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Laser-Assisted Control of Epistaxis in Hereditary Hemorrhagic Telangiectasia: A Systematic Review

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Abstract

Objectives: Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu disease, causes recurrent mucous membrane hemorrhage, especially epistaxis. In this systematic review, we discuss the efficacies of the three most common laser photocoagulation treatments for HHT-related epistaxis.

Methods: A systematic literature search was conducted in PubMed and MEDLINE from database inception to March 2019. Studies reporting epistaxis outcomes following Argon, neodymium-doped yttrium aluminum garnet (Nd:YAG), and Diode laser photocoagulation for HHT were included. Chi-squared and Barnard's exact tests were utilized to detect differences in reduced epistaxis frequency and intensity rates.

Results: 15 out of 157 published studies met our eligibility criteria, spanning a collective 362 patients. Argon, Nd:YAG, and Diode laser therapy reduced epistaxis frequency in 90.4%, 88.9%, and 71.1% of patients, respectively, and reduced epistaxis intensity in 87.8%, 87.2%, and 71.1% of patients, respectively. Diode laser photocoagulation significantly underperformed in both outcome measurements when compared to Argon (frequency: $p = 0.005$; intensity: $p = 0.034$) and Nd:YAG (frequency: $p = 0.012$; intensity: $p = 0.041$). There was no significant difference between Argon and Nd:YAG in reducing HHT epistaxis frequency ($p = 0.434$) or intensity ($p = 0.969$). Categorizing HHT patients by clinical severity demonstrated a higher rate of improvement in the mild-moderate group compared to the severe group in both Argon ($p < 0.001$) and Nd:YAG ($p < 0.001$) therapeutic methods. While no significant differences were found in rates of improved epistaxis outcomes between Argon and Nd:YAG in mild-moderate HHT patients (frequency: $p =$

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0.061; intensity: $p = 0.061$), Nd:YAG demonstrated greater rates of reduction in epistaxis frequency ($p = 0.040$) and intensity ($p = 0.028$) than Argon among severe HHT patients.

Conclusions: HHT is a lifelong disease, plaguing patients with debilitating epistaxis. Intranasal laser photocoagulation of telangiectasias using Argon or Nd:YAG laser therapy can yield improved epistaxis outcomes compared to Diode laser photocoagulation. In severe cases of HHT, Nd:YAG laser therapy provides greater improvements in epistaxis outcomes than Argon photocoagulation.

Keywords

hereditary hemorrhagic telangiectasia; Osler-Weber-Rendu; laser; photocoagulation; epistaxis

Introduction

Hereditary hemorrhagic telangiectasia (HHT), or Osler-Weber-Rendu disease, is an inherited autosomal dominant vascular disorder which predisposes individuals to abnormal formation of telangiectasias throughout the skin, mucosa, and viscera. [1] HHT may present with the classic triad of recurrent epistaxis, telangiectasias, and family history of related signs and symptoms. Although telangiectasias can lead to a life-threatening hemorrhage in the brain, lung, and liver, HHT most commonly manifests in the head and neck as recurrent epistaxis. [2] Due to its unpredictable and often severe nature, HHT-related epistaxis can be a significant detriment on patients' quality of life. [3–5]

Most cases of HHT-related epistaxis can be controlled conservatively with nasal humidification and nasal trauma avoidance, but these interventions do not prevent the natural progression of telangiectasia growth. A frequently utilized method of mitigating HHT-related epistaxis involves fiberoptic laser photocoagulation of nasal mucosal telangiectasias, a technique first introduced in 1981. [6] This procedure is particularly effective in small punctate lesions, despite it being costly or unavailable in many remote centers. [7,8] Despite these challenges, there has been increased utilization of this technique across otolaryngology practices, leading to improved HHT-related epistaxis management and quality of life. [3,9,10] Among the most well-studied and successful laser treatments are Argon, neodymium-doped yttrium aluminum garnet (Nd:YAG), and Diode laser photocoagulation, which differ in their technical and optical properties. Argon laser operates 70% at 488nm (blue) and 30% at 514nm (green), and is characterized by its medium absorption, low scattering, and low depth of penetrance (0.44mm). Much of its absorption is due to its blue and green radiation, which is highly absorbed by oxyhemoglobin's red pigmentation. Nd:YAG laser operates at 1064nm and is characterized by its low absorption, strong scattering, and high depth of penetrance (4.6mm). Diode laser operates at 800-1000nm and, similarly, has low absorption, medium scattering, and high depth of penetrance (3.5mm). Nd:YAG and Diode lasers both emit near-infrared radiation and lack any special chromophores that would facilitate their absorption. Of the three lasers, Argon's volume of coagulation as a function of irradiation time is greatest, followed by Diode, and then Nd:YAG laser. [11] Potassium titanyl phosphate (KTP) laser has also recently gained popularity for its medium absorption, low scattering, and low depth of penetrance (0.39mm). Similar to Argon laser, KTP operates at a green (532nm) wavelength, enabling it to be specifically absorbed by oxyhemoglobin [11,12] However, despite its growing prominence in epistaxis treatment, few studies have evaluated its efficacy in improving epistaxis outcomes in HHT patients. [13,14]

Advancements in laser technology and their incorporation in clinical practices require standardization and guidelines for specific applications. For instance, a multi-institutional collaboration in 2014 [15] led to a consensus on laser therapy for traumatic scars, paving the way for future developments in the field. Therefore, establishing algorithms to employ specific laser modalities in different clinical scenarios could be an important step in improving patient outcomes. In this study, we perform a systematic review of published studies to elucidate both the absolute and comparative efficacies of Argon, Nd:YAG, and Diode laser therapies in alleviating HHT-related epistaxis.

Methods

The design and conduct of this study were in accordance to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analyses. [16] Institutional Review Board consideration was not applicable since patient information beyond those already published in the literature was not used. We conducted a thorough literature search of PubMed and Ovid MEDLINE from database inception to March 2019 to identify case series, prospective and retrospective cohort studies, and randomized controlled trials involving Argon, Nd:YAG, or Diode laser-assisted photocoagulation of HHT-related telangiectasias (Figure 1). Database queries were performed using “Hereditary Hemorrhagic Telangiectasia” or “Osler-Weber Rendu” and “laser” keywords in conjunction with filters for primary studies reporting on “Human” subjects. 131 abstracts were evaluated and studies with fewer than 5 subjects (e.g., case reports) were excluded to reduce publication bias. The resulting 93 full-text articles were narrowed down to 15 studies to be included for analysis by using the following exclusion criteria: (1) laser type was not described; (2) data for primary outcome variables was not provided; (3) reported outcome data was unclear and could not be dichotomized; (4) HHT management involved more than one laser or treatment type. Each article was independently evaluated by two authors (A.A. and K.G.) to consider for data inclusion. If disagreement occurred for inclusion, the senior author (E.K.) acted as the final arbitrator.

For each study, patient demographics, sample size, laser type, and laser efficacy were collected. Due to heterogeneity in measurement instruments used to report epistaxis outcomes, we evaluated the lasers’ efficacies by reduction in rates of epistaxis frequency and intensity. In studies where epistaxis frequency or intensity was indicated according to a numeric scale, a numerical decrease in symptom severity was considered a reduction in the outcome variable. Otherwise, reductions in epistaxis frequency or intensity were marked strictly as they were written in the articles. Additionally, studies did not apply standard criteria for classifying HHT severity. As a result, some studies either dichotomized (mild or severe) or trichotomized (mild, moderate, or severe) HHT severity. For the purposes of quantitative analysis, collected data on HHT severity was dichotomized as mild-moderate or severe. Statistical analyses were performed using MATLAB (MathWorks Inc., Massachusetts, USA). To assess for statistical differences in epistaxis outcomes between laser types, the Chi-square test of independence or, in cases of a small sample size, Barnard’s exact test was applied. A p-value of < 0.05 was considered statistically significant.

Results

A total of 157 articles were identified in the initial search, of which 15 studies met inclusion criteria. Summaries of the patient demographics and outcome variables reported by these studies are listed in Table 1. This accounted for a total of 362 patients treated. The mean age was 51.5 years (n=197 patients), with approximately 48% of the patients being males. The lasers most commonly investigated were Nd:YAG (n=6 studies), followed by Argon (n=6 studies) and diode (n=3 studies). The average sample sizes for studies reporting Argon, Nd:YAG, and Diode laser therapies were 24 (range: 12-43), 29 (range: 6-45), and 15 (range: 8-20) patients. No complications or deaths from treatment were noted in any of the studies.

Argon, Nd:YAG, and Diode laser therapy reduced epistaxis frequency in 132 (90.4%), 152 (88.9%), and 32 (71.1%) of patients, respectively (Figure 2). Epistaxis intensity reduced in 115 (87.8%), 123 (87.2%), and 32 (71.1%) of patients following Argon, Nd:YAG, and Diode laser photocoagulation, respectively (Figure 3). Rates of epistaxis frequency reduction were significantly different between Argon and Diode laser therapy (χ^2 [2, N = 191] = 10.56, p = 0.005) and between Nd:YAG and Diode laser therapy (χ^2 [2, N = 216] = 8.92, p = 0.012). Moreover, there were significant differences in rates of epistaxis intensity reduction between Argon and Diode laser therapy (χ^2 [2, N = 176] = 6.77, p = 0.034) as well as Nd:YAG and Diode laser therapy (χ^2 [2, N = 186] = 6.39, p = 0.041). No significant differences were found between Argon and Nd:YAG laser photocoagulation for rates of epistaxis frequency reduction (χ^2 [2, N = 317] = 0.20, p = 0.907) and intensity reduction (χ^2 [2, N = 272] = 0.02, p = 0.991).

Seven studies [17–23] identified patients' HHT severity as mild-moderate (n = 127) or severe (n = 41) prior to treatment. Comparisons between the two severity categories demonstrated a higher rate of improvement in epistaxis outcomes in both Nd:YAG ($p < 0.001$) and Argon ($p < 0.001$) laser therapies (Table 2). No significant differences were found in rates of improved epistaxis outcomes between Argon and Nd:YAG in mild-moderate HHT patients (frequency: p = 0.061; intensity: p = 0.061); however, Nd:YAG demonstrated higher reduction rates in epistaxis frequency (p = 0.040) and intensity (p = 0.028) than did Argon among severe HHT patients.

Discussion

This systematic review assesses the efficacies of Argon, Nd:YAG, and Diode laser therapies in alleviating HHT-related epistaxis. We evaluated 15 studies for epistaxis outcomes (frequency and intensity) following laser treatment in patients with HHT. Argon and Nd:YAG laser treatments both provided higher rates of reduced epistaxis frequency and intensity than did Diode laser photocoagulation. A subset analysis of Argon and Nd:YAG laser therapy outcomes demonstrated a high success rate of 93% and 100%, respectively, in reducing epistaxis symptoms in mild to moderate HHT. While Argon and Nd:YAG were, on average, similarly efficacious in alleviating epistaxis, our sub-analysis of various HHT severities demonstrated a significantly higher reduction of epistaxis frequency and intensity after Nd:YAG compared to Argon treatments among severe cases of HHT.

Lund and Howard suggested that the treatment of choice for recurrent epistaxis should be dictated on the patient's HHT severity. [18] Measures of HHT severity include overall patient health status, quantity and size of nasal telangiectasia, and number of necessary blood transfusions. Argon, Nd:YAG, and Diode photocoagulation therapies are considered minimally invasive procedures suitable for mild to moderate cases of HHT. [24] These lasers enable accurate control over the extent of coagulation, thereby reducing morbidity and risk of septal perforation. Additionally, the minimal resulting trauma to the nasal mucosa opens the opportunity for repeated treatment with minimal post-operative hospitalization. Some studies have suggested that frequent therapeutic intervention and revision via laser coagulation could put patients at an increased risk for septal perforation. [21,25] However, multiple studies have confirmed the safety of laser photocoagulation in treating HHT-related epistaxis. For example, Zhang *et al.* noted no post-operative complications using an Nd:YAG laser to manage 72 patients with epistaxis. [26] Lennox *et al.* also reported a lack of complications following Argon photocoagulation in 19 HHT patients. [17] Additionally, Fiorella *et al.* reported no short- or long-term complications from Diode laser treatment on 20 HHT patients. [27] Therefore, with minimal associated complications, laser photocoagulation can serve as an effective treatment of choice for initial intervention.

In addition to the aforementioned laser therapies, KTP laser treatment serves as another photocoagulative technique that has recently gained in prominence for alleviating HHT-related epistaxis. [13] In a retrospective study of 11 HHT patients, Levine demonstrated that KTP lasers could be reliably employed to treat epistaxis with high efficacy and low morbidity. [28] KTP laser possesses coagulative properties comparable to those of Argon lasers and similarly emits green radiation that is specifically absorbed by oxyhemoglobin's red pigmentation. Since KTP is only moderately absorbed by its target tissue, its radiation distribution consists of both direct and scattered radiation. [11] Since degree of scattering is directly correlated to the thermal damage a laser produces outside its target vaporization site, this property can be suggestive of a laser's precision. [28] While KTP laser scatters, its degree of scattering is comparable to that of Argon and less than those of Nd:YAG and Diode lasers. Additionally, KTP's depth of penetration is 11.4% lower than that of Argon, making it one of the more precise lasers. [11] This increased depth precision reduces damage to the septal mucosa and decreases risks for septal perforation. However, this property also makes KTP lasers less suitable than deeper penetrating lasers like Nd:YAG when treating nasal telangiectasias that are caused by a submucosal plexus of vessels. [29] Additionally, Siegel *et al.* reported that the average length of time between Nd:YAG and KTP laser interventions was 16.3 and 11.7 months, respectively. [12] Therefore, while KTP could pose a lower risk of peripheral tissue injury, Nd:YAG may provide HHT patients with a longer period of symptomatic relief. Due to a paucity of studies examining the efficacy of KTP lasers in treating HHT-related epistaxis, we could not incorporate it into our quantitative calculations and included it here as part of a qualitative analysis.

Similarly, pulsed dye laser (PDL, 595nm) is another laser modality for treating HHT-related epistaxis that current literature lacks sufficient data for quantitative analysis. While PDL has been effective in photocoagulating smaller capillaries, there has been little reported success in treating larger vessels. [30–32] In a study of 9 HHT patients, Harries *et al.* demonstrated that reductions in epistaxis frequency could be achieved after an average of three treatments. [31]

However, Haye *et al.* reported that a series of two PDL treatments only provided epistaxis improvements in 1 of 7 HHT patients. [32] Therefore, patients might only experience symptomatic relief after undergoing several PDL treatments. Furthermore, since PDL is expensive and not commonly available in most outpatient suites, it is not as practical and frequently used as other laser modalities. [30]

In our analysis of severe cases of HHT, 0% and 34% of Argon- and Nd:YAG-treated patients, respectively, were found to have improvements in epistaxis symptoms. Although our subset analysis of Argon and Nd:YAG laser photocoagulation demonstrated a lower treatment efficacy in severe HHT, Shah *et al.* has demonstrated high efficacy of Argon laser therapy in reducing epistaxis frequency, intensity, and duration in patients with severe epistaxis and a history of blood transfusions. [33] Therefore, while laser therapy has shown to be primarily effective for mild and moderate epistaxis, cases of severe HHT-related epistaxis might benefit from treatment via a trial of laser photocoagulation before resorting to septodermoplasty or Young's procedure. Moreover, combining laser photocoagulation with topical therapies has shown potential in further improving epistaxis outcomes. A randomized control study in 2002 investigated the use of topical estrogen in combination with Argon laser therapy and demonstrated its greater reductions in epistaxis frequency and intensity compared to Argon photocoagulation alone. [34] Some studies have also demonstrated that concurrent use of bevacizumab (Avastin) with laser treatment could yield superior epistaxis outcomes compared to laser treatment alone. [35,36] These studies show potential in de-escalating interventions for HHT-related epistaxis, both in milder and more severe cases of HHT.

Past and recent standard of care for patients with severe recurrent epistaxis has consisted of invasive surgical operations such as septodermoplasty and Young's procedure. [24] However, these procedures can result in notable complications such as recurrence in as early as 2 years after treatment, or olfactory loss and nasal respiratory obstruction. [37–41] On the other hand, in addition to their discussed safety superiority, laser treatments have shown to lead to significant quality of life (QOL) improvements. Since epistaxis can be induced by simple activities such as drinking and putting on clothes, there is a large social and psychological burden on HHT patients who experience recurrent epistaxis. [18] In 2017, Kuan *et al.* utilized the Sinonasal Outcome Test-22 questionnaire to demonstrate longer-term (> 45 days after treatment) improvements in HHT patients' mental well-being following laser therapy for their epistaxis. [3] However, HHT is a progressive lifelong disease where regrowth of telangiectasias remains a possibility even months to years after treatment. This was demonstrated in a 2-year QOL study, where Karapantzos *et al.* demonstrated significant improvements in QOL and mental health outcomes following laser therapy. However, in this time, nearly 70% of patients were reported to have had recurrences and needed one or more repeat laser treatments. [10] Additionally, in a 2011 prospective study, Jørgensen *et al.* found, on average, no significant improvements in HHT patients' QOL in as soon as 6 months after laser treatment. [42] Therefore, while laser therapy can serve as a safer and less invasive remedy to HHT-related epistaxis than surgical intervention, its benefits are limited by its temporary effects and need for repeated treatments.

Though we took great care in collecting the relevant studies and performing the appropriate analyses, this study has several limitations. A systematic review comprised of a collective several studies suffers from a lack of homogeneity in treatment guidelines and measurement of outcome variables. There also exists heterogeneity in the studies' patient baselines and follow-up timelines that is difficult to control or standardize. Moreover, differences in measurement instruments used to report epistaxis outcomes necessitated binarizing reductions in epistaxis frequency and severity for the purpose of analytic calculation. The categorization of HHT severity as mild, moderate, and severe also lacks standardization, with many studies using varying combinations of the number of blood transfusions and the epistaxis frequency and intensity as determining factors of HHT severity. [17–23] A recently validated scoring index known as the Epistaxis Severity Score (ESS) presents future studies investigating HHT-related epistaxis the prospect of classifying patients' HHT severity according to this standardized measure. [43] For some outcome variables such as change in quality of life, many studies did not utilize standardized templates. This presents an opportunity for future studies to consider incorporating a newly proposed epistaxis-specific quality-of-life questionnaire (EQQoL) [44] for further investigation. Lastly, the rarity of HHT makes it difficult for any single author or institution to perform each laser type on an adequate number of patients. This leads to increased susceptibility for type II error and false negative conclusion. Regardless of these limitations, this systematic review is the first to demonstrate a qualitative and quantitative comparison among common laser treatments for management of HHT epistaxis, which we hope will pave the path for future development of consensus and guidelines.

Conclusion

Laser photocoagulation of intranasal telangiectasias using Argon or Nd:YAG laser therapy yields greater reductions in epistaxis frequency and intensity compared to Diode laser treatment. Despite its relatively low rate of success in the context of severe HHT, an initial trial of Argon or Nd:YAG laser therapy could sufficiently improve epistaxis symptoms to mitigate the need for invasive surgical treatment.

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References

1. Guttmacher AE, Marchuk DA, White RI. Hereditary Hemorrhagic Telangiectasia. N Engl J Med. 2005;33(14):918–924. doi:10.1179/136174205×45237
2. Shovlin CL, Guttmacher AE, Buscarini E, et al. Diagnostic criteria for Hereditary Hemorrhagic Telangiectasia (Rendu- Osler-Weber Syndrome). Am J Med Genet. 2000;91(1):66–67. doi:10.1002/(SICI)1096-8628(20000306)91:1<66::AID-AJMG12>3.0.CO;2-P [PubMed: 10751092]
3. Kuan EC, Peng KA, Thompson CF, Suh JD, Wang MB. Sinonasal quality of life outcomes following laser treatment of epistaxis related to hereditary hemorrhagic telangiectasia. Lasers Med Sci. 2017;32(3):527–531. doi:10.1007/s10103-017-2144-7 [PubMed: 28116537]
4. Dheyauldeen SA, Abdelnoor M, Bachmann-Harildstad G. The natural history of epistaxis in patients with hereditary hemorrhagic telangiectasia in the Norwegian population: A cross-sectional study. Am J Rhinol Allergy. 2011;25(4):214–218. doi:10.2500/ajra.2011.25.3616 [PubMed: 21819756]

5. Holderried M, Baur M, Pfister M. Impact of Hereditary Hemorrhagic Teleangiectasia on Quality of Life. Open Otorhinolaryngol J 2014;4(1):55–61. doi:10.2174/1874428101004010055
6. Parkin JL, Dixon JA. Laser photocoagulation in hereditary hemorrhagic telangiectasia. Otolaryngol - Head Neck Surg. 1981;89(2):204–208. doi:10.1177/019459988108900212 [PubMed: 6787514]
7. Luk L, Mace JC, Bhandarkar ND, Sautter NB. Comparison of electrosurgical plasma coagulation and potassium-titanyl-phosphate laser photocoagulation for treatment of hereditary hemorrhagic telangiectasia-related epistaxis. Int Forum Allergy Rhinol. 2014;4(8):640–645. doi:10.1002/alr.21328 [PubMed: 24719397]
8. Sautter NB, Smith TL. Treatment of Hereditary Hemorrhagic Telangiectasia–Related Epistaxis. Otolaryngol Clin North Am. 2016;49(3):639–654. doi:10.1016/j.otc.2016.02.010 [PubMed: 27267016]
9. Poje G, Kavanagh MM. Hereditary hemorrhagic telangiectasia — laser treatment of epistaxis. Ear, Nose Throat J. 2017;96(9):E10–E14.
10. Karapantzos I, Tsimpiris N, Goulis DG, Van Hoecke H, Van Cauwenberge P, Danielides V. Management of epistaxis in hereditary hemorrhagic telangiectasia by Nd:YAG laser and quality of life assessment using the HR-QoL questionnaire. Eur Arch Oto-Rhino-Laryngology. 2005;262(10):830–833. doi:10.1007/s00405-004-0911-0
11. Eichler J, Goncalves O. A Review of Different Lasers in Endonasal Surgery: Ar-, KTP-, Dye-, Diode-, Nd-, Ho- and CO2-Laser. Med Laser Appl. 2002;17(3):190–200.
12. Siegel MB, Keane WM, Atkins JP, Rosen MR. Control of epistaxis in patients with hereditary hemorrhagic telangiectasia. Otolaryngol - Head Neck Surg. 1991;105(5):675–679. doi:10.1177/019459989110500507 [PubMed: 1754250]
13. Harvey RJ, Kanagalingam J, Lund VJ. The Impact of Septodermoplasty and Potassium-Titanyl-Phosphate (KTP) Laser Therapy in the Treatment of Hereditary Hemorrhagic Telangiectasia-Related Epistaxis. Am J Rhinol. 2008;22(2):182–187. doi:10.2500/ajr.2008.22.3145 [PubMed: 18416977]
14. Masuda Y, Tanabe T, Ohmae Y, et al. Using the KTP Laser to Control Epistaxis in Patients with Hereditary Hemorrhagic Telangiectasia. Otolaryngol Clin Pract. 2004;97(12):1075–1081. doi:10.5631/jibirin.97.1075
15. Anderson RR, Donelan MB, Hivnor C, et al. Laser Treatment of Traumatic Scars With an Emphasis on Ablative Fractional Laser Resurfacing. JAMA Dermatology. 2014;150(2):187–193. doi:10.1001/jamadermatol.2013.7761 [PubMed: 24336931]
16. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151(4):264–269. [PubMed: 19622511]
17. Lennox PA, Harries M, Lund VJ, Howard DJ. A retrospective study of the role of the argon laser in the management of epistaxis secondary to hereditary haemorrhagic telangiectasia. J Laryngol Otol. 2007;111(01):34–37. doi:10.1017/s0022215100136370
18. Lund VJ, Howard DJ. A Treatment Algorithm for the Management of Epistaxis in Hereditary Hemorrhagic Telang iectasia. Am J Rhinol. 1999;13(4):319–322. doi:10.2500/105065899782102890 [PubMed: 10485021]
19. Bergler W, Riedel F, Baker-schreyer A, Juncker C, Hormann K. Argon Plasma Coagulation for the Treatment of Hereditary Hemorrhagic Telangiectasia. Laryngoscope. 1999;109(1):15–20. [PubMed: 9917033]
20. Kluger PB, Shapshay SM, Hybels RL, Bohigian KR. Neodymium-Yag Laser Intranasal Photocoagulation in Hereditary Hemorrhagic Telangiectasia. Laryngoscope. 2006;97(12):1397–1401. doi:10.1288/00005537-198712000-00004
21. Folz BJ, Tennie J, Lippert BM, Werner JA. Natural history and control of epistaxis in a group of German patients with Rendu-Osler-Weber disease. Rhinology. 2005;43(1):40–46. [PubMed: 15844501]
22. Shapshay SM, Oliver P. Treatment of Hereditary Hemorrhagic Telangiectasia by Nd-YAG Laser Photocoagulation. Laryngoscope. 2006;94(12):1545–1556. doi:10.1288/00005537-198412000-00003

23. Rebeiz EE, Parks S, Shapshay SM. Management of epistaxis in hereditary hemorrhagic telangiectasia with neodymium: Yttrium-aluminum-garnet laser photocoagulation. Oper Tech Otolaryngol - Head Neck Surg. 1991;2(3):177–182. doi:10.1016/S1043-1810(10)80052-1
24. Pagella F, Matti E, Chu F, et al. Argon plasma coagulation is an effective treatment for hereditary hemorrhagic telangiectasia patients with severe nosebleeds. Acta Otolaryngol. 2012;133(2):174–180. doi:10.3109/00016489.2012.718097 [PubMed: 23066781]
25. Hanks JE, Hunter D, Goding GS, Boyer HC. Complications from office sclerotherapy for epistaxis due to hereditary hemorrhagic telangiectasia (HHT or Osler-Weber-Rendu). Int Forum Allergy Rhinol. 2014;4(5):422–427. doi:10.1002/alr.21287 [PubMed: 24431220]
26. Zhang J, Cao L, Wei C. Randomized controlled trial comparing Nd:YAG laser photocoagulation and bipolar electrocautery in the management of epistaxis. Lasers Med Sci. 2017;32(7):1587–1593. doi:10.1007/s10103-017-2285-8 [PubMed: 28707034]
27. Fiorella ML, Lillo L, Fiorella R. Diode laser in the treatment of epistaxis in patients with hereditary haemorrhagic telangiectasia. Acta Otorhinolaryngol Ital. 2012;32(3):164–169. http://www.ncbi.nlm.nih.gov/pubmed/22767981%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3385056. [PubMed: 22767981]
28. Levine HL. Endoscopy and the ktp/532 laser for nasal sinus disease. Ann Otol Rhinol Laryngol. 1989;98(1):46–51. doi:10.1177/000348948909800110 [PubMed: 2910188]
29. Byahatti SV, Rebeiz EE, Shapshay SM. Hereditary Hemorrhagic Telangiectasia: What the Otolaryngologist Should Know. Am J Rhinol. 2007;11(1):55–62. doi:10.2500/105065897781446829
30. Hartnick CJ, Dailey S, Franco R, Zeitels SM. Office-based pulsed dye laser treatment for hemorrhagic telangiectasias and epistaxis. Laryngoscope. 2003;113(6):1085–1087. doi:10.1097/00005537-200306000-00033 [PubMed: 12782829]
31. Harries PG, Brockbank MJ, Shakespeare PG, Carruth JAS. Treatment of hereditary haemorrhagic telangiectasia by the pulsed dye laser. J Laryngol Otol. 1997;111(11):1038–1041. doi:10.1017/S0022215100139283 [PubMed: 9472572]
32. Haye R, Austad J. Hereditary haemorrhagic teleangiectasia: Unsuccessful treatment with the flashlamp-pulsed dye laser. Rhinology. 1992;30(2):135–137. [PubMed: 1411099]
33. Shah RK, Dhingra JK, Shapshay SM. Hereditary hemorrhagic telangiectasia: A review of 76 cases. Laryngoscope. 2002;112(5):767–773. doi:10.1097/00005537-200205000-00001 [PubMed: 12150604]
34. Bergler W, Sadick H, Götte K, Riedel F, Hörmann K. Topical estrogens combined with argon plasma coagulation in the management of epistaxis in hereditary hemorrhagic telangiectasia. Ann Otol Rhinol Laryngol. 2002;111(3):222–228. doi:10.1177/000348940211100306 [PubMed: 11913682]
35. Chen S IV, Karnezis T, Davidson TM. Safety of intranasal Bevacizumab (avastin) treatment in patients with hereditary hemorrhagic telangiectasia-associated epistaxis. Laryngoscope. 2011;121(3):644–646. doi:10.1002/lary.21345 [PubMed: 21344447]
36. Simonds J, Miller F, Mandel J, Davidson TM. The effect of bevacizumab (Avastin) treatment on epistaxis in hereditary hemorrhagic telangiectasia. Laryngoscope. 2009;119(5):988–992. doi:10.1002/lary.20159 [PubMed: 19194865]
37. Lesnik GT, Ross DA, Henderson KJ, Joe JK, Leder SB, White RI. Septectomy and Septal Dermoplasty for the Treatment of Severe Transfusion-Dependent Epistaxis in Patients with Hereditary Hemorrhagic Telangiectasia and Septal Perforation. Am J Rhinol. 2007;21(3):312–315. doi:10.2500/ajr.2007.21.3017 [PubMed: 17621815]
38. Ross DA, Nguyen DB. Inferior Turbinectomy in Conjunction with Septodermoplasty for Patients with Hereditary Hemorrhagic Telangiectasia. Laryngoscope. 2004;114(4):779–781. doi:10.1097/00005537-200404000-00037 [PubMed: 15064642]
39. Gluckman JL, Portugal LG. Modified young's procedure for refractory epistaxis due to hereditary hemorrhagic telangiectasia. Laryngoscope. 1994;104(9):1174–1177. doi:10.1288/00005537-199409000-00023 [PubMed: 8072369]

40. Hosni AA, Innes AJ. Hereditary haemorrhagic telangiectasia: Young's procedure in the management of epistaxis. J Laryngol Otol. 1994;108(9):754–757. doi:10.1017/S0022215100128026 [PubMed: 7964136]

41. Lund VJ, Howard DJ. Closure of the nasal cavities in the treatment of refractory hereditary haemorrhagic telangiectasia. J Laryngol Otol. 1997;111(1):30–33. doi:10.1017/s0022215100136369 [PubMed: 9292127]

42. Jørgensen G, Lange B, Wanscher JH, Kjeldsen AD. Efficiency of laser treatment in patients with hereditary hemorrhagic telangiectasia. Eur Arch Oto-Rhino-Laryngology. 2011;268(12):1765–1770. doi:10.1007/s00405-011-1677-9

43. Hoag JB, Terry P, Mitchell S, Reh D, Merlo CA. An epistaxis severity score for hereditary hemorrhagic telangiectasia. Laryngoscope. 2010;120(4):838–843. doi:10.1002/lary.20818 [PubMed: 20087969]

44. Ingrand I, Ingrand P, Gilbert-Dussardier B, et al. Altered Quality of Life in Rendu-Osler-Weber Disease Related to Recurrent Epistaxis. Rhinology. 2011;49(2):155–162. doi:10.4193/Rhino09.138 [PubMed: 21743869]

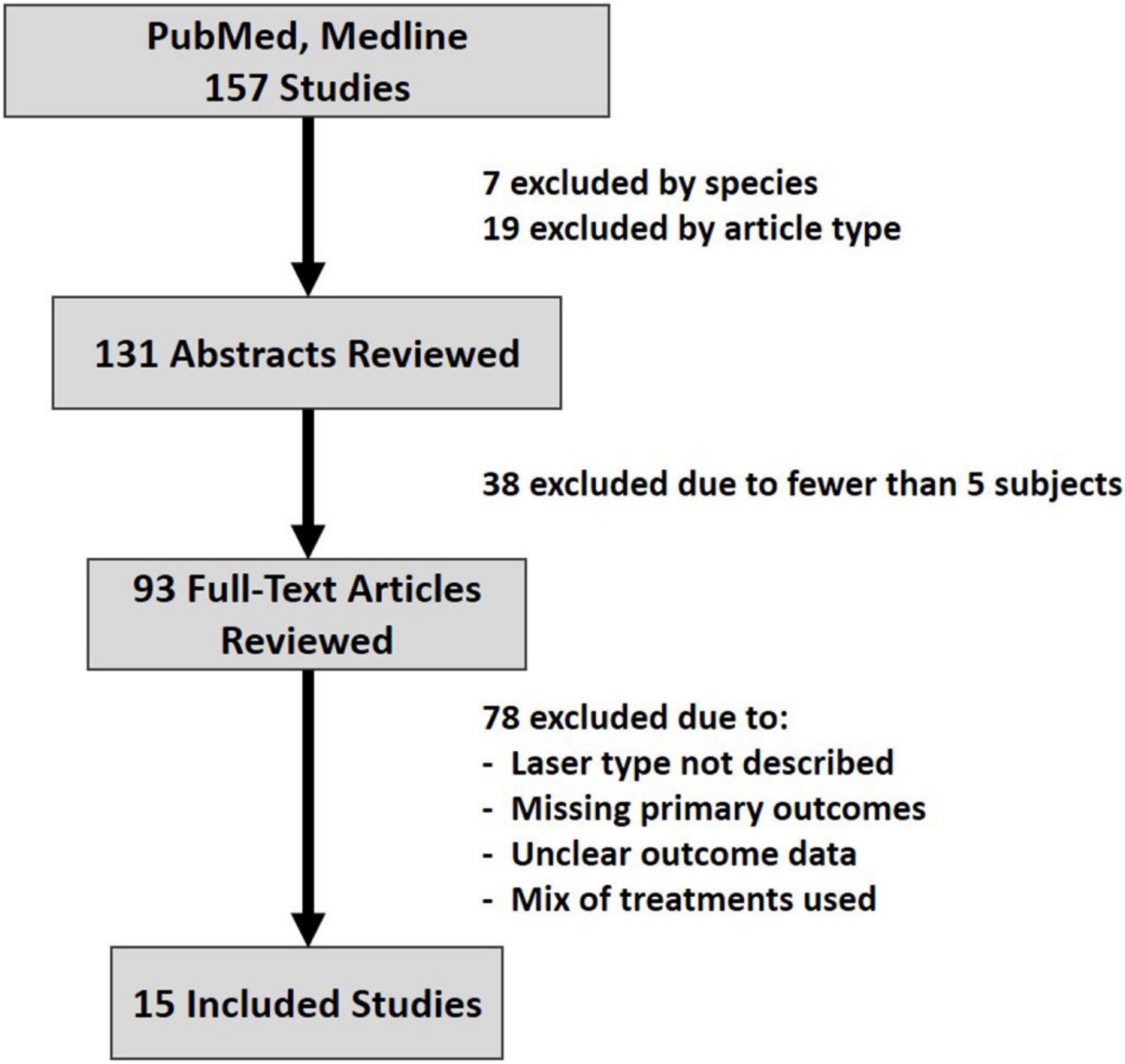

Figure 1:
Flowchart of study inclusion.

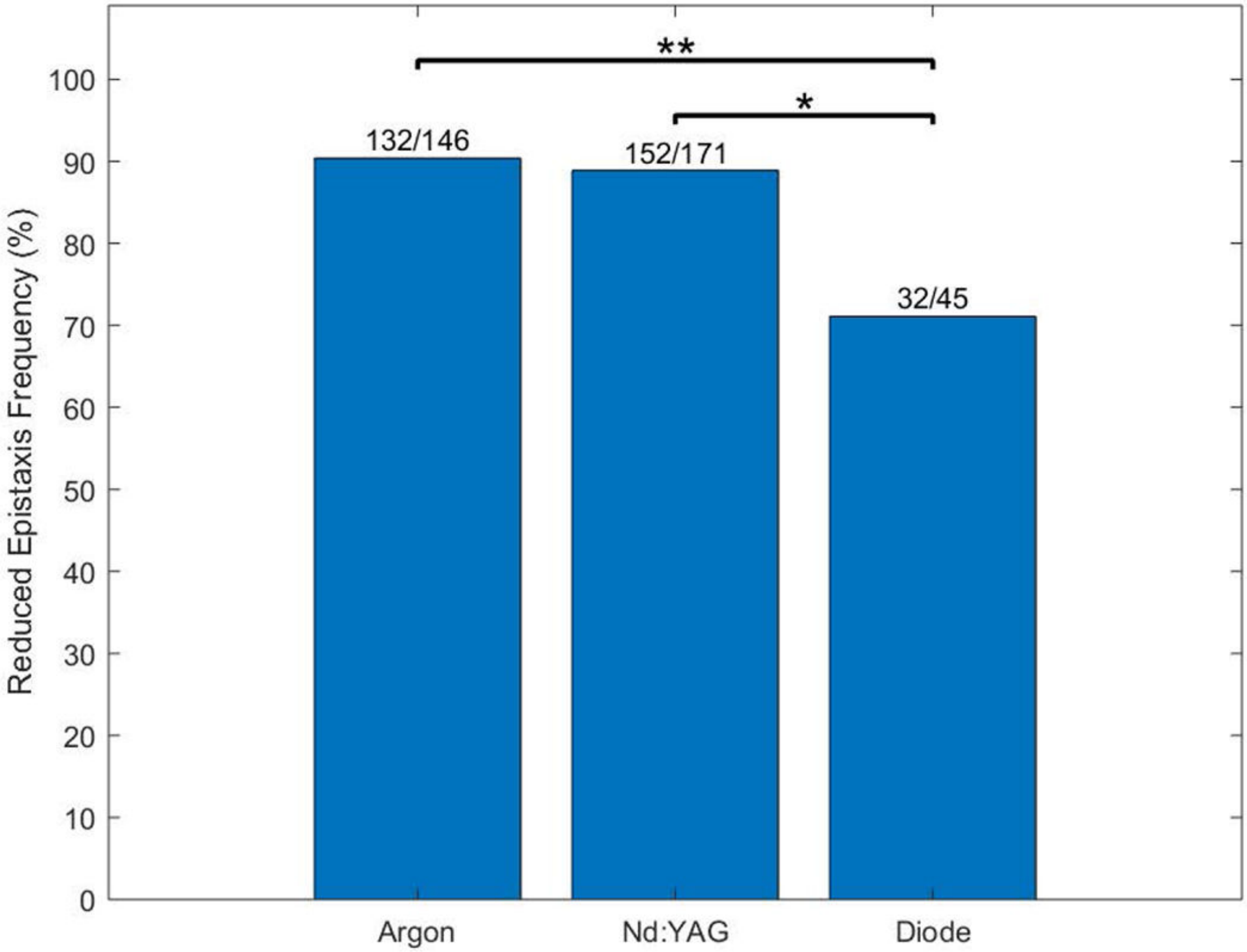

Figure 2:

Rates of reduced epistaxis frequency among patients who underwent Argon (n = 146), Nd:YAG (n = 171), or Diode (n = 45) laser treatment for HHT. * indicates $p < 0.05$. ** indicates $p < 0.01$.

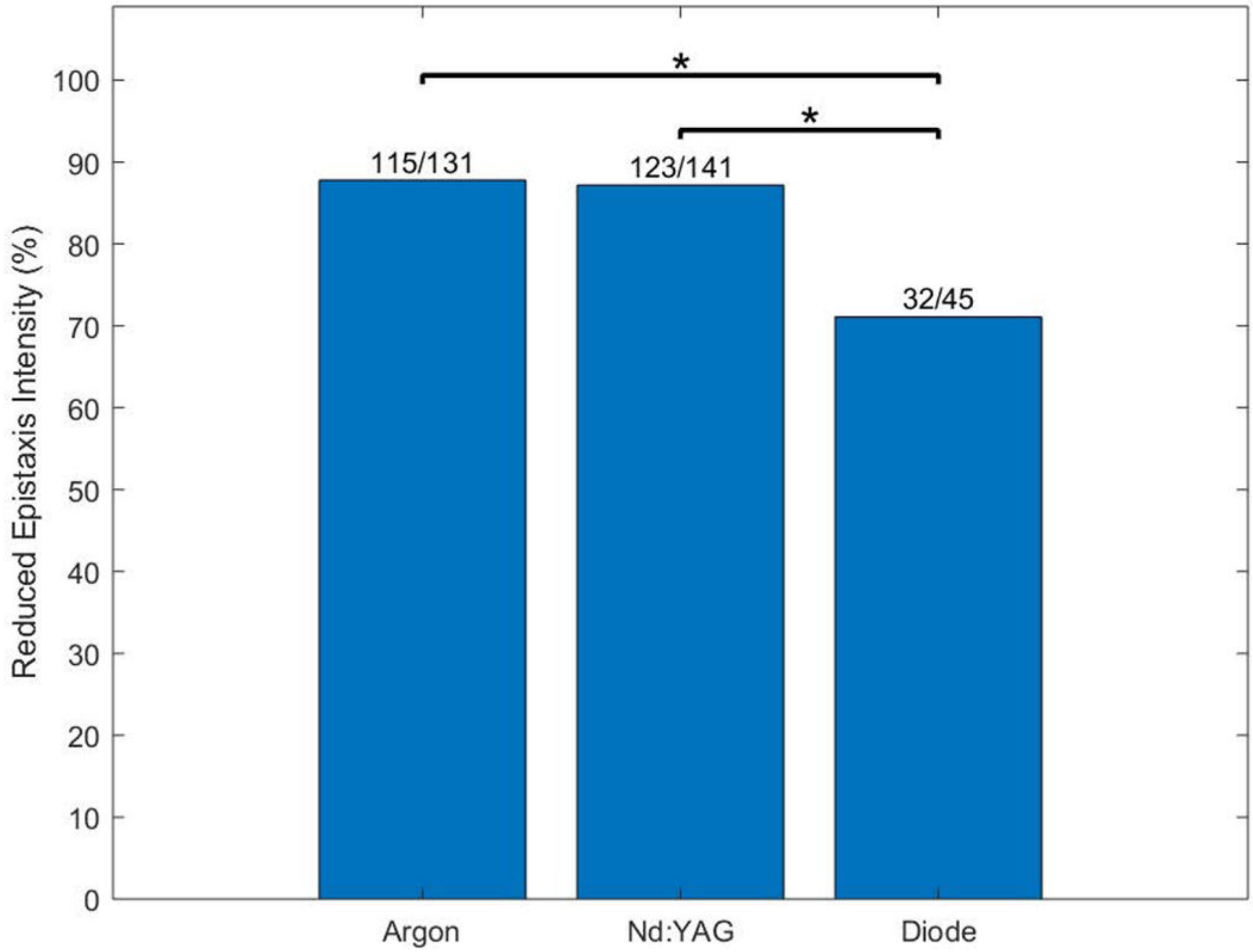

Figure 3:
Rates of reduced epistaxis intensity among patients who underwent Argon (n = 146), Nd:YAG (n = 171), or Diode (n = 45) laser treatment for HHT. * indicates $p < 0.05$.

Table 1:

Summary of patient demographics and outcome variables for each analyzed study.

Study	Study Years	Sample Size (% F)	Mean Age (range, yr)	Follow-up (mo)	Laser Type	Reduced Epistaxis Frequency (%)	Reduced Epistaxis Intensity (%)
Haye 1991	1986-1989	15	N/A (30-70)	6+	Argon	15 (100)	N/A
Lennox 1997	1991-1995	19	N/A (15-68)	6-31	Argon	14 (73.7)	14 (73.7)
Lund 1999	1991-1997	18 (55.6)	55 (15-85)	6-72	Argon	14 (77.8)	14 (77.8)
Bergler 1999	1998-1999	12	N/A (8-68)	1	Argon	12 (100)	10 (83.3)
Sadick 2003	1997-2000	43	N/A	20+	Argon	41 (95.3)	41 (95.3)
Pagella 2006	1997-2004	43	52.3 (26-76)	6	Argon	36/39 (92.3)	36/39 (92.3)
Shapshay 1984	N/A	6 (16.7)	50.5 (25-86)	6-9	Nd:YAG	5 (83.3)	5 (83.3)
Kluger 1987	1982-1987	17 (58.8)	48.4 (9-86)	2-42	Nd:YAG	14 (82.4)	15 (88.2)
Rebeiz 1991	1982-1990	41	N/A	12-96	Nd:YAG	35 (85.4)	35 (85.4)
Werner 1997	1987-1996	32	N/A	< 24	Nd:YAG	30 (93.8)	30 (93.8)
Kuhnel 2005	N/A	30 (50.0)	53.8 (15-77)	N/A	Nd:YAG	30 (100)	N/A
Folz 2005	1998-2003	49 (61.2)	55 (15-77)	8-60	Nd:YAG	38/45 (84.4)	38/45 (84.4)
Hopf 2002	2000-2002	8	N/A (1-83)	4-24	Diode	8 (100)	8 (100)
Fiorella 2012	2005-2010	20 (35.0)	52.5 (21-70)	3	Diode	7 (35)	7 (35)
Poje 2017	2008-2012	17 (58.8)	34 (15-57)	12	Diode	17 (100)	17 (100)

Table 2:

Rates of reduced epistaxis frequency and intensity in mild-moderate (n = 127) and severe (n = 41) HHT following Argon (n = 49) or Nd:YAG (n = 119) laser treatment.

Reduced Epistaxis Frequency				
Laser Type	**Mild-Moderate**	**Severe**	**Score Statistic**	***p*-Value**
Argon	37/40	0/9	5.83	< 0.001
Nd:YAG	87/87	11/32	8.33	< 0.001
Score Statistic	5.59	2.06		
***p*-Value**	0.061	0.040		
Reduced Epistaxis Intensity				
Laser Type	**Mild-Moderate**	**Severe**	**Score Statistic**	***p*-Value**
Argon	37/40	0/9	5.83	< 0.001
Nd:YAG	87/87	12/32	8.09	< 0.001
Score Statistic	5.59	2.18		
***p*-Value**	0.061	0.028		