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Most effective method for the management of physiologic gingival hyperpigmentation: A systematic review and meta-analysis

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Abstract

Background and Aim:

Gingival hyperpigmentation is an esthetic problem. The aim of the present study was to identify most effective treatment modality for managing generalized physiological gingival pigmentation.

Materials and Methods:

A systematic review and meta-analysis were done (1919 to October 2018) using PubMed, CINHAL, Dental and Oral Science, and manual searches. Twenty-five articles were finally reviewed. Only human clinical trials were considered with physiological gingival pigmentation treated with different depigmentation methods and compared with surgical stripping. The outcome was the achievement of gingival depigmentation and its recurrence. RevMan software was used for data analysis.

Results:

Of 26,132 articles, 25 met the inclusion criteria. Seventeen were randomized control trials and 8 were nonrandomized control trials. Most of the studies were on laser. The control group was scalpel surgery. Majority of studies showed no difference in compared treatment modality. A meta-analysis compared laser ablation with surgical stripping revealed a nonsignificance difference regarding recurrence ($P = 0.75$) and depigmentation ($P = 0.23$) and a statistically significant difference regarding postoperative pain favoring laser ablation ($P \leq 0.05$).

Conclusions:

Surgical stripping has been the conventional treatment of choice, but our review showed that new techniques are equally effective or even better. Laser especially diode laser was the most frequently used technique and showed better esthetic outcomes, less pain, faster healing, and patients' preference and satisfaction after treatment. However, laser showed more regimentation at 6-month evaluation. More good quality randomized controlled trials with different depigmentation methods are needed to draw strong conclusions.

Key words: Cryosurgery, electro-cautery, gingival hyperpigmentation, laser therapy, melanin

INTRODUCTION

An esthetic smile does not only create an impact on the viewers but it also enhances the personality and self-confidence of the individual.[1] Various factors contribute to the composition of an esthetic smile such as shape, color, and position of teeth and gingiva.[1] Of these, the color of gingiva plays a significant role in the overall smile esthetics.[1] The color of gingiva is affected by some factors, including the thickness of the epithelium, the degree of keratinization, size of blood vessels, and color pigments within the epithelium.[2]

Normal color of the gingiva is mainly due to the melanin pigment produced by melanocytes present in the basal and supra-basal layer of the epithelium, excessive melanocytic activity leads to hyperpigmentation.[3] Gingival hyperpigmentation can be physiological or pathological.[3] Physiological hyperpigmentation is genetic and does not pose any health concerns, whereas pathological hyperpigmentation is a health concern and can occur due to a variety of reasons.[3] These include endocrine disorders, ingestion of heavy metals, Kaposi's sarcoma and smoking, etc.[3]

Physiological hyperpigmentation clinically manifests as variable amount of diffuse melanin pigmentation in the gingiva.[4] It varies among different races.[4] Pigmentation is more prevalent on the labial surface of the attached gingiva than the lingual or palatal surface.[5,6] It is an important esthetic concern, especially in patients with high smile line. Studies have reported that people perceive the pink color of gingiva as more acceptable and appealing than the dark-colored gingiva.[7,8,9] The dark patches on the facial gingiva are also associated with the adverse psychological effects.[7,8,9]

Different treatment modalities are available for the management of gingival hyperpigmentation that can be broadly classified into two categories: methods that remove pigments and methods that mask the pigment.[10,11] Removal of pigment can be done by surgical and nonsurgical or chemical methods.[10,11] Surgical methods mainly include scalpel surgery, laser ablation, bur abrasion, electrocautery, cryosurgery, and radiosurgery.[10,11] Nonsurgical method mainly refers to chemical cauterization.[10,11] The methods that mask the gingival pigments include gingival grafting procedures and use of acellular dermal matrix allograft, etc.[10,11]

All these treatment modalities have their own advantages and disadvantages. In addition to the known complications such as postoperative pain, bleeding, discomfort, the difficulty of the procedure, and delayed wound healing, the most common problem associated with the above is the mentioned treatment modalities is the recurrence of the pigmentation.[12,13,14]

Various studies had been conducted to identify the best treatment for gingival hyperpigmentation with conflicting results. Some studies were in favor of scalpel surgery, some favored laser ablation and some reported no differences among different treatment modalities.[12,13,14] Previous systematic reviews conducted on this topic were either based on poor evidence-based studies or have taken only one treatment modality into consideration.[15,16] Therefore, the aim of the present systematic review and meta-analysis was to identify the most effective treatment modality for physiological gingival hyperpigmentation in light of the best available evidence.

MATERIALS AND METHODS

Protocol and registration

The registration of the review protocol was done at PROSPERO (CRD42017072470), an international database of prospectively registered systematic reviews. It was done to avoid any unplanned duplication of the review on this topic. We strictly adhered to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-analysis) guidelines.[17,18] Our review question was: "Which is the most effective treatment modality for managing generalized physiological gingival hyperpigmentation?" PRISMA statement and Cochrane Handbook for Systematic Reviews of Interventions was referenced in reporting the results of this review.[19,20]

Eligibility criteria

The following PICOS model was employed: Participants: patients presenting with generalized physiological gingival hyperpigmentation; Intervention: cryosurgery, laser, electrocautery, radiofrequency, graft, chemical cauterization; Comparison: surgical stripping; Outcome: primary outcome: recurrence of gingival pigmentation and secondary outcome: amount of depigmentation achieved and procedural complications; Studies: clinical trials (randomized and nonrandomized), articles published only in the English language, *in vivo* studies. Review articles, single-arm experimental studies, case reports, commentaries, case series, letters to the Editor and unpublished articles were excluded.

Search strategy

A comprehensive literature search was performed from 1919 to October 2018. All clinical trials (randomized or nonrandomized) done on the human gingival tissues were explored in three major health science databases (PubMed [NLM] CINAHL Plus, EBSCO Dent, and Oral Science). Manual search on the Google Scholar and in the database for registered clinical trials in the Medline, clinicaltrials.gov, greylit.org, opengrey.eu and Trove was performed to identify any gray literature and unpublished data. MESH terms included different permutations of: (melanin OR gingiva OR pigmentation OR hypopigmentation OR hyperpigmentation OR gingival hyperpigmentation OR depigmentation) AND (laser therapy OR cryosurgery OR electrocautery OR bur abrasion OR gingival graft OR ascorbic acid gel).

Screening and data extraction

Initially, one of the investigators reviewed the total search results to exclude any duplications or studies that are not relevant to the research question. The eligibility of studies of the relevant studies was evaluated individually by the three investigators based on the titles followed by evaluation of the abstract, objective, outcome, study design, availability of full-text articles. Any disagreement was resolved after discussion with the fourth author. These final selected articles were thoroughly evaluated for inclusion in the systematic review, whereas others were excluded after scrutiny with duly mentioned reasons. Data was extracted from the finally included studies on a customized self-structured pro forma.

Risk of bias

The quality of randomized clinical trials was evaluated using the risk of the bias assessment tool (The Cochrane collaboration's tool) by three investigators separately.[19] Conflicts over the review were discussed and resolved after consultation with the fourth investigator. Using the risk of the bias assessment tool, the studies were assigned as having a high, low, or unclear risk of bias.

Statistical analysis

Data from the included studies were processed for both qualitative and quantitative analyses. Review Manager Version 5.3.5 (The Nordic Cochrane Centre, the Cochrane Collaboration, Copenhagen, Denmark)was used for meta-analysis (for studies with quantitative data).[20] Heterogeneity among the selected studies was evaluated using the I^2 statistic. Random effect model was used for the computation of a summary effect for the majority of the outcomes where I^2 was high and fixed effect model where the value of I^2 was low. Pair-wise meta-analysis was conducted for the primary outcomes (amount of depigmentation, recurrence rate) and secondary outcome (postoperative pain, wound healing, intra/postoperative bleeding, procedure time, and patient preference). The level of significance (α) was set at ≤0.05.

RESULTS

Study selection

A total of 26,132 studies were identified after detailed literature search. Initial screening was done to remove duplicate studies, studies in language other than English and irrelevant titles. A total of 4989 studies with relevant titles were further scrutinized based on eligibility criteria. After removing studies on basis of irrelevant objective, protocols only, no abstract, no full text, *in vitro* studies, different study designs, only 25 studies[12,13,14,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42] were finally selected to be included for data extraction. The PRISMA flow chart of the process is shown in Figure 1.

Study characteristics

Out of 25 clinical trials, 17 were randomized trials and 8 were nonrandomized trials.[12,13,14,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42] A total of 437 participants were evaluated in the selected studies. Suryavanshi *et al*.[40] contributed maximum number of patients (n = 40), whereas Mahesh *et al*.[29] contributed minimum (n = 4). The age range of the participants was between 10 and 60 years in all studies except Gera *et al*.,[26] Suryavanshi *et al*.[40] and Bhardwaj *et al*.[32] who did not mention it and Ribeiro *et al*.[14] who reported the mean age of participants only. Most studies reported gender distribution of patients except Gera *et al*., Kumar *et al*.[25] and Basha *et al*.[23] Minimum follow-up was of 24 h, and the maximum follow-up was of 15 months.[36,27] Out of 25 studies, 17 studies compared laser,[12,14,21,22,23,25,26,28,30,31,32,34,36,37,38,39,41] 3 compared cryosurgery,[13,24,42] 2 electrocautery,[27,35] one radiosurgery[29] and 2 combination of laser and electrocautery, laser and graft.[33,40] The control group in all the studies was surgical stripping. Different types of lasers have been used in the included studies which include Diode, ErYAG, NdYAG, and CO_2 lasers. Majority of the studies have studied the diode laser.[21,22,25,26,30,32,33,35,36,38,39,40] Rest used Nd-YAG[23,12,14,28] and Er-YAG laser [Table 1].[31,34,37] The parameters assessed in the included studies along with the measurement scale are mentioned in Table 2.

Outcomes of included studies

Out of a total of 25 included studies, 16 studies[12,13,14,21,22,23,26,27,28,29,30,34,38,39,40,42] reported recurrence of pigmentation. Majority of the studies reported no significant difference for recurrence of pigmentation, two studies[22,42] supported scalpel surgery, one study favored cryosurgery[13] and one study supported diode laser [Table 3].[21] Ten out of 25 studies have reported no significant between the compared treatment modalities for depigmentation level achieved.[21,22,23,24,27,31,33,35,41,42] 16 out of 25 studies reported postoperative pain and discomfort.[12,13,14,21,22,23,24,25,27,28,31,34,36,37,41,42]

Majority of the studies reported pain both after 24 h and 1 week, few studies also reported pain after 3 and 6 months. Nine studies[12,21,22,23,25,30,36,37,41] reported that laser is more comfortable and produces less postoperative pain, two studies were in favor of cryosurgery[13,42] and remaining showed no difference [Table 3].[14,27,28,31,34]

Six studies reported intra-operative and immediate postoperative bleeding.[21,22,23,30,31,34] All studies[22,23,30,31,34] favor laser except one[23] which showed no significant difference. Six studies reported wound healing after different treatment modalities.[21,22,25,31,33,34] Out of six studies, two favored laser,[31,34] one favored scalpel,[22] and remaining showed no difference between compared modalities.[21,25,33] Three studies reported patient preference and procedure time[14,23,31] and majority of the studies favored laser [Table 3].

Results of meta-analysis

Meta-analysis was performed for seven outcomes. These were a recurrence of pigmentation, depigmentation achieved, pain or discomfort after the procedure, wound healing, intra- and postoperative bleeding, procedure time, and patient preference. We need at least two studies on a similar technique for meta-analysis. Due to limited or no studies on other interventions only those studies which compared laser ablation with surgical stripping underwent meta-analysis. Random effect model was used for the computation of the summary effect for most outcomes and fixed effect model was used where the value of I^2 was low. Out of total 16 studies[12,13,14,21,22,23,26,27,28,29,30,34,38,39,40,42] that reported recurrence only 4 studies[12,14,22,23] underwent meta-analysis due to heterogeneity in technique, insufficient or different follow-up time and inconsistent measurement scale [Figure 1]. The result of meta-analysis showed that the risk of recurrence of pigmentation at 3 months was more in scalpel surgery group, but the difference was not statistically significant (risk ratio 0.85; 95% confidence interval [CI], 0.46, 1.57) (I^2 = 0%, P = 0.60). Meta-analysis also shoed that on 6 month follow-up recurrence of pigmentation was more in laser ablation group when compared to scalpel surgery group, but the difference was not statistically significant (risk ratio 1.08; 95% CI, 0.68, 1.72) (I^2 = 41%, P = 0.75) [Figures 1 and 2a, b].

Out of 10 studies[14,21,23,24,27,31,33,35,41,42] that reported depigmentation, only 4 studies[14,21,23,31] underwent meta-analysis reason being heterogeneity in data regarding depigmentation technique. The forest plot depicts that laser and scalpel surgery both are equally effective, and the difference was not statistically significant (weighted mean difference 0.10; 95% CI, −0.07, 0.27) (I^2 = 0%, P = 0.23) [Figures 1 and 3].

Out of 16 studies[12,13,14,21,22,23,25,27,28,30,31,34,36,37,41,42] that reported pain only 8 studies[14,21,23,28,31,34,36,37] underwent meta-analysis because rest of studies vary in terms of techniques and inconsistent measurement scale and the results showed that laser is associated with less postoperative pain immediately but not significant statistically (weighted mean difference − 0.06; 95% CI, −1.07, 0.95) (I^2 = 88%, P = 0.91) and on the 7th postoperative day, there is significantly less pain in laser treated site as compared to surgical stripping (weighted mean difference − 0.37; 95% CI, −0.73, −0.00) (I^2 = 35%, P = 0.05) [Figures 1 and 4a, b].

Out of 6 studies that reported wound healing[21,22,25,31,33,34] only two underwent meta-analysis[21,34] and the results were in favor of laser but not statistically significant (weighted mean difference 0.20; 95% CI, −0.07, −0.47) (I^2 = 29%, P = 0.16) [Figure 1 and 5].

Six studies reported intra- and post-operative bleeding, only 4 underwent meta-analysis and the results revealed that there was significantly less bleeding during the procedure when the laser was used as compared to scalpel surgery (weighted mean difference − 1.07; 95% CI, −1.62, −0.52) (I^2 = 83%, P = 0.0002) [Figures 1 and 6].

Three studies reported procedure time[14,23,31] and two[14,23] underwent meta-analysis and the results favored laser, but the result was not statistically significant (weighted mean difference − 4.71; 95% CI, −10.27, 0.86) (I^2 = 94%, P = 0.10) [Figures 1 and 7].

Only two studies reported patient preference and underwent meta-analysis, and the results showed that patients preferred laser as compared to scalpel surgery, but the results were not statistically significant (weighted mean difference 1.36; 95% CI, 0.48, 3.82) (I^2 = 78%, P = 0.56) [Figures 1 and 8].

Risk of bias

The studies were evaluated for the risk of bias using the Cochrane's collaboration tool.[19,20] Due to the type of surgical intervention used in the test and control groups blinding of participants was not possible so the highest risk of bias was reported for blinding of the participant. Randomization was done in 13 out of 17 randomized clinical trials except for five in which the method used was unclear, and no randomization in eight studies which were quasi-experimental. Allocation concealment was either missing or unclear in all the studies. Measures that were used for blinding of the outcome assessors were mentioned in eight studies only. No subjects in any of the included studies fail to complete the trial hence the attrition bias was nonexisting. Authors adequately reported the outcomes under consideration in the studies except for one study who failed to completely report the outcome. Other biases remained unclear. Details are given in Figure 9a and b.

DISCUSSION

Several treatment modalities are available for the removal of gingival hyperpigmentation among those conventional scalpel surgery is still the most widely used therapy as it is simple and cost-effective compared to other techniques.[43] Choice of treatment modality is usually based on clinician expertise, preference, and cost. There is a lack of high level of evidence to recommend the best treatment option for gingival hyperpigmentation. After a thorough literature search, we identified two systematic reviews previously reported on this topic one by Lin *et al*.[16] in 2014 who compared all the treatment modalities, but the main shortcoming was the level of evidence of the included studies, all the studies were either case report or case series that generate a poor evidence. Another recent systematic review was done by Abduljabbar *et al*.[15] in which only one treatment modality laser ablation was taken into consideration, therefore due to limitations in the previous studies we generated our review question to identify the most effective treatment modality for the management of physiological gingival pigmentation.

Although different treatment modalities were compared in this review, the majority of the included trials were on laser and due to limited or no clinical trials reported on other treatment modalities most of our results are based on comparison between laser and scalpel technique and only this comparison group underwent meta-analysis.

We tried to address publication bias by searching for grey literature on different websites. After thorough search we found many studies but only one unpublished dissertation met our inclusion criteria, rest were excluded. Details are given in Table 1.

Every treatment has its own advantages and disadvantages, but the most common problem with all the depigmentation procedure is the recurrence of pigmentation. Majority of the included studies reported no significant difference for recurrence between the compared treatment modalities.[12,14,23,26,28,30,34,38,39,40] Laser treatment groups showed greater recurrence as compared to scalpel technique. Meta-analysis further supported the result. Other systematic review by Abduljabbar *et al*.[15] also reported the same. However, Lin *et al*.[16] reported less recurrence in electrocautery, cryosurgery, and laser group as compared to scalpel and bur abrasion group. The results could be biased as it was done on case reports and case series.

Recurrence is due to migration of melanocytes from adjacent tissues. Excessive sunlight exposure, hormonal changes, genetic and ethnic factors.[8,44] it also includes incomplete removal of pigment due to less depth of penetration of some lasers except for Nd-YAG laser which has greater depth of penetration and hence less recurrence.[12] laser work by biomodulation which at one end increase the rate of healing while on the other end stimulate migration of adjacent melanocytes resulting in faster recurrence.[12] Recurrence is more common in interdental papilla as it is difficult to treat due to proximity to vital tooth structure[14]

Advantages of lasers reported in the included studies are less postoperative pain due to formation of coagulum on wound surface acting as biological seal,[14,21,22,23,25,28,30,37,41] better wound healing,[31,33,34] less discomfort,[12,21,22,23,25,30,36,37,41] less bleeding[21,22,30,31,34] and more patient satisfaction and preference[23] and less chairside time[14,23] these results were further supported by meta-analysis. The diode laser is the most frequently used laser in the studies. It targets mainly soft tissue, and hence hard tissues are protected. However, studies have reported that it results in incomplete removal of pigmented tissue.[34]

Despite the advantages of laser in achieving esthetic outcomes, it is technique sensitive, require expensive instruments and proper training before usage. If used inappropriate, it can result in damage to hard and soft tissue.[14,44,45,46] Studies have recommended using multiple sessions of the laser at a low power setting instead of a single session and using long pulse duration to prevent recurrence and avoid damage to vital structures.[31,37]

Healing occur by secondary intention in surgical stripping causing more discomfort as compared to laser, especially in cases of thin gingival biotype, care should be taken to prevent exposure of alveolar bone.[14] It has also been reported in our systematic review and supported by meta-analysis. Surgical stripping was associated with less recurrence in majority of the studies as it completely removes the gingival epithelium and connective tissue along with the pigment.[22,42] Other advantages include easy and cost-effective treatment.[24] The major disadvantage associated with this technique is bleeding, raw, and painful tissue surface due to open nerve endings, longer procedure time as reported in multiple studies and supported by meta-analysis.[14,22,23,12,41,21,30,34] Recommendations include careful excision of soft tissue, periodontal dressing covering the lesion, adequate local anesthesia.

Cryosurgery destroy tissue by freezing it using cryogens.[47,48] There is no need of local anesthesia, and it was also associated with less postoperative pain and bleeding as reported in studies.[13,42] other advantages reported include less cost, good esthetic outcome, less recurrence, and less technique sensitive.[13,24] Postoperative swelling and difficulty in controlling the penetration depth constitute the disadvantages of this technique.[45]

Electro-cautery is also a commonly employed technique for depigmentation. It results in delayed wound healing, requires more expertise and equipment.[27,33,35] Incorrect use of equipment leads to damage soft and hard tissues of the oral cavity.[27,33,35]

After thorough literature search, it can be said that this is the first systematic review on gingival depigmentation techniques that is based on high level of evidence-based studies RCTs and N-RCTs, structured and first meta-analysis done on this topic. Multiple treatment modalities were taken into consideration to make the results more generalizable. Risk of bias of the individual studies and of the overall systematic review was assessed. The limitations are that no conclusive inference regarding cryosurgery, electro-surgery, radiosurgery, and other techniques could be drawn because of the limited data, follow-up time was limited, limited included studies, inconsistent appraisal methods of outcomes across studies. Although we tried to address publication bias, there are chances of missing studies published in other languages. We recommend performing more good quality randomized controlled trials with strict inclusion and exclusion criteria, longer follow-up period, larger sample size, and comparison of different depigmentation methods.

CONCLUSIONS

Surgical stripping has been the conventional treatment of choice as it was convenient, cost effective and less technique sensitive, but our review showed that new techniques are equally effective or even better than conventional scalpel surgery when different parameters were assessed. Laser especially diode laser was the most frequently used technique and showed better esthetic outcomes, less pain, faster healing and most important patients' preference and satisfaction after treatment. However, lasers were associated with more recurrence at 6-month follow-up. We had limited studies on other techniques, but the few included studies reported that cryosurgery and electro-cautery and radiosurgery can be alternative for scalpel surgery in terms of esthetic outcomes achieved. Limitations should be kept in mind, such as special equipment needed, adequate training, cost of treatment, and clinician preference. The results of our systematic review should be considered with caution as included studies have high risk of bias. We need more good quality randomized control trials on different currently used techniques to generate strong conclusions.

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Conflicts of interest

There are no conflicts of interest.

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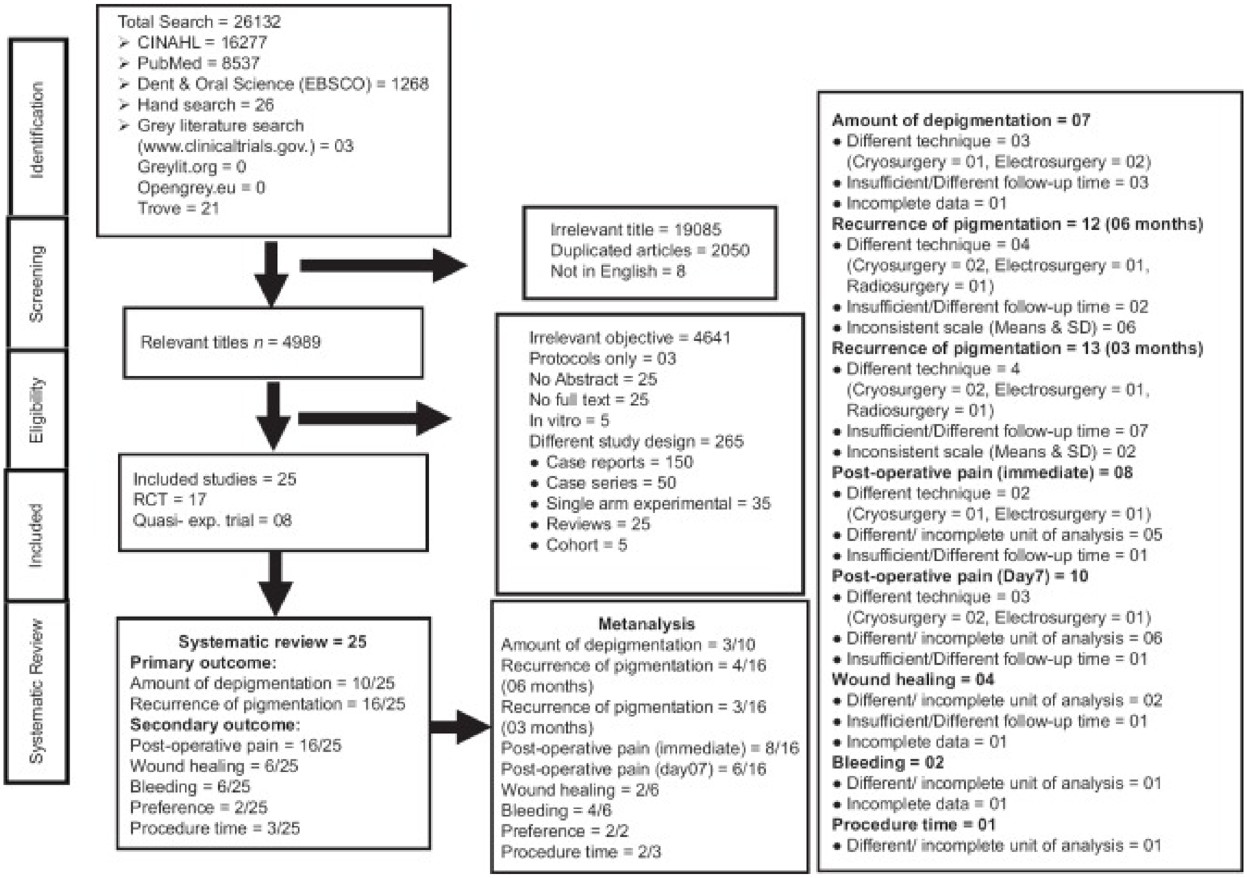
Figures and Tables

Figure 1



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Literature search PRISMA Flowchart

Table 1

Characteristics of Included studies

Author	Publication years	Journal	Study design	Age (years)	Gender	Comparison techniques	Follow-up (months)
Bakutra	2017	International Journal of Health Science	RCT	18-30	Male=12, female=8	Diode laser	12
Narayankar	2017	Contemporary Clinical Dentistry	RCT	20-60	Male=20, female=5	Cryosurgery	6
Suragimath	2016	Laser Medical Sciences	RCT	18-40	Male=7, female=5	Diode laser	12
Gera	2016	Journal of Dental Speciality	RCT	-	-	Diode laser	3
Kumar	2015	Journal of Clinical and Diagnostic Research	RCT	20-40	-	Diode laser	3
Basha	2015	Photomedicine and Laser Surgery	RCT	18-38	-	Nd-YAG laser	6
Ribeiro	2014	Laser Medical Sciences	RCT	39.82±11.44	63%female	Nd-YAG laser	6
Rahmati	2014	Journal of Dental Shiraz University Medical sciences	RCT	10-31	Male=5, female=15	Cryosurgery	1
Hedge	2013	Journal of Periodontology	RCT	18-50	Male=15, female=20	Nd-YAG and CO2 laser	6
Nagati	2017	Global Journal of Health Science	Non-RCT	18-30	Male=12, female=8	Diode laser	6

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ND-YAG – Neodymium-doped yttrium aluminum garnet; Er-YAG – Erbium-doped yttrium aluminium garnet; NA – Not available; RCT – Randomized control triall; NRCT – Non-randomized control trial; FGG – Free gingival graft

Table 2

Parameters evaluated in included studies with their measurement scale

Author	Esthetic score/depigmentation	Recurrence/repigmentation	Postoperative pain/discomfort	Bleeding	Wound healing	Ti
Bakutra	-	Hedin index	VAS	Visual	Visual	-
Narayankar	-	GPI	VAS	-	-	-
Suragimath	DOPI, photographs	-	VAS	Scale 1-4	Scale 1-4	D
Gera	DOPI score	DOPI	-	-	-	-
Kumar	-	-	VAS	-	Healing index	-
Basha	-	DOPI	VAS	Score 0-3	-	Ti
Ribeiro	VAS	-	Yes	-	-	Ti
Rahmati	Yes	-	Questionnaire	-	-	-
Hedge	DOPI, Hedin index	DOPI	VAS	-	-	-
Gupta	DOPI	-	VAS	-	Visually	-
Grover	-	-	VAS	-	-	-
Mahesh	Pigmentation index	-	-	-	-	-
Nagati		DOPI, Hedin index	VAS	Score 0-3		Ti
Mahajan		DOPI				
Gholami	Hedin index/DOPI	Hedin index/DOPI	VAS	Scale 1-4	Healing index	
Alhabashneh	DOPI	-	VAS	Scale 1-4	Means and SD	Ti
Kaarthikiyan			VAS			
Suryavanshi	DOPI	DOPI	VAS		Healing index	
Sagar	Image analysis software	Image analysis software				
Gufran	DOPI					
Ipek			VAS			

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DOPI – Dummet oral pigmentation index; VAS: Visual Analogue Scale; SD – Standard deviation; GPI – Gingival pigmentation index

Table 3

Outcomes in included studies

Serial number	Author (follow-up months)	Outcomes	Preferred treatment (P-value)
		Recurrence of pigmentation procedure (%/mean±SD)	
1	Bakutra (6)	Scalpel (20%), diode laser ablation (50%)	Surgical stripping (≤0.05)
2	Narayankar (3)	Scalpel (20%), cryosurgery (8%)	Cryosurgery (not reported)
3	Suragimath (12)	Scalpel (25%), diode laser (0%)	Diode laser (not reported)
4	Gera (3)	Scalpel group (53%), diode laser (46%)	Both (not reported)
5	Basha (6)	Scalpel (80%), Nd-YAG laser (65%)	Both (0.294)
6	Ribeiro (6)	Scalpel (45.5%), Nd-YAG laser (45.5%)	Both (>0.05)
7	Hedge (6)	Scalpel (21.4%), Er-YAG laser (28.6%), CO2 laser (22.8%)	Both (>0.05)
8	Gupta (15)	Scalpel (46.7%), electro surgery (26.7%)	Both (not reported)
9	Grover (3)	Scalpel (35%), diode laser (20%)	Both (≤0.288)
10	Mahesh (3)	Scalpel (mean=1.3), radiosurgery (Mean=0.42)	Both (not reported)
11	Nagati (6)	Scalpel (mean±SD) (0.35±0.67), diode laser (0.5±0.827)	Both (≤0.72)
12	Mahajan (3, 6, 9)	Scalpel (mean±SD) (0.474±0.342), diode laser (0.251±0.287)Scalpel (mean±SD) (0.574±0.443), diode laser (0.389±0.465)Scalpel (mean±SD) (0.648±0.457), diode laser (0.451±0.450)	Laser (≤0.040) (3 months)Both (≤0.118) (6 months)Both (≤0.146) (9 months)
13	Sagar (2,3,6)	Scalpel (mean±SD) (117.69±19.19), diode laser (85.13±19.56)Scalpel (mean±SD) (119.74±21.79), diode laser (83.77±11.45)Scalpel (mean±SD) (109.80±20.88), diode laser (100.85±24.49)	Laser (≤0.001)Laser (≤0.001)Both (≤0.63)
14	Suryavanshi (3)	Scalpel (18.57%), electrocautery (19.66%), FGG (0%), laser (1.6%)	Both
15	Gholami (12)	Scalpel (mean±SD) (0.71±0.49), diode laser (0.66±0.49)	Both (≤0.071)
16	Parvez (3)	Scalpel=0%, cryosurgery=0% (1 month)Scalpel=20%, cryosurgery=60% (2 months)Scalpel=0%, cryosurgery=10%	Both (1 month)Scalpel (2

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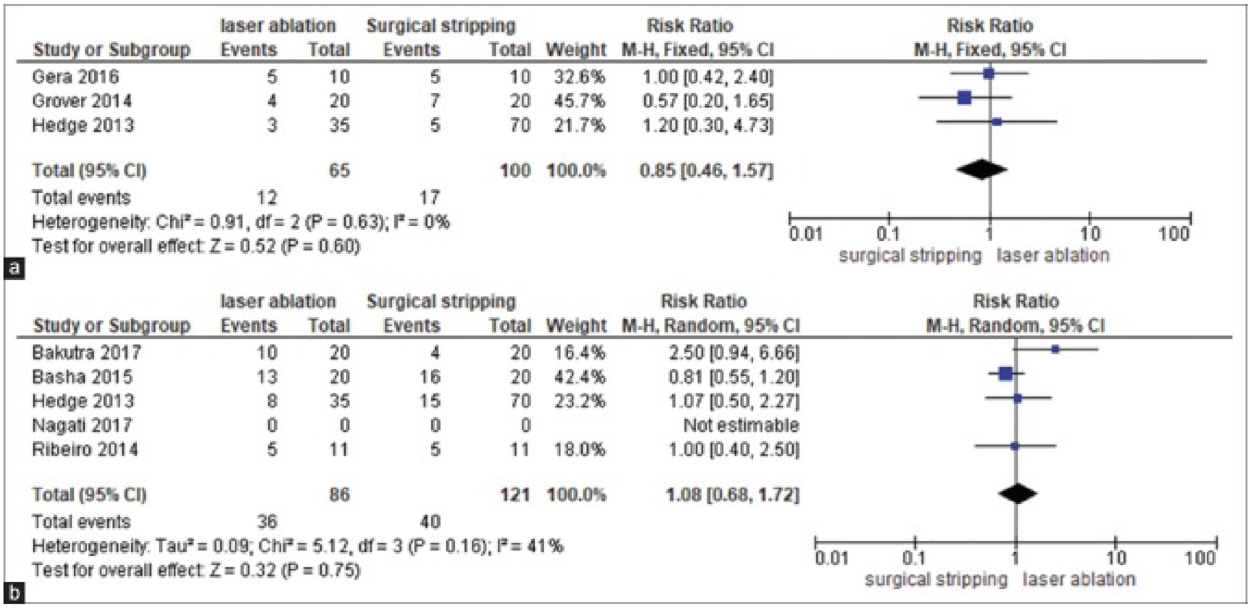
ND-YAG – Neodymium-doped yttrium aluminum garnet; Er-YAG – Erbium-doped yttrium aluminium garnet; SD – Standard deviation; FGG – Free gingival graft; *P* – *P*-value

Figure 2

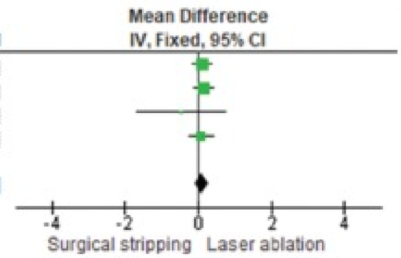


(a) Forest plot presenting risk ratio for recurrence of pigmentation between laser ablation and surgical stripping at 3 months; (b) Forest plot presenting risk ratio for recurrence of pigmentation between laser ablation and surgical stripping at 6 months

Figure 3

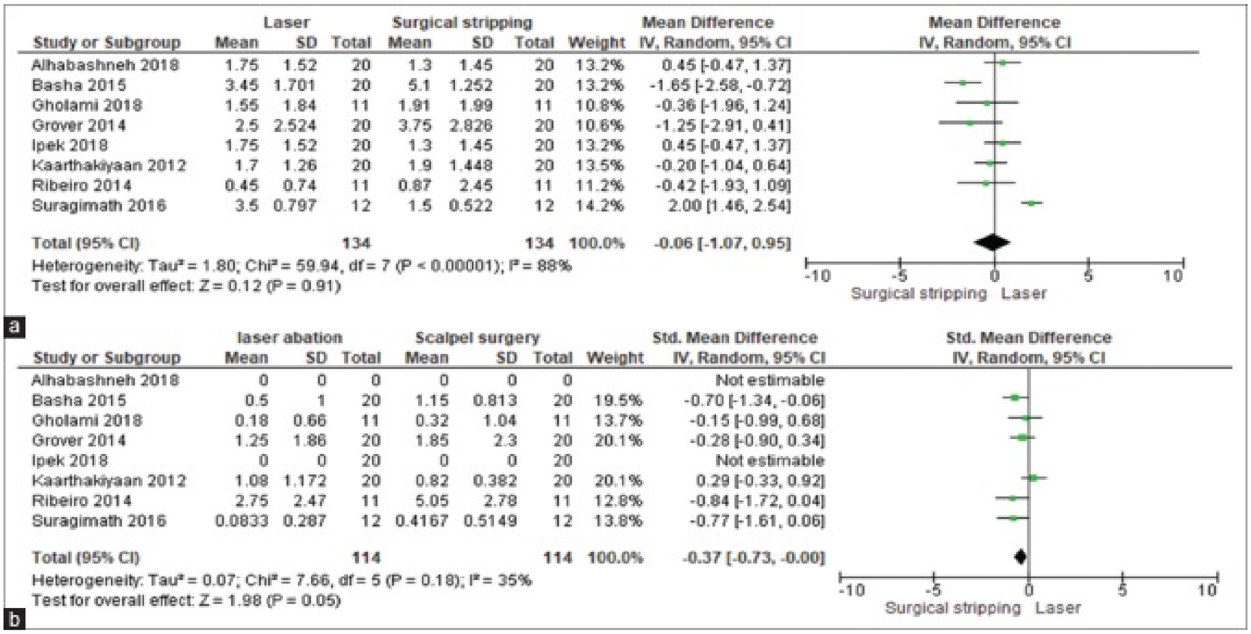
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Surgical stripping Mean	Surgical stripping SD	Surgical stripping Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Alhabashneh 2018	0.3	0.47	20	0.2	0.41	20	37.7%	0.10 [-0.17, 0.37]
Basha 2015	0.8	0.41	20	0.65	0.489	20	36.0%	0.15 [-0.13, 0.43]
Ribeiro 2014	8.6	1.9	11	9.07	0.82	11	1.9%	-0.47 [-1.69, 0.75]
Suragimath 2016	0.31	0.48	12	0.23	0.36	12	24.4%	0.08 [-0.26, 0.42]
Total (95% CI)			**63**			**63**	**100.0%**	**0.10 [-0.07, 0.27]**

Heterogeneity: $Chi^2 = 0.97$, $df = 3$ ($P = 0.81$); $I^2 = 0\%$
Test for overall effect: $Z = 1.20$ ($P = 0.23$)



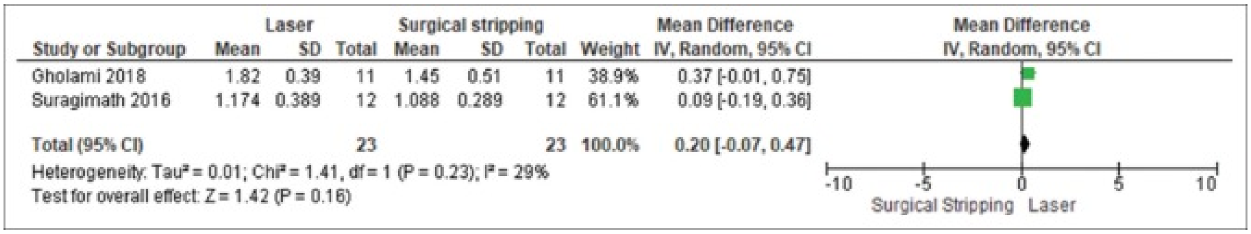
Forest plot presenting mean difference for depigmentation between laser ablation and surgical stripping

Figure 4



(a) Forest plot presenting mean difference for postoperative pain/discomfort as observed on 1st postoperative day between laser ablation and surgical stripping; (b) Forest plot presenting mean difference for postoperative pain/discomfort as observed on 7th postoperative day between laser ablation and surgical stripping

Figure 5

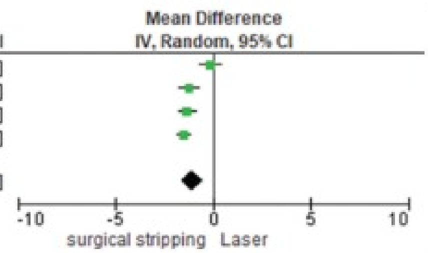


Forest plot presenting Mean difference for wound healing between laser ablation and surgical stripping at 1 week

Figure 6

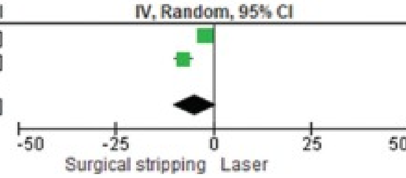
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Surgical stripping Mean	Surgical stripping SD	Surgical stripping Total	Weight	Mean Difference IV, Random, 95% CI
Basha 2015	1.65	0.745	20	1.8	1.005	20	23.5%	-0.15 [-0.70, 0.40]
Gholami 2018	1.68	0.71	11	2.91	0.61	11	23.4%	-1.23 [-1.78, -0.68]
Nagati 2017	0.7	0.65	20	2	0.79	20	25.5%	-1.30 [-1.75, -0.85]
Suragimath 2016	1.417	0.514	12	2.91	0.288	12	27.6%	-1.49 [-1.83, -1.16]
Total (95% CI)			**63**			**63**	**100.0%**	**-1.07 [-1.62, -0.52]**

Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 17.25$, df = 3 (P = 0.0006); $I^2 = 83\%$
Test for overall effect: Z = 3.79 (P = 0.0002)



Forest plot presenting mean difference for intraoperative bleeding during laser ablation and surgical stripping

Figure 7

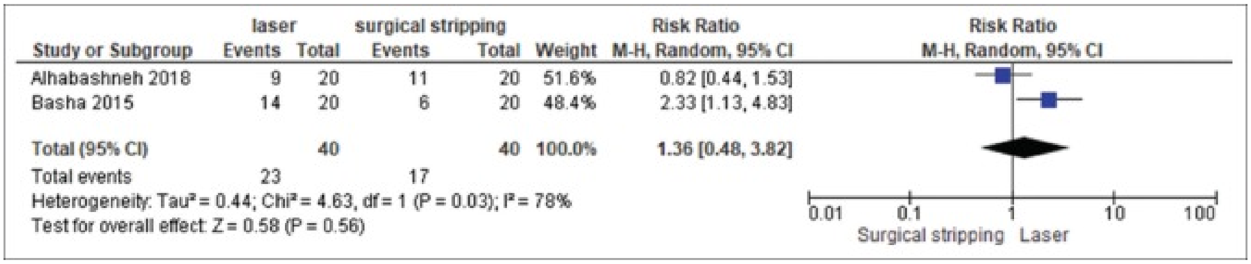


Study or Subgroup	Laser Mean	Laser SD	Laser Total	Surgical stripping Mean	Surgical stripping SD	Surgical stripping Total	Weight	Mean Difference IV, Random, 95% CI
Basha 2015	5.1	2.125	20	7.05	2.114	20	51.5%	-1.95 [-3.26, -0.64]
Ribeiro 2014	6.55	2.55	11	14.18	2.96	11	48.5%	-7.63 [-9.94, -5.32]
Total (95% CI)			**31**			**31**	**100.0%**	**-4.71 [-10.27, 0.86]**

Heterogeneity: Tau² = 15.21; Chi² = 17.56, df = 1 (P < 0.0001); I² = 94%
Test for overall effect: Z = 1.66 (P = 0.10)

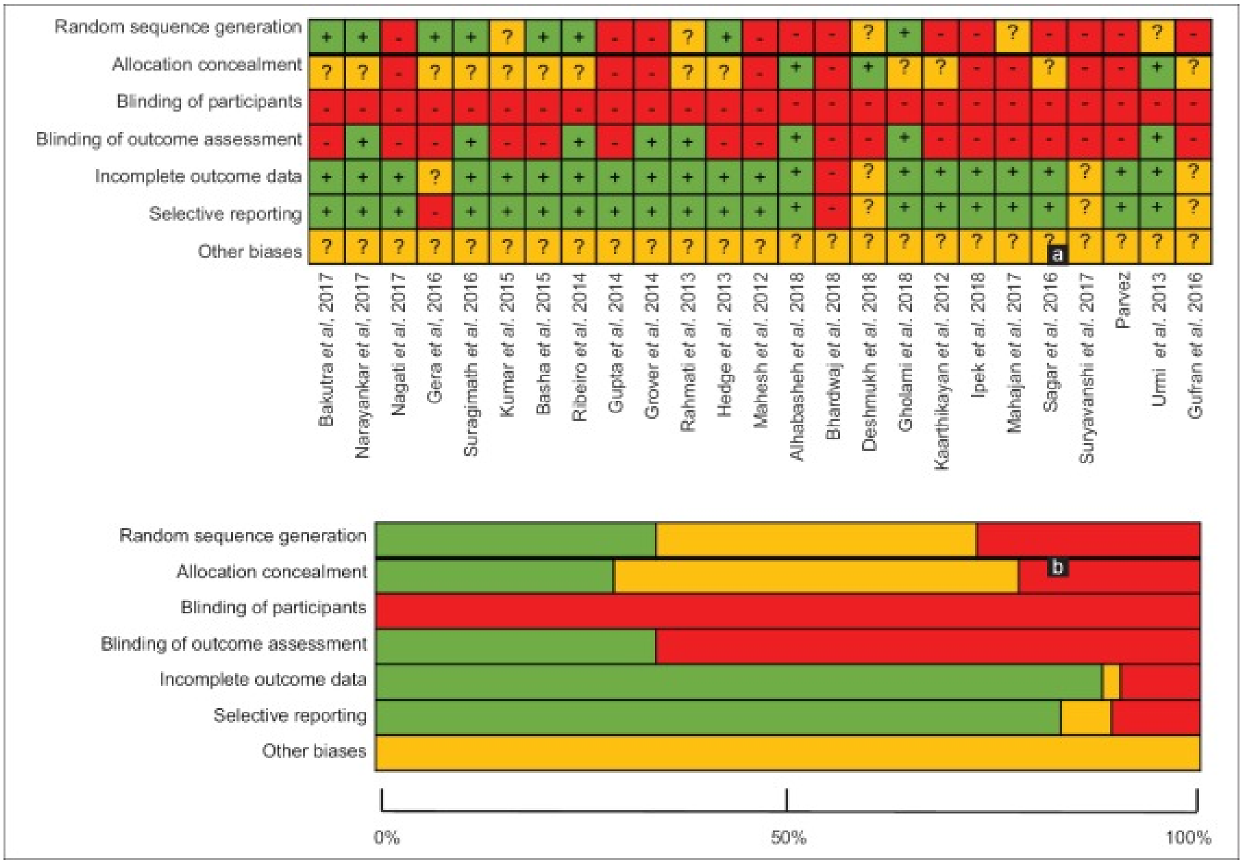
Forest plot presenting mean difference for procedure time between laser ablation and surgical stripping

Figure 8



Forest plot presenting risk ratio for patient preference for laser ablation and surgical stripping

Figure 9



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(a) Risk of bias of individual studies; (b) Risk of bias of overall studies