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REVIEW ARTICLE

Cosmetic

A Practical Review of the Management of *Xanthelasma palpebrarum*

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Background: *Xanthelasma palpebrarum* is the most common type of xanthomatous lesion. Various methods for treating *Xanthelasma palpebrarum* have been reported. We conducted a systematic review to evaluate the efficacy and associated complications of different treatment methods, and we summarized these findings as a practical review designed to be clinically useful, accessible, and impactful.

Methods: The PubMed and Embase databases were searched to identify clinical studies that reported on outcomes and complications of different methods of *Xanthelasma* treatment. The electronic databases were searched from January 1990 to October 2022. Data on study characteristics, lesion clearance, complications, and recurrences were collected.

Results: Forty-nine articles (including 1329 patients) were reviewed. The studies reported on surgical excision, laser modalities, electrosurgical techniques, chemical peeling, cryotherapy, and intralesional injection. The majority of studies were retrospective (69%) and single-arm (84%). Surgical excision combined with blepharoplasty and skin grafts showed excellent outcomes for large *Xanthelasma*. CO_2 and erbium yttrium aluminum garnet (Er:YAG) were the most commonly studied lasers and showed more than 75% improvement in over 90% and 80% of patients, respectively. Comparative studies reported better efficacy for CO_2 laser than both Er:YAG laser and 30%–50% trichloroacetic acid. Dyspigmentation was the most encountered complication.

Conclusions: Different methods for the treatment of *Xanthelasma palpebrarum* have been reported in the literature, with moderate to excellent efficacy and safety profiles depending on the size and location of the lesion. Surgery is more appropriate for larger and deeper lesions, whereas laser and electrosurgical techniques can be used in smaller and more superficial contexts. Only a limited number of comparative studies have been conducted, and novel clinical trials are necessary to further augment appropriate treatment selection. *(Plast Reconstr Surg Glob Open 2023; 11:e4982; doi: 10.1097/GOX.0000000000004982; Published online 24 May 2023.)*

INTRODUCTION

Xanthelasma palpebrarum (XP) is characterized by periorbital fatty depositions underlying the skin surface. Frequently referred to as "*Xanthelasma*," XP lesions have variable presentations ranging from raised, waxy-appearing, yellowish-colored plaques to red-brown macules, papules, or nodules of variable consistency. They are often distributed symmetrically and can either be multiple or coalescing. Overall, the prevalence is approximately 4% with peak incidence in the fourth and fifth decades of life.[1–3]

XP is the most common type of xanthoma (>95%), a pathology defined by localized infiltrates of lipid-laden histiocytes called "foam cells" that are accompanied by endothelial and fibroblastic cell proliferation. The lesions are primarily located either within the upper dermis or in the perivascular and periadnexal areas.[2,4,5] While hyperlipidemia is a known cause of XP, it is only present in 33% to 40% of patients. Other factors, such as familial

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dyslipidemia type II and III, have also been shown to have associations with XP.[6] Although the diagnosis can usually be established from clinical features alone, a serum lipid profile is recommended to detect these lipid metabolism disorders if present. Additionally, because XP has been shown to be associated with both nonalcoholic fatty liver disease and hypothyroidism,[7,8] a liver panel and thyroid function tests are warranted to further identify associated conditions. More atypical lesions may present in the setting of adult orbital xanthogranulomatous diseases or other mucocutaneous pathologies.[5,9]

Although typically asymptomatic and benign, XP lesions can be disfiguring and cause patients to seek cosmetic treatment. Several therapeutic methods have been described in the literature thus far, including surgical excision, laser therapy, chemical peeling, cryotherapy, radiofrequency ablation (RFA), plasma sublimation, and dermabrasion. Although surgical excision is the conventional treatment and remains the most commonly used method, it carries concerns about scarring and ectropion.[10] Alternatively, lasers destroy foam cells in perivascular areas via thermal energy produced from tissue absorption of laser waves.[11] Topical trichloroacetic acid (TCA) works by dissolving lipids and coagulating proteins. Electrosurgical techniques, such as RFA and plasma sublimation, cause vaporization of targeted tissue in the epidermis and superficial dermis, where XP lesions mostly reside.[12] These varied mechanisms have led to varied results and complications profiles.

Herein, we conducted a systematic review of the literature to summarize the different treatment methods for XP and to compare their efficacy profiles and complications. We hope this will help guide contemporary, practical, evidence-based treatment of XP by medical providers.

METHODS

Literature Search

We followed the Preferred Items for Reporting of Systematic Reviews and Meta-analyses (PRISMA) statement to conduct this review.[13] An electronic search was performed to collect all publications from January 1990 through October of 2022. PubMed and Medline databases were searched for original English articles on clinical outcomes of XP treatment. The query for the PubMed database search was as follows: ("xanthomatosis"[MeSH Terms] OR "xanthomatosis"[All Fields] OR "xanthelasma"[All Fields]) AND ("palpebra*"[All Fields] OR "eyelids"[MeSH Terms] OR "eyelids"[All Fields]). The bibliographies of the included studies were also queried for additional sources.

Selection Criteria

Studies were included if they reported objective data on clearance, recurrence, and complications of any treatment method for XP. The exclusion criteria included the following: (1) case series with fewer than five patients; (2) review articles, editorials, letters, comments, and conference abstracts; (3) studies that were not in English; (4) studies evaluating cases through telephone or postal surveys; and (5) studies with insufficient or unclear data about recurrences and complications.

Data Extraction

The titles and abstracts were screened to determine whether studies met the inclusion criteria, and the relevant articles were selected for full-text review. Data collected for each study consisted of study characteristics, treatment characteristics, follow-up period, aesthetic outcomes, complications, and recurrences. For aesthetic outcomes, only data from objective size measurements were extracted. Lesion clearance was defined as the percentage of an XP lesion cleared per individual patient treatment. When applicable according to the format of reporting, clearance data were categorized as poor (<25%), fair (25%–50%), good (51%–75%), and excellent (>75%), and data were combined for each treatment method. The incidence of complications, including dyspigmentation (hypo- and hyperpigmentation), persistent erythema, scar (atrophic or hypertrophic), ectropion, and infections, were recorded regardless of severity or persistence. Outcomes were extracted if they were explicitly reported as present or absent. Recurrence was assessed in studies reporting a follow-up period longer than 6 months. Because some degree of scarring usually follows surgical excision, we screened for postoperative complications such as deformities. The level of evidence of the included studies was assessed based on the ASPS Evidence Rating Scale for Therapeutic Studies.[14]

RESULTS

Search Results

Our literature search retrieved 506 potentially relevant publications, and another six were found through handsearching the references of the included articles (Fig. 1). We screened 311 publications by title and abstract after duplicates were removed. We identified 74 publications for full-text review, with 49 meeting our inclusion criteria. Common reasons for exclusion at full-text review were not reporting on our prespecified outcomes, non-English papers, and letter or abstract publication. The PRISMA flow diagram is presented in Figure 1.

Treatment Modalities

Supplemental Digital Content 1 provides an overview of the characteristics of the included studies. (**See table, Supplemental Digital Content 1,** which displays the characteristics of the included studies. **http://links.lww.com/PRSGO/C546**.)

Thirty studies reported outcomes of laser therapies, including carbon dioxide (CO_2) (n = 11),[15–25] erbium-doped yttrium aluminum garnet (Er:YAG) (n = 7),[26–32] neodymium-doped yttrium aluminum garnet (Nd:YAG; n = 6),[31,33–37] argon (n = 4),[30,38–40] pulsed dye (n = 2),[41,42]

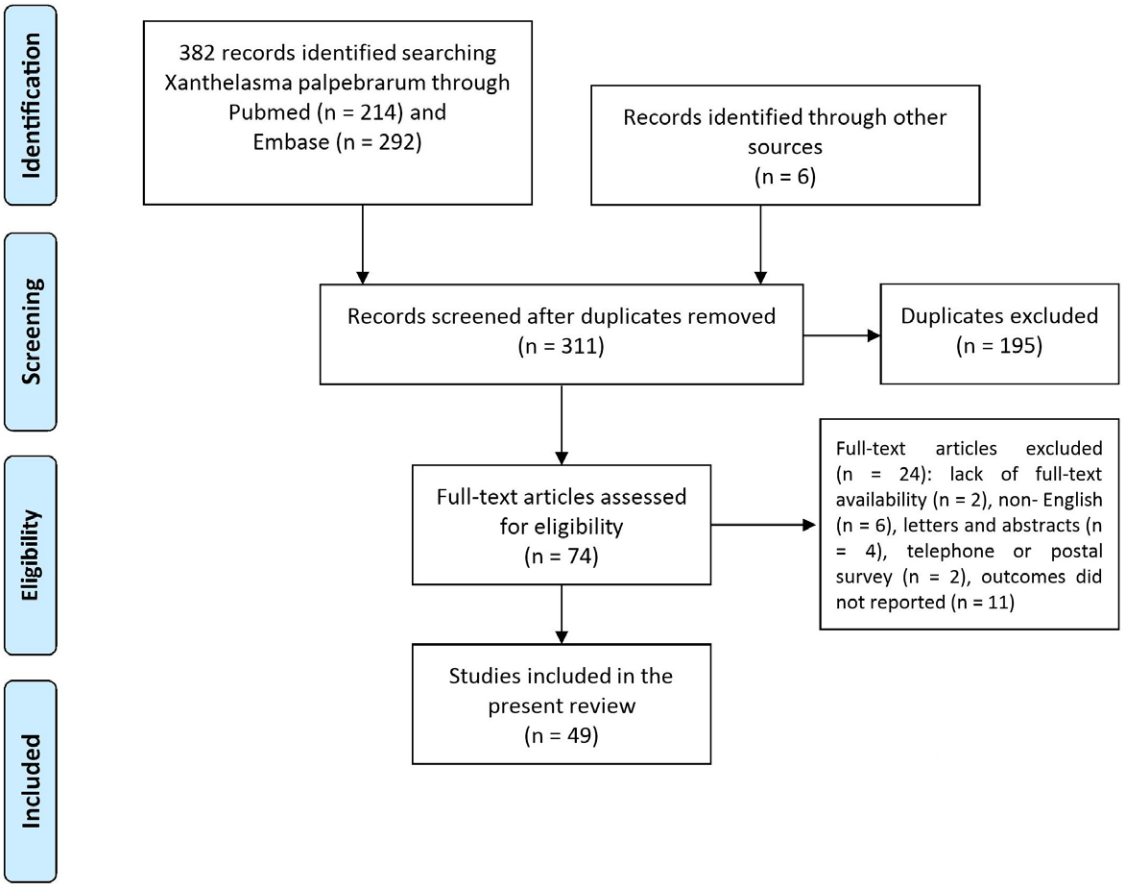

Fig 1. PRISMA flow diagram.

diode (n = 1),[43] and potassium titanyl phosphate (KTP) (n = 1)[44] lasers.

The remainder of the studies reported on surgery (n = 8),[10,45–50] RFA (n = 3),[51–53] plasma sublimation (n = 1),[54] voltaic arc dermabrasion (n = 1),[55] intralesional injection (n = 2),[56,57] topical therapies [bichloracetic acid (n =1),[58] TCA (n = 7)],[18,20,29,52,59–61] and cryotherapy (n = 1).[61] Thirty-four (69%) studies were retrospective with an evidence level of III and IV, and 13 (27%) were prospective with level II evidence. There were 41 single-arm and eight comparative studies among the included publications. The number of treatment sessions ranged from one to four for laser and electrosurgical techniques, one to six for topical therapies, and one to two for intralesional injections.

Surgery

One study utilized surgical removal of XP lesions with healing by secondary intention on 28 patients and reported excellent outcomes in all but two, who had recurrences.[45] Another study utilized an incision made along the upper margin of XP lesions followed by lifting the skin containing the lesions above the orbicularis oculi muscle. Lesions were then excised from the dermal side of the flap using microscissors. Recurrences were observed in two of eight patients, neither of which further recurred within one year of revision.[46] Three of the four patients with recurrences noted in these two studies had uncontrolled hypercholesterolemia, and one had primary biliary cirrhosis.

Six studies reported on techniques combining XP excision with blepharoplasty and skin grafts or flaps.[10,47–50,62] One study used full-thickness skin grafts from blepharoplasty for large lesions (>1.5 cm); upper eyelid positions were unaffected postoperatively. No recurrences occurred at a mean follow-up of 3 years, but two patients had hyperpigmentation.[48] Three studies used reconstruction by various local advancement flaps from blepharoplasty in a total of 32 patients.[10,50,62] No recurrences were noted at more than 6 months follow-up. In two other studies, reconstruction after large XP resection was done with a combination of local flaps and skin grafts obtained from blepharoplasty. They reported 3% and 8% recurrence rates during the 6 to 12-month postoperative periods.[47,49]

Laser

The outcomes from 23 of 30 studies on laser are presented in Fig. 2A and Supplemental Digital Content 2. (**See Supplemental Digital Content 2**, which displays the outcomes and complications of each treatment modality. **http://links.lww.com/PRSGO/C547**.) Overall, the clearance rates were poor in 10.3% of cases, fair in 6.7%, good in 12%, and excellent in 71%. CO_2 laser achieved excellent clearance in 94% of cases, Er:YAG in 80%, Nd:YAG in 45%, and pulsed dye

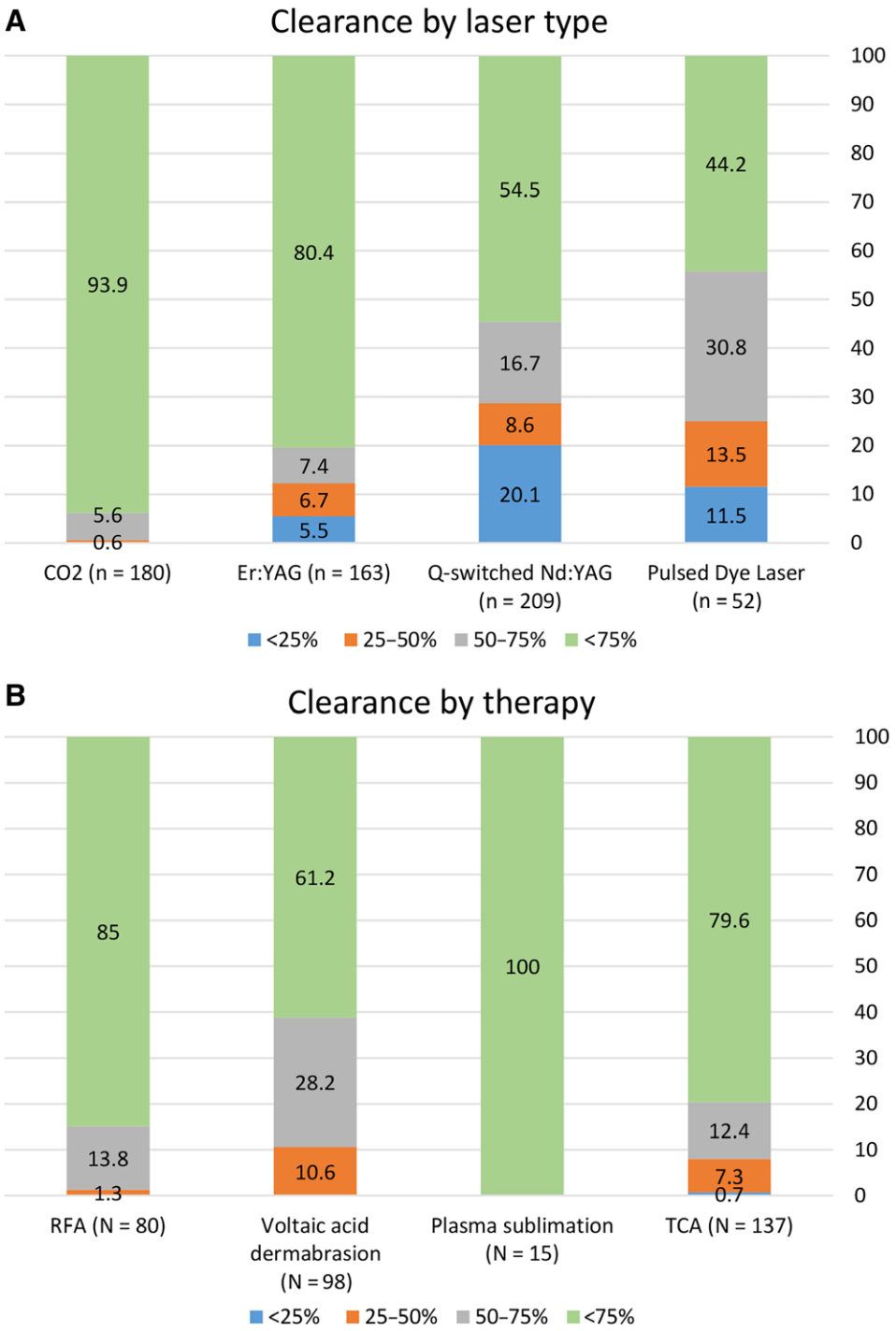

Fig 2. Lesion clearance rates by each treatment method. A, Clearance by laser type. B, Clearance by therapy.

lasers in 44%. As for argon laser, a complete resolution was achieved in 84% of cases, but the remaining 16% showed reduction in size only.[38–40] Single studies on diode and KTP lasers reported that 25% of cases treated with diode had over 60% clearance, whereas 97% of lesions treated with KTP were almost cleared after the final session.[43,44]

The total rates of dyspigmentation, scarring, and recurrence among laser therapies were determined for CO_2 (16%, 6%, and 10%, respectively), Er:YAG (11%, 2%, and 20%), Nd:YAG (9%, 7%, and 31%), argon (7%, 0%, and 21%), pulsed dye (7%, 0%, and 0%), diode (31%, n/a, and n/a), and KTP (3%, 0%, and 43%) lasers. [26–28,30,40,44] (**See table, Supplemental Digital Content 3**, which displays the complications and recurrence rates among included studies **http://links.lww.com/PRSGO/C548**.)

Electrosurgical

The clearance rates for RFA, plasma sublimation, and voltaic arc dermabrasion are presented in Figure 2B and Supplemental Digital Content 2. (**http://links.lww.com/PRSGO/C547**). Three studies evaluating RFA for XP treatment in a total of 80 cases showed good to excellent lesion clearance in 98.8% of cases.[51–53] The rate of dyspigmentation varied among studies from 20% to 50%, and scarring was only reported in one study, which complicated 40% of cases. In the two studies tracking recurrence, the total rate was 3% (two of 65 patients).[53,63] In separate studies, the rates of dyspigmentation were 0% and 1% for plasma sublimation and voltaic arc dermabrasion, respectively, and no recurrences were noted at over 6 months follow-up using either technique (**Supplemental Digital Content 3**, **http://links.lww.com/PRSGO/C548**)[54,55]

TCA Peel

The combined results of five studies reporting on TCA peeling in a total of 137 cases showed excellent lesion clearance in 83% of cases. Total rates of dyspigmentation, scarring, and recurrence in these patients were 44%, 9%, and 17%, respectively.[29,52,59–61]

Comparative Studies

Among studies that compared different modalities, fractional CO_2 laser had superior efficacy in treating XP lesions over fractional Er:YAG laser despite requiring fewer treatment sessions to show clinical improvement. No differences in complications or recurrence rates were reported between these two modalities.[32] Although CO_2 laser was no different than 70% TCA in lesion clearance, it was more effective than 30% to 50% TCA. Likewise, 70% TCA was more effective than 35% and 50% TCA strengths. Posttreatment dyspigmentation was more frequent in 70% TCA than both lower TCA concentrations and CO_2 laser, but the recurrence rates were similar among these groups.[18,20]

One study comparing Er:YAG laser and 70% TCA found no significant differences in the clearance of XP lesions or complication rates between the two modalities.[29] Another study comparing the clinical efficacy of Er:YAG versus Nd:YAG laser showed a higher proportion of patients with excellent lesion clearance in the Er:YAG group, but they also required more treatment sessions. The rates of complications and recurrences were similar between the two groups.[31]

One study demonstrated that a single session of 100% TCA was more effective than cryotherapy in resolving xanthelasma but was also associated with higher rates of hypo- and hyperpigmentation along with scar development.[61]

DISCUSSION

This review summarizes the evidence on the efficacy and complications of different modalities in the treatment of XP. Most of the included literature reported on laser and other nonsurgical methods, whereas only eight (16%) articles evaluated surgical methods. The evidence comprises eight comparative and 41 single-arm studies. Surgical techniques resulted in a total recurrence rate of less than 5%. Nonsurgical modalities demonstrated variable efficacy profiles. Notably, laser studies collectively demonstrated greater than 75% lesion clearance in 71% of patients, with recurrence rates ranging from 10% to 31% in lasers with multiple publications investigating their use. Dyspigmentation was the most common side effect overall, followed by problematic scarring.

Surgery has been the conventional method of XP treatment, especially in lesions involving the deeper dermis. In small lesions, simple excision with primary closure or healing by secondary intention has been shown to be safe and leave minimal pigmentary changes or scarring.[45,46] However, because excision of larger XP lesions increases the risk of eyelid retraction, ectropion, and dyspigmentation, these procedures generally require reconstruction with a skin graft or flap to prevent these complications. Recent literature has mostly focused on methods incorporating blepharoplasty with skin grafts or flaps.[10,47–50] Among the included studies, both collective complication and recurrence rates were 0.5%. However, despite reconstructive techniques to mitigate scarring, surgery is an invasive procedure requiring either local or systemic anesthesia, and can still lead to some degree of scarring, eyelid deformities, or dyspigmentation as postoperative complications.[64]

Laser therapy is a potentially ideal option for XP treatment when lesions are localized to the superficial dermis.[30] Ablative lasers, like CO_2 and Er:YAG, destroy perivascular foam cells and coagulate dermal vessels through rapid heating and vaporization of intracellular water.[63] Additionally, different laser modes carry different functional properties. Continuous mode CO_2 laser therapy renders a high concern of scarring and dyspigmentation due to its unpredictable penetration.[16] Alternatively, ultrapulsed- and superpulsed-mode CO_2 lasers deliver microscopic beams of light in a grid pattern. These modes have been studied abundantly and have been reported to be safe and effective (Fig. 3). They have shown superior efficacy than Er:YAG laser and 30%–50% TCA but no difference in efficacy from 70% TCA.[18,20] In separate studies, Er:YAG laser has also demonstrated efficacy and side-effect profiles comparable to those of TCA 70%, along with Argon laser.[29,30]

Other modalities using nonablative lasers, including Nd:YAG, argon, pulsed dye, and KTP lasers, have been reported in the literature to have promising safety and efficacy profiles. Due to their shorter wavelengths and reduced penetration, they are primarily indicated in the treatment of smaller, superficial lesions at early stages. They also often require multiple treatment sessions.[30]

Electrosurgical techniques such as RFA, plasma sublimation, and voltaic arc dermabrasion have been introduced as new methods of XP treatment with mixed results. RFA is recommended in cases where there are multiple lesions with indistinct borders or close proximity to the eyes.[51] Plasma sublimation allows for control over the depth of tissue destruction, thus minimizing pain and trauma and implicating it in the use of periocular lesions as well.[54]

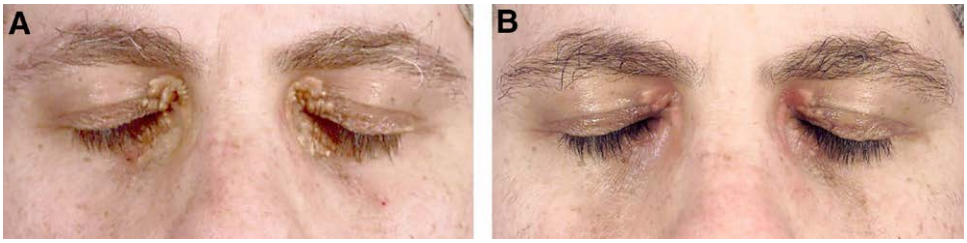

Fig. 3. A 45-year-old White man with a several-year history of *Xanthelasma* of the bilateral medialanthal area was treated with a high-energy, pulsed CO_2 laser ablation (300 mJ, 60 W) by making three passes in each area. A, Preoperative view; B, 6-week postoperative view. © 2002 Wolters Kluwer Health, Inc. Used with permission from Rohrich RJ, Janis, JE, Pownell PH. *Xanthelasma palpebrarum*: a review and current management principles. *Plast Reconstr Surg*. 2002;110:1310–1314. The Creative Commons license does not apply to this content. Use of the material in any format is prohibited without written permission from the publisher, Wolters Kluwer Health, Inc. Please contact permissions@lww.com for further information.

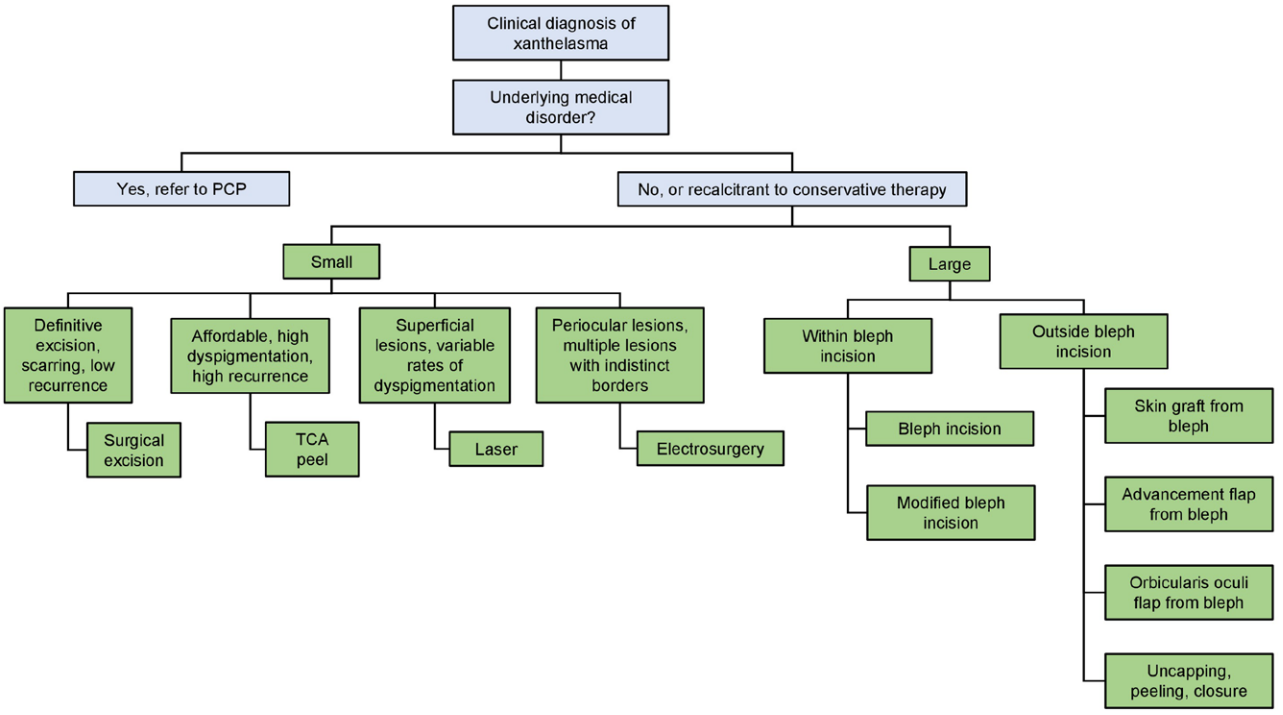

Fig 4. Display of the algorithmic approach for the management of XP.

TCA peeling is a simple and affordable method for XP treatment that has been previously shown to achieve satisfactory outcomes, especially with repeated treatments.[59] Among the studies included in this review, over 80% of patients experienced more than 75% improvement. However, these studies also reported dyspigmentation and recurrence rates exceeding 30% (**Supplemental Digital Content 3, http://links.lww.com/PRSGO/C548**.). Evaluation of three different strengths of TCA indicated that best results are achieved with 100% TCA in papulonodular lesions, 70% or 100% TCA in flat plaques, and 50% TCA in macular lesions.[59] Compared with other treatment modalities, it is less effective than CO_2 laser, has a higher dyspigmentation rate, and requires more treatment sessions.[18,20] Regarding cryotherapy, TCA is more efficacious yet leads to higher complication rates.[20,61] Notably, the depth of tissue penetration by the chemicals is not predictable, which increases the risk of ocular damage and further complications.[30] Based on the above discussion, we have developed an algorithmic approach for the management of XP relying on the size and location of the lesions (Fig. 4).

CONCLUSIONS

Xanthelasma palpebrarum is a benign, yet disfiguring, disease that can subject patients to high degrees of cosmetic discomfort. Treatment strategies are abundant, yet proper selection in the right setting remains a challenge. In this

comprehensive review, we have investigated the literature regarding the efficacy and complication rates of each therapeutic modality. The primary limitation is the predominance of single-arm studies and corresponding dearth of comparative studies to inform treatment selection of modalities with overlapping indications. Additionally, several studies were excluded from the review due to variations in outcomes that precluded consistent analysis with other studies. Nonetheless, our findings underscore the compelling evidence that surgery with blepharoplasty incision in addition to skin grafting or flap coverage is an excellent option for large XP lesions. Additionally, laser treatments have shown remarkable efficacy. TCA is an inexpensive and effective modality, especially in high doses repeated adequately. All strategies have adverse effects that should be weighed against their benefits. In future studies, authors should aim to conduct comparative and, ideally, prospective trials that will empower clinicians to better select between two favorable therapeutic options.

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DISCLOSURES

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