



# Hyaluronidase injection vs direct surgery in surgical rhinoplasty patients treated with non-surgical nasal reshaping with hyaluronic acid filler: a systematic review

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## Abstract

**Background** Non-surgical nasal reshaping with hyaluronic acid filler is a well-established procedure performed in order to ameliorate nasal appearance and considered a valid alternative to surgical rhinoplasty in selected patients. The aim of this systematic review is to evaluate, in patients looking for surgical rhinoplasty who already received nSNR with HA, if hyaluronidase injection before surgery is to prefer instead of direct surgery in order to reduce/avoid intra-operative troubles in performing a rhinoplasty.

**Methods** The literature search was carried out on electronic PubMed and Cochrane Library databases identifying 567 articles up to May 19th, 2021. Number of patients, outcomes and complications were extracted.

**Results** Three retrospective articles were eligible for inclusion in the review. Thirteen patients were operated on for rhinoplasty who previously received nSNR with HA. Six received hyaluronidase injections before surgery and 7 underwent directly to surgery. Among the 7 who went straight to surgery, in 5 of them, 6 months was the specified time lapse between last HA injection and surgery. Among the ones receiving hyaluronidase injection before surgery, the time lapse reported was 6 months for 1 patient, 3 months for 2 patients, 2 months for 1 patient and 7 days for 1 patient. Post-operative complications were not recorded.

**Conclusions** Either direct surgical approach or hyaluronidase injection first seems to be a viable option with the total absence of post-operative complications. When direct surgery is preferred, it could be demanding and customized informed consent should be released to the patients prior to surgery.

Level of evidence: Not gradable.

**Keywords** Hyaluronidase · nSNR · Nasal reshaping · Hyaluronic acid · Rhinoplasty

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## Introduction

Nowadays, non-surgical nasal reshaping (nSNR) with hyaluronic acid (HA) filler is a well-established procedure performed in order to ameliorate nasal appearance, although not all nasal deformities, such as septal deviations or bulbous tip, can be faced with this approach [1–10]. nSNR is one of the fastest growing aesthetic procedures in last 10 years, and the published medical literature in this field is an evidence of it [1–16]. nSNR, also known as rhinofiller, is a medical procedure based on the injections of filler in several nasal areas in order to project them: the projection achieved is able to camouflage unpleasant nasal deformities. E.g., in order to reduce nasal hump perception is possible to inject over the radix, projecting the overlying soft tissues and reducing the fronto-nasal angle depth [16]; in case of nasal tip drooping, it is possible to inject HA over the anterior nasal spine and/or between medial crura, this maneuvers are able, performed alone or in conjunction, to project the tip of the nose and solve an unpleasant nasal drooping [17].

During the time, HA filler injections have been also proposed as a useful tool in nasal post-surgical deformities in order to avoid secondary surgery [18]; patients have shown to be more prone to non-surgical corrections after a previous rhinoplasty instead of surgery [19].

HA fillers were firstly introduced in the European market in 1998, later on, in 2002 also in the Northern American one. HA fillers were introduced in order to treat facial lines and wrinkles by dermal injections, and a mainstay of HA fillers was the temporary correction due to the self-resorption of HA once injected [20]. During the time, HA fillers have also been used for several “off-label” procedures and have been injected in all the facial layers, from the periosteum up to the dermis [20–23]. HA fillers are usually resorbed within 4 to 6 months if injected into the dermis due to the presence of hyaluronidase [24], an hydrolytic enzyme able to catabolize HA. Nonetheless, if HA injections are performed in deeper facial layers, such as over the periosteum, the results are long lasting, persisting for over 3 years [20, 21].

The first medical reports regarding nSNR with HA were published around 2006 [4], although this procedure has evolved over time [5–11]: HA drops injected for nasal reshaping can be considered and used as “cartilage grafts” that are routinely applied during surgical rhinoplasties [5].

However, as soon as nSNR was described, vascular complications became the physicians’ nightmare when performing this procedure [25–28]. A better knowledge of nasal vascular impairment management with the use of hyaluronidase [29–33], a better knowledge regarding “where” to inject, and the use of the filler with the right rheology make this procedure considered safe with a low rate of severe complications [2, 5, 11].

Rhinofiller is considered a valid alternative to surgical rhinoplasty in selected patients because this procedure is safe, effective and also long lasting [2]; for all these reasons, an increasing number of patients are seeking, and have sought, nSNR with HA [3, 8].

On the other hand, also surgical rhinoplasty is one of the most requested and performed facial aesthetic procedures and is not so unusual to have a patient looking for surgical rhinoplasty after having a nSNR [34, 35]. The long-lasting result secondary to HA injection over the nose leads to several questions: first of all, “how should a surgeon approach a nose previously injected with HA?”

Guidelines about this topic are lacking.

## Objective

The aim of the present systematic review is to evaluate, in patients looking for surgical rhinoplasty who already received nSNR with HA, if hyaluronidase injection before surgery is to prefer instead of direct surgery in order to reduce/avoid intra-operative troubles in performing a rhinoplasty.

## Materials and methods

### Eligibility criteria

The methods and the inclusion criteria of this work were specified and documented in a protocol, according to quality standards described in the PRISMA 2020 checklist [36].

The following focus question was developed according to the population, intervention, comparison and outcome (PICO) study design. In patients looking for surgical rhinoplasty, who already received nSNR with HA (P), is hyaluronidase injection before surgery (I) to be preferred to direct surgery (C) in order to reduce/avoid intra-operative troubles in performing a rhinoplasty (O)? The studies eligible for review were English-written articles describing if hyaluronidase injections were suggested or not before approaching a rhinoplasty in a previously HA injected nose. The study design included were techniques studies, retrospective studies, prospective studies.

Articles were excluded when not reporting data regarding rhinoplasty in previously injected noses with HA. Editorials, letters and commentaries were excluded. Reference lists of all articles were examined to identify other potentially pertinent studies.

### Information sources

The research was carried out on electronic PubMed and Cochrane Library databases identifying articles from May 1998 to May 2021. The search was conducted up to May

19th, 2021. Article language was limited to English using the provided filters.

### Search strategy

The keywords were used and combined with Boolean operators, adapted for every database, both as text words and Medical Search Headings (MeSH terms) as follows: hyaluronidase AND nose; hyaluronidase AND rhinoplasty; hyaluronidase AND surgical rhinoplasty; hyaluronidase AND aesthetics; hyaluronidase AND clinical application; filler AND surgical rhinoplasty; hyaluronic acid AND surgical rhinoplasty; (((hyaluronic acid) AND (rhinoplasty)) NOT (nonsurgical)) NOT (non-surgical).

### Selection and data collection process

Two reviewers (R.F., G.L.G.) performed eligibility assessment, full-text inclusion and data extraction independently. Disagreements between reviewers were resolved by consensus. When consensus was not reached, a senior member mediated (R.R.). A standard chart form of the obtained data was prepared to facilitate comparison among the articles.

### Data items

The following data from each study were extracted: author, date, study design, number of patients, outcomes and complications.

### Study risk of bias assessment

Two independent reviewers (G.L.G., R.F.) performed quality assessments of the included studies; in cases of discrepancies in the results, they consulted a third senior reviewer (R.R.). ROBINS-I tool was used to assess non-randomized studies. Five levels (low, moderate, serious, critical or no information) were used to present the risk of bias [37]. The robvis visualization tool web app was used to create “traffic light” plots of the domain level judgements for each individual result and weighted bar plots of the distribution of risk-of-bias judgements within each bias [38].

### Effect measures

Intra-operative issues, post-operative results and any other variables were listed and expressed as integer numbers and percentage.

## Results

### Study selection

The PubMed and Cochrane Library database search identified 567 articles: 167 were duplicate articles, while 400 studies were screened for title, abstract and language. Eight full-text articles were finally selected for further evaluation. Of the 8 papers, 5 were excluded: 2 letters, 1 French language article, 2 did not discuss about rhinoplasty in patients already injected with HA. The selection process identified 3 retrospective articles as eligible for inclusion in the review (Fig. 1).

### Study characteristics

The review process identified a total of 3 studies: Heden, Bektas et al., and Ramos et al. [10, 19, 34]. Thirteen patients were evaluated, 6 received hyaluronidase injections before surgery and 5 underwent surgery directly. In all studies, intra-operative issues, post-operative complications and result evaluation were assessed (Table 1).

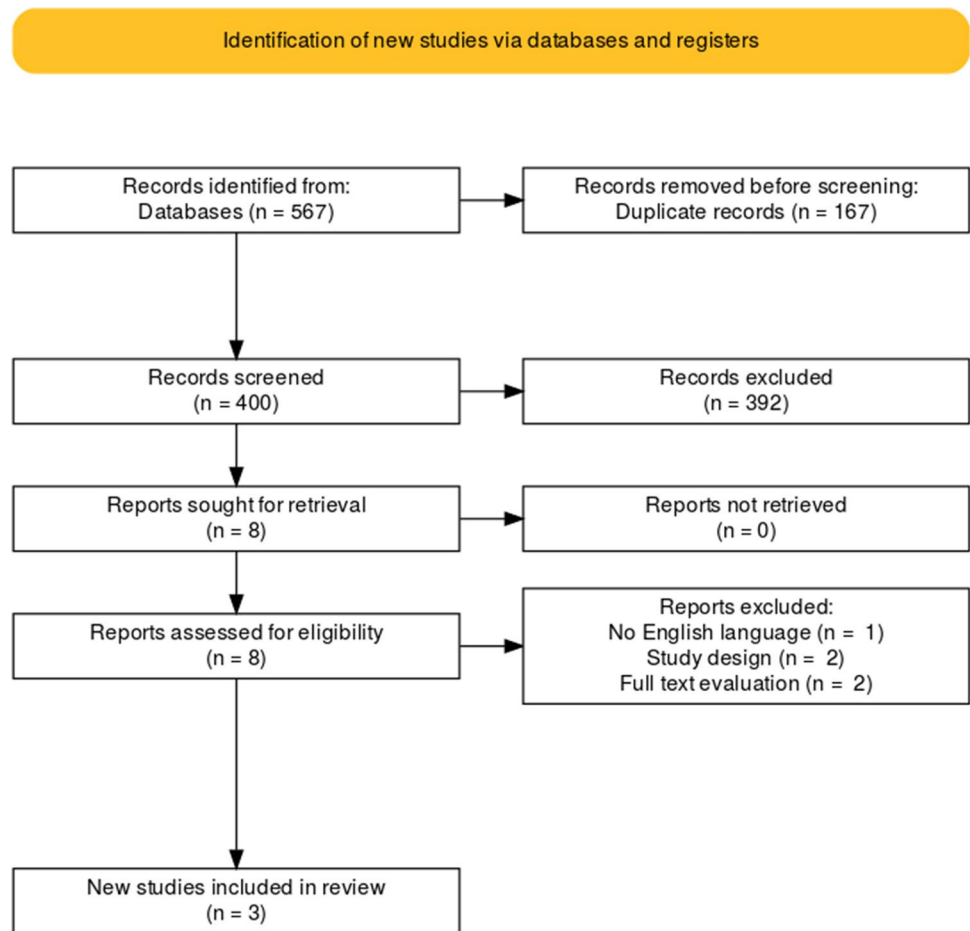
### Risk of bias in studies

The analysis of the paper quality assessment is presented in Figs. 2 and 3.

### Results of individual studies

In 2016, Heden retrospectively reviewed his clinical experience with HA gel for nasal reshaping from 1997 to 2012. More than 250 patients were treated, although the article focused on HA injections performed between 1998 and 2012 with those executed during 1998, 2005 and 2012 selected for detailed review. A total of 75 patients were finally considered: fifty-five patients (73%) received HA injection instead of rhinoplasty; twenty (27%) received HA injection as a secondary correction after rhinoplasty; five patients (7%) underwent rhinoplasty as a secondary procedure to HA fillers. Among the 5 patients who underwent rhinoplasty as a secondary procedure to HA fillers, the time lapse between filler procedures and secondary rhinoplasty was > 6 months. The reasons for secondary rhinoplasty include that duration of the filler was too short (2 patients), a more drastic effect was sought (1 patient) and the HA injection was a door opener for rhinoplasty (2 patients) [19].

In 2020, Bektas and colleagues presented a paper about nasal filling in plastic surgery practice under three headings: primary nasal filling, nasal filling for post-rhinoplasty defects and rhinoplasty after hyaluronidase injection in dissatisfied filling patients. Nasal filling patients from July 2015 to March 2020 were divided and analyzed in three groups:

**Fig. 1** Flow diagram of literature search and study selection

(a) primary nasal filling was provided to 62 patients, (b) nasal filling for post-rhinoplasty defect was provided to 18 patients and (c) rhinoplasty after hyaluronidase injection was performed in five patients who are not satisfied with results. The five patients who had primary nasal filling with HA but not satisfied with results have undergone rhinoplasty. In all the cases, the filler was dissolved with hyaluronidase before surgery. The operation time was decided following consultation with the patient. Authors stated “*after hyaluronidase treatment, the patient should wait for at least a week, but it would be better to wait longer*”. One patient underwent rhinoplasty after 6 months from hyaluronidase treatment, two patients underwent rhinoplasty after 3 months from hyaluronidase treatment, one patient underwent rhinoplasty after 2 months from hyaluronidase treatment and one patient underwent rhinoplasty after 7 days from hyaluronidase treatment. Intra-operative course was uneventful. No filling residue was observed in the supraperichondrial plane. No scarring was observed in the areas of previous injections. Dorsal skin flaps were normal in color and capillary return after the operation. No complication was observed. Bruising and swelling were seen much the same when compared to other rhinoplasty cases. After surgery, no patients needed

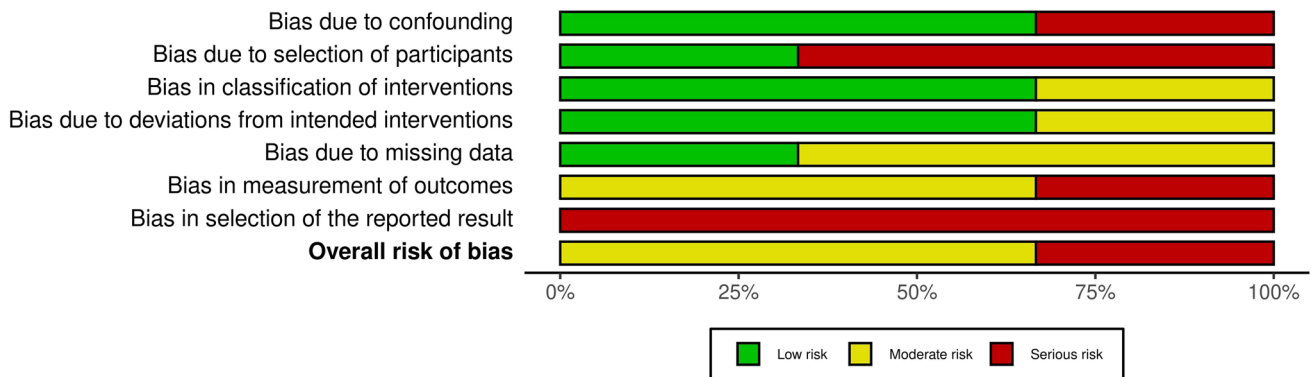
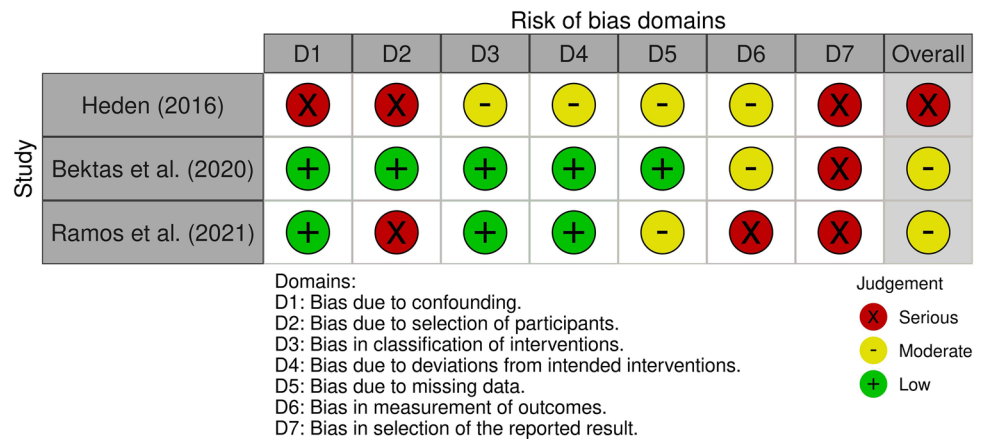
revision operations. Physical examination and assessment of the postoperative photographs showed that aesthetically pleasing results have been achieved. No functional problems were observed. No any other complications were recorded. The postoperative results were considered satisfactory [10].

In 2021, Ramos and colleagues released a specific paper regarding the management of patients seeking surgical rhinoplasty with previous nasal injections of hyaluronic acid. In this article, the authors suggest to inject hyaluronidase only when HA was injected into nasal soft tissue and a surgical removal of HA, performing concomitant rhinoplasty, when the filler was injected over the periosteum (in the same layer of musical dissection); 3 patients were evaluated. In the first case, hyaluronidase was injected before surgery, 1 week after change was noticeable with removal of filler and no edema. In 2 more cases, rhinoplasty was performed with no prior application of hyaluronidase. Among them, in one case, HA gel was found and removed during the first incision of the rhinoplasty; in the second one, at the radix, the HA was removed through an 18G needle with a 5-mL syringe to produce a fan tunnel while an aspiration process was in progress. Once the HA was identified, it was manually removed through the tunnel previously made. After that,

**Table 1** Synthesis of results

Author (year)	Treated patients	Reasons for surgery after nSNR	Hyaluronidase injections before surgery	Direct surgery	Time lapse between HA injection or hyaluronidase injection and surgery	Intra-operative issues	Post-operative complications	Outcome evaluation
Heden P. (2016)	5	<ul style="list-style-type: none"> <li>• Duration of the filler was too short (2 patients)</li> <li>• A more drastic effect was sought (1 patient)</li> <li>• HA injection was a door opener for rhinoplasty (2 patients)</li> </ul>	0	5	At least 6 months before last HA injection	Not reported	None	Self-assessment scale
Bektas G, et al. (2020)	5	Not satisfied with the result (5 patients)	5	0	<ul style="list-style-type: none"> <li>• 1 patient underwent rhinoplasty after 6 months from hyaluronidase treatment</li> <li>• 2 patients underwent rhinoplasty after 3 months from hyaluronidase treatment</li> <li>• 1 patient underwent rhinoplasty after 2 months from hyaluronidase treatment</li> <li>• 1 patient underwent rhinoplasty after 7 days from hyaluronidase treatment</li> </ul>	None	None	Physical examination and postoperative photographic evaluation
Ramos HHA, et al. (2021)	3	<ul style="list-style-type: none"> <li>• Not satisfied (1 patient)</li> <li>• Not reported (2 patients)</li> </ul>	1	2	Not reported	In one case were direct surgery was performed at the radix, the HA was removed through an 18G needle with a 5 mL syringe to produce a fan tunnel while an aspiration process was in progress	None	Photographic evaluation

**Fig. 2** ROBINS-I traffic light plot bias assessment



**Fig. 3** ROBINS-I weighted summary plot bias assessment

it was identified that the gel masked anatomic abnormalities, such as a low radix and boxy tip [34].

**Results of synthesis**

Data extraction from the 3 articles evaluated allowed us to list a total of 13 patients operated on for rhinoplasty who previously received nSNR with HA. Six received hyaluronidase injections before surgery and 7 underwent directly to surgery. Among the 7 who went straight to surgery, just in 5 of them, the time lapse between last HA injection and surgery was approximately specified, at least 6 months. Among the 6 receiving hyaluronidase injection before surgery, the time lapse between hyaluronidase injection and surgery was specified only in 5 of them: reports shows 6 months for 1 patient, 3 months for 2 patients, 2 months for 1 patients and 7 days for 1 patient.

Among the 13 participants, post-operative complications were not recorded. About intra-operative issues, just in one patient who underwent directly to surgery, it was reported that at the radix, the HA was removed through an 18G needle with a 5-mL syringe to produce a fan tunnel while

an aspiration process was in progress. In 2 more patients directly operated on, it was specified that HA was detected during dissection and easily removed. In all the cases previously injected with hyaluronidase, HA or scarring was never detected during surgery. The evaluation of the results was performed with a self-assessment scale in one research, and with photographic evaluation in the other 2 (Table 1).

**Discussion**

The nose is a keystone in facial aesthetic and up to the end of the twentieth century, the surgical approach was the only way to reshape the nose. Since the introduction of HA fillers, pioneering approaches have been proposed, and several reports of “alternative” uses of HA fillers, such as nose reshaping, buttocks reshaping, genitourinary syndrome treatment and labia majora restoration, have been published [5, 21, 22, 39–42].

Nowadays, nSNR is considered a valuable alternative to aesthetic surgical nasal reshaping in selected cases; no functional improvement can be achieved although some authors advocate the opposite [2, 19]. Nasal reshaping with HA filler

seems to be preferred instead of surgery due to the absence of the “surgical fear”, days off after surgery and for economic reasons: nSNR is in fact cheaper compared to surgical rhinoplasty [12, 19]. Moreover, non-surgical corrections of nasal post-surgical deformities are another indication that let this procedure obtain approval by both patients and surgeons [19].

Although the nose is considered a dangerous zone to be injected, due to the high-density vascular network, many researches have described “operative safe ways” in order to avoid vascular complications [5, 27]. Moreover, researchers suggested the importance of using the “right filler to use” in order to avoid vascular compressions thus performing safer nasal injections [5, 43].

Impending necrosis following vascular impairment can be secondary to intravascular injections (embolization) or extravascular compression [24, 29, 32]. To avoid embolization, perpendicular injection, releasing HA above nasal bones and/or cartilage has been proposed. Nevertheless, even with deep injections, vascular impairment can be induced due to *ab-extrinsico* filler compression [5]. For the aforementioned reasons, the choice of a HA filler with a not too high  $G'$  should be preferred, although the lower the  $G'$  is, the lower is the projection achieved [43].

Finally yet importantly, every time a nose is approached with HA filler, a careful evaluation of the skin refill should be tested at the end of the procedure and in case of supposed impending necrosis, hyaluronidase injection is mandatory [19, 31, 33].

During last 10 years, the number of papers speaking about nSNR has raised up, highlighting the long-lasting results after the injections [20, 35]. In a recent letter released by Rauso et al., the presence of HA was detected during a surgical rhinoplasty performed over 24 months after the injections [44]; moreover, several reports shows that only in a few percentage of patients the clinical result is vanished within 12 months from the injections [5, 6, 10, 19, 20]. At the same time, surgical rhinoplasty is one of the five most requested procedure worldwide; therefore, it is easy to understand why rhinoplasty surgeons are facing an increasing number of patients looking for surgical rhinoplasty after receiving nSNR [35, 45].

Theoretically, there are three approaches [34]:

- 1 wait, even years, until the filler is clinically resorbed;
- 2 remove or “try to remove” all the filler during surgery;
- 3 inject hyaluronidase and then perform surgery.

In the first case, wait, even years, until the filler is clinically resorbed could be questionable due to unpredictable long-lasting results achieved in injected noses. While some published researches describe long-lasting results of this technique up to 3 years, Heiden reported how patients look

for surgical rhinoplasty after nSNR because the duration of the filler was considered as too short.

Pre-injective pictures, self-provided by patient, could be useful to have an idea of the baseline appearance of the nose, although this is not an objective evaluation method, especially in the last few years due to photo editing filters often applied through social networks. Bektas et al. highlighted the role of ultrasound (US) examination before having surgical rhinoplasty in order to be sure of total HA resorption. HA filler is a resorbable filler, although when injected in nasal area seems to give unpredictable long-lasting results; because of this and the aforementioned reasons, it is not possible to affirm when HA will be totally resorbed before performing a surgical rhinoplasty: clinical examination and US examination are key points during pre-surgical clinical examination.

In the second case, remove or “try to remove” all the filler during surgery is another option to choose. Surgical removal of previously injected HA has been suggested when the layer of HA injection is supposed to be at the same layer where the surgical dissection will be performed, usually the supra-perichondrial one. In these cases, the use of US examination has been advocated as a useful tool in order to detect the location of the HA too. However, if a rhinoplasty surgeon decides to approach a previously injected nose directly with surgery, it is of pivotal importance to clearly state to the patients that is not possible to assure that all HA could be removed during rhinoplasty, and that the final result could change during the years if HA is not totally removed.

The main questionable aspect to this approach is related to medico-legal sphere: what happens if HA is not totally removed during surgery? What happens if during the post-operative period the results worsen due to HA resorption?

A customized consent form should be released to the patient, clearly explaining all the surgical issues related to the presence of HA into the area to be operated on, in order to avoid litigations.

The third approach is represented by the injection of hyaluronidase in order to dissolve previously injected HA before having surgery. Hyaluronidase injection is a worldwide renown procedure; once injected, hyaluronidase is able to dissolve HA filler and it may be really helpful in cases of side effects, such as foreign body reaction, unpleasant results or in order to avoid vascular problems secondary to occlusion or compression of the vessels [29–31, 33, 46].

Although hyaluronidase injection is safe, it must be underlined that not all HA fillers respond similarly to this drug: the effectiveness of HA resorption following hyaluronidase injection is strictly related to the rheology of the filler itself [47]. Therefore, during the first consultation, the physician should retrieve as much information as possible to identify the specifics of the previously injected HA filler, since more than a session of hyaluronidase injections

could be necessary to achieve complete resorption. One more question can be raised regarding the amount of waiting time. Bektas empirically stated: “*after hyaluronidase treatment, the patient should wait for at least a week, but it would be better to wait longer*”. Theoretically, the hyaluronidase is a hydrolytic inflammatory enzyme and sudden surgical approach following hyal injection could be potentially associated with intra- and post-operative issues due to tissue inflammation. Even so, intra-operative difficulties or post-operative scarring were not reported in the eligible researches.

Among the 3 options to face a rhinoplasty in previously injected noses, no consensus are reached.

In the present systematic review, we identified only 3 papers that analyzed the matter in hand [10, 19, 34]. Direct surgical approach or hyaluronidase injections before surgery have been both advocated. Post-operative complications were never recorded in both groups. Intra-operative issues were described just in one case where direct surgery was performed, and in order to remove the previously HA from the radix “*an 18G needle with a 5 mL syringe was used to produce a fan tunnel while an aspiration process was in progress, then manually removal through the tunnel previously made was performed*” [10]. In 2 more patients, directly operated on, HA was easily detected and removed during nasal dissection. In all the cases where hyaluronidase was injected prior to surgery, neither HA nor scarring was detected during surgery [10]. Since surgical rhinoplasty is one of the most performed facial aesthetic procedures, only in 2020 ASAPS stated that 55,436 procedures were performed in USA, and at the same time non-surgical rhinoplasty is among the fastest-growing aesthetic procedures worldwide; the collected sample of our work may not be representative [35, 39].

## Conclusions

The approach of patients looking for surgical rhinoplasty who already received nSNR is a topic without scientific evidence. Either direct surgical approach or hyaluronidase injection first seems to be viable options with the total absence of post-operative complications. When direct surgery is preferred, it could be demanding and customized informed consent should be released to the patients prior to surgery. Larger case–control studies with long follow-ups are necessary to understand if in patient seeking surgical rhinoplasty who already received nSNR, the injection of hyaluronidase prior to surgery is indeed mandatory, recommended or not.

**Author contribution** Conceptualization, R.R. and P.B.; methodology, N.Z. and M.P.; data curation, P.C. and D.B.; investigation, R.F.; validation, V.F.; writing—original draft preparation, R.R.; writing—review and editing, G.L.G.; project administration, G.F.N. All authors have read and agreed to the final version of the manuscript.

**Data availability** Data are available upon request.

## Declarations

**Ethics approval** This article is a review. No ethical approval is required.

**Consent to participate** Not applicable.

**Consent for publication** Not applicable.

**Competing interests** Raffaele Rauso, Romolo Fragola, Giovanni Francesco Nicoletti, Nicola Zerbinati, Pierfrancesco Cirillo, Dario Bertossi, Valerio Finocchi, Michele Pascali, Pierfrancesco Bove and Giorgio Lo Giudice declare no competing interests.

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