Is nasal closure an effective treatment for severe refractory epistaxis in HHT? A scoping review and narrative synthesis

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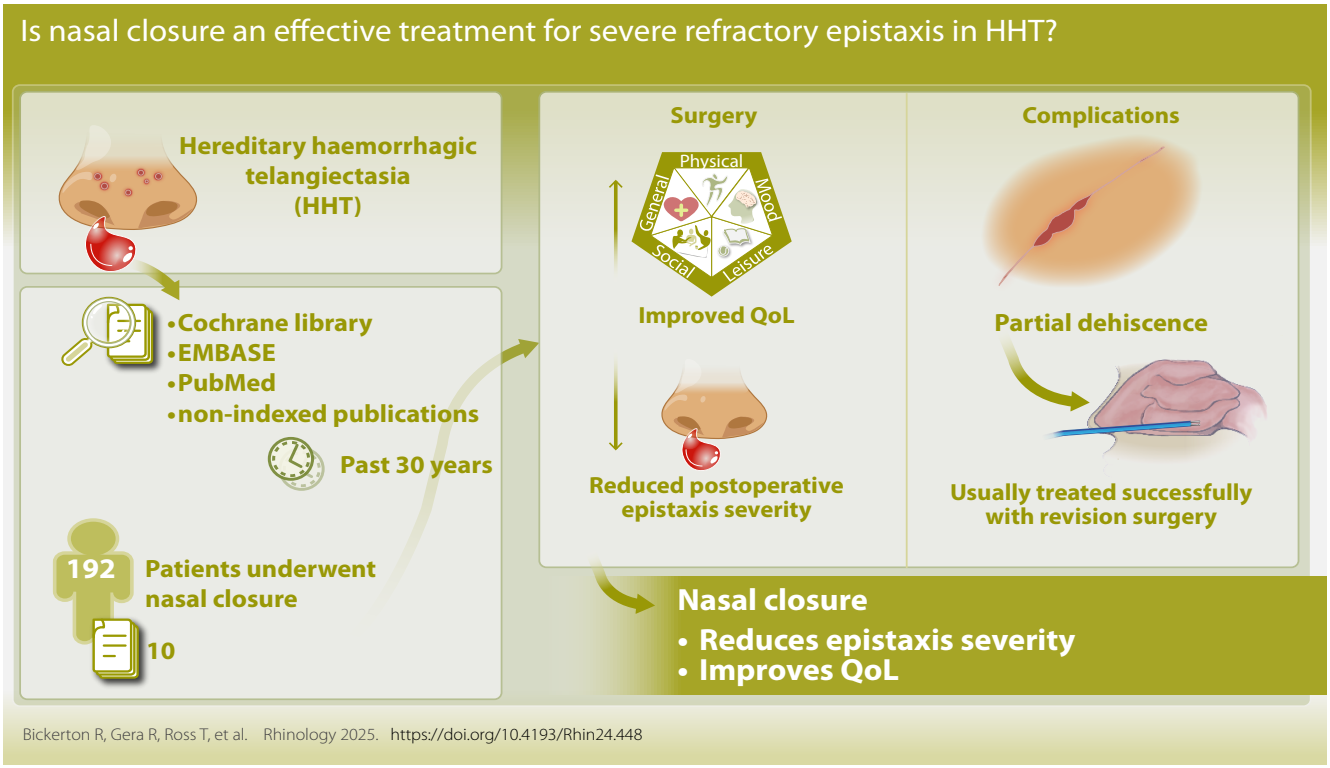

Abstract

Introduction: Hereditary haemorrhagic telangiectasia (HHT) is an uncommon genetic disorder characterised by recurrent, severe epistaxis which poses significant management challenges. Nasal closure has emerged as a treatment for refractory cases, however there is limited research on its outcomes. We aim to consolidate existing evidence to assess its efficacy and safety.

Methods: We conducted a systematic search of the Cochrane library, EMBASE, PubMed and non-indexed publications from the past 30 years. Two independent reviewers extracted data and assessed bias from included studies. Findings were summarised via narrative synthesis due to heterogeneity of included studies.

Results: 192 patients from ten studies underwent nasal closure. Frequently used outcome measures were validated epistaxis severity scores, Glasgow Benefit Inventory and haemoglobin trends. Surgery improved quality of life and reduced epistaxis severity post-operatively. Partial dehiscence is a frequently reported complication which is usually successfully treated with revision surgery.

Conclusions: Nasal closure reduces epistaxis severity, improving quality of life in patients with severe, refractory HHT-related epistaxis, providing a valuable treatment option for the most challenging cases. The strength of our conclusions is limited by the heterogeneity of outcome measures. To our knowledge, this is the largest pooled database of patients who have undergone nasal closure.

Key words: epistaxis, hereditary haemorrhagic telangiectasia, HHT, nasal closure, systematic review

Introduction

Hereditary haemorrhagic telangiectasia (HHT) is a rare inherited disorder characterised by the formation of arterio-venous malformations in the skin, mucous membranes and visceral organs, occurring in around 1 in 6000 Europeans [1]. Key diagnostic features, as defined by the Curacao diagnostic criteria (Figure 1), include the presence of mucocutaneous telangiectasia, visceral arterio-venous malformation, a history of recurrent epistaxis, and a positive family history (first degree relative) [2].

Genetic testing confirms the diagnosis and identifies its genetic subtype, typically involving mutations in the endoglin (ENG) or activin receptor-like kinase 1 (ACVRL1) genes [3]. This has relevance in predicting phenotypical symptoms, such as the distribution of arteriovenous malformations [4]. Genetic counselling is an important factor in diagnosis and management.

Carriers of these mutations, inherited in an autosomal dominant manner, can develop arteriovenous malformations in the gastrointestinal tract, lungs and brain, alongside widespread mucocutaneous telangiectasia in the nasal and oral cavities. Patients are treated by a multidisciplinary team including but not limited to haematologists, rhinologists, respiratory physicians, gastroenterologists [1]. However, the most debilitating symptom for many patients is recurrent spontaneous epistaxis, affecting over 90% of HHT patients [5] and significantly impacting their quality of life [6].

Presence of telangiectasia in the nasal mucosa can result in recurrent severe epistaxis. These abnormal blood vessels are thin-walled and lack contractile elements due to the lack of elastin, making the epistaxis found in HHT characteristically difficult to treat [7]. Management is multimodal, involving conservative, medical and surgical treatments frequently used in tandem.

An international standard for best evidence-based management has been established by VASCERN, the European Reference Network on Rare Multisystemic Vascular Diseases [1].

Patients are educated on basic first aid for epistaxis and provided with means to control bleeding. Rotating moisturising nasal creams (Naseptin®, Bactroban®, Fusidin®) are used to moisten nasal mucosa and reduce its friability [8]. Topical and oral tranexamic acid can also be used to control bleeding [9,10]. Absorbable packs such as Kaltostat® or NasoPore® may also prove useful for patients to self-administer [11]. Embolisation is used primarily in emergencies for major bleeds. Topical polidocanol sclerotherapy has also been shown to be effective in a large European case series [12].

Bevacizumab, an anti-VEGF monoclonal antibody which prevents the formation of telangiectasia, has shown great promise in early studies with topical and systemic use [13]. However, recent reviews have highlighted a relatively short duration of effect [14]; furthermore, its use is contraindicated in patients with arteriopathy, risk factors for or recent thromboembolic events, and severe pulmonary hypertension, which are comorbidities frequently seen in HHT patients [15,16]. Thalidomide is another systemic anti-angiogenic agent which is used in a very small proportion of HHT patients [1] due to its potential for adverse events, in particular peripheral neuropathy [16].

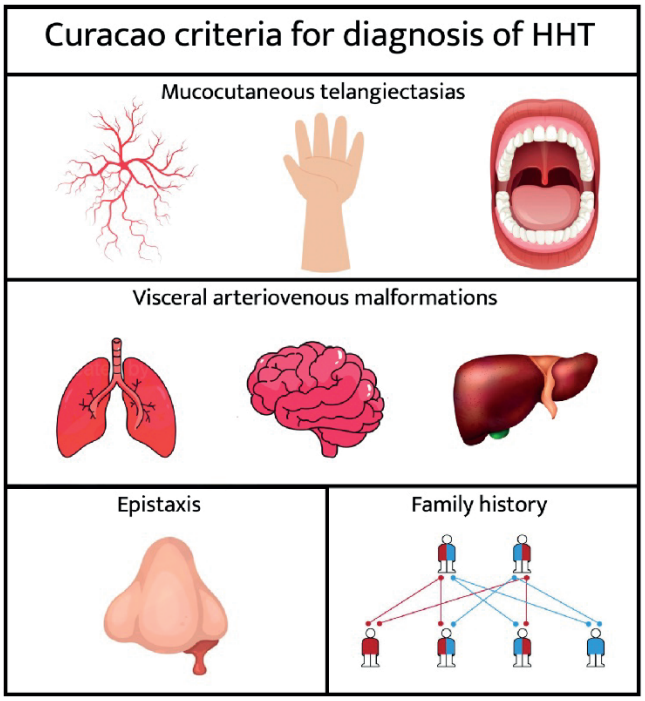

Figure 1. Curacao criteria for diagnosis of HHT.

Surgical interventions are fundamental in the management of HHT-related epistaxis, and are indicated where topical, local non-invasive management is insufficient in control of symptoms [1]. Ablation of telangiectasiae using electrocautery, coblation, KTP laser or argon photocoagulation is frequently used [17], however over-treatment can risk septal perforation. Nasal septodermoplasty, which involves the raising of a split thickness skin graft to cover the nasal mucosa, is another option available to the rhinologist where laser treatments should fail [18].

For the most severe, refractory cases, closure of the nasal airway is the final treatment option. Originally pioneered by Austen Young for atrophic rhinitis and colloquially termed the 'Young's procedure' [19], this involves closure of the nasal vestibules using mucocutaneous flaps. It was initially described using two mucocutaneous flaps. Closing the nasal airway eliminates the drying effect of constant airflow, keeping mucosa moist and less friable

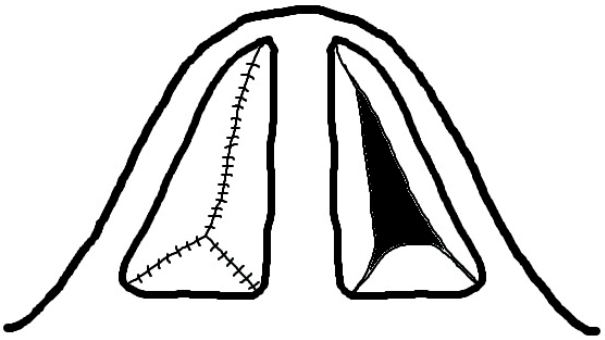

Figure 2. Modified nasal closure using the three-flap technique.

[20]. In the late 1990s, Lund and Howard modified the original procedure to a three-flap procedure, now known as the modified Young's procedure, or modified nasal closure (Figure 2) [21].

The evidence for nasal closure in severe, refractory HHT-related epistaxis is limited to a handful of case series given the rarity of HHT as a disease entity, all of which predominantly report positive outcomes. Consequently, no established criteria for surgery have been suggested in the literature to date.

Objective, aims, question

Our objective is to conduct a scoping review of all available evidence evaluating the efficacy of nasal closure for patients with severe refractory HHT-related epistaxis. This is with the aim to provide informed management recommendations, suggest criteria for surgery, advice for further research and to establish a reporting standard for centres publishing their outcomes of modified nasal closure in the future.

The primary review question is as follows: Is nasal closure a safe and effective management option for patients with refractory epistaxis secondary to hereditary haemorrhagic telangiectasia?

Materials and methods

Registration

This scoping review was prospectively registered on PROSPERO database in February 2024 under registration number CRD42024511489. The protocol can be found in Appendix 1. PROSPERO is an international prospective register of systematic reviews with open access which aims to avoid duplication of reviews and ensure robust methodology.

Search strategy

A literature review was performed in accordance with the "Preferred Reporting Items for Systematic Reviews and Meta-Analysis" (PRISMA) guidelines [22]. The literature search was performed in February 2024 across Cochrane Library (CENTRAL), EMBASE, PubMed and clinical trial registers. The search strategy used the

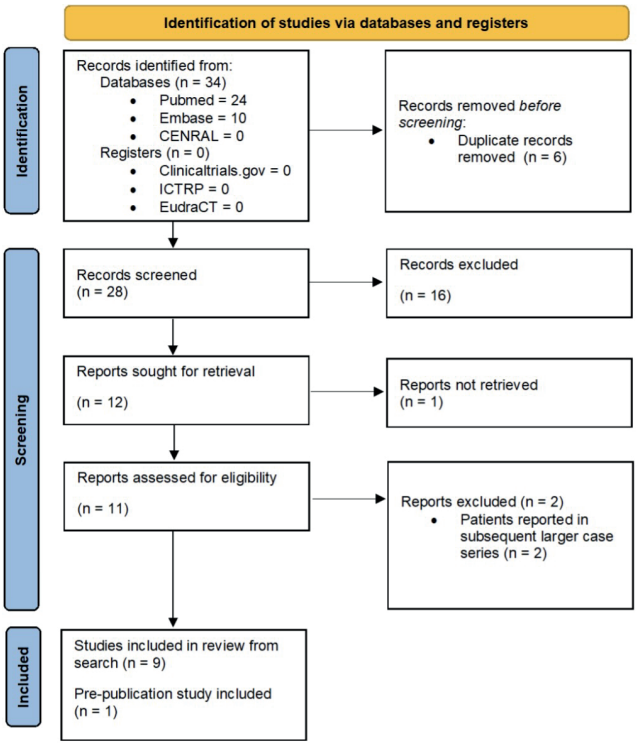

Figure 3. PRISMA flow diagram for included studies.
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

keywords "Hereditary haemorrhagic telangiectasia" or "HHT" or "Osler-Weber-Rendu", combined with "nasal closure" or "Young's procedure". The full search strategy can be seen in Appendix 2. We were prepared to include case reports or series, observational studies, case-control/cohort and randomised controlled studies. Non-English language papers were excluded. There were no limitations on the date of publication.

A "PICO" (population, intervention, comparator, outcome) search strategy was used. The population included any age, sex, ethnicity or nationality patient with HHT and persistent severe epistaxis despite conventional management. The intervention studied was modified nasal closure. The comparator group comprised patients with severe epistaxis who did not undergo nasal closure.

The main outcomes reviewed were:

1) Efficacy of the procedure in controlling epistaxis, evaluated through changes in pre- and post-operative haemoglobin concentrations, transfusion frequency, and epistaxis severity scores (ESS).
2) Patient reported outcome measures related to quality of life, including scores such as Glasgow Benefit Inventory

Table 1. Included studies, study design, demographics and duration of follow up.

Author	Design	Number of participants	Mean age (range)	M:F	Bilateral: unilateral	Mean follow up, months (range)
Lund et al. 2017	Case series	100	63.6 (27-85)	51:49	87:13	68 (6-264)
Anderson et al. 2020	Case series	10	62.4	5:5	9:1	66
Thompson et al. 2018	Case-control	5 cases 8 controls	64.6 cases 67.4 controls	1:4 cases 3:5 controls	5:0	70 (SD 3.65)
Richer et al. 2012	Case series	43	61 (31-77)	28:15	38:5	34 (6 -84)
Ichimura et al. 2011	Case series	7	65.3 (54-80)	4:3	5:2	44 (13-66)
Timmins et al. 2014	Case series	13	64.3 (33-75)	9:4	13:0	49 (13-110)
Gluckman and Portugal 1994	Case series	3	50 (48-52)	2:1	3:0	55 (24-92)
Esteves et al. 2015	Case series	4	55.5 (38-68)	2:2	4:0	19 (12-26)
Bickerton et al. 2024	Case series	5	65 (44-76)	3:2	4:1	34
Hosni and Innes 1994	Case series	2	58 (53 and 63)	2:0	2:0	14 years

Table 2. Included studies and outcomes.

Author	Number of participants	ESS pre-op	ESS post-op	Mean GBI (range)	Mean Hb increase	Rate of dehiscence or pinhole (%)
Lund et al. 2017	100	9.42	0.54	53.43 (25-83)		10/100 (10%)
Anderson et al. 2020	10			38.05	28	3/10 (30%)
Thompson et al. 2018	5 cases 8 controls					
Richer et al. 2012	43			44 (17-70)	46.8	13/43 (30%)
Ichimura et al. 2011	7					4/7 (57%)
Timmins et al. 2014	13	7.88	0.97	Three-flap 77.3 (55.6-100) Two-flap 56.3 (8.3-83.3)		8/13 (62%)
Gluckman and Portugal 1994	3					1/3 (33%)
Esteves et al. 2015	4					
Bickerton et al. 2024	5	7.8	0.4	49.2 (-6-83)	47.2	3/5 (60%)
Hosni and Innes 1994	2					

(GBI), a validated patient reported outcome measure which is widely used in research evaluating otorhinolaryngological interventions [23].

Post-operative complications were also reviewed.

Data collection and analysis

Searches were conducted as per the above criteria to identify relevant papers. Duplicates were manually excluded. Titles and abstracts were screened for inclusion and exclusion, followed by full text assessment for final inclusion. This process is summarised in the PRISMA flow diagram (Figure 3). Additionally, references from included papers were cross-checked for relevance by reviewers RB and RG, with discrepancies resolved by a third reviewer, TR.

Data extraction from included papers was performed by two independent reviewers, RB and RG. Extractions broadly included study characteristics, patient demographics, the nature of the intervention and the outcomes used. Any discrepancies between reviewers were resolved through discussion with a third reviewer, TR.

Quality assessment

Bias assessment was conducted using the tool proposed by Murad et al. [24] by the two independent reviewers RB and RG. Questions 4, 5 and 6 were deemed not applicable for the included case series, as these questions pertain to pharmacological treatment rather than surgical interventions. Any differences in bias assessments were resolved with a third reviewer, TR.

Synthesis of results

Due to a heterogeneity of study design and reported outcomes

among the included papers, data was synthesised using a narrative synthesis rather than a meta-analysis, summarising the efficacy of treatment in controlling epistaxis and patient reported outcome measures.

Results

Study selection

The initial literature search yielded 34 results. The study selection process is illustrated in Figure 3. From these results, 28 abstracts were screened, and 13 full texts were reviewed. Ultimately, nine publications met the eligibility criteria and were included in the review. One pre-publication study was included from our own centre; this was subsequently accepted for publication in May 2024. Nine included studies were case series, and one was a case-control study. These publications are summarised in Table 1, which includes study characteristics, patient demographics, the nature of the intervention and the outcome measures used.

One senior author, VJ Lund, had published three separate case series on patients who underwent modified nasal closure for HHT-related epistaxis at their centre over the past 20 years. Upon contacting the author, it was confirmed that the most recent paper, with the largest cohort, included data from all patients involved in the prior studies. Therefore, the two preceding case series were excluded to prevent duplication of data. Three studies identified had authors affiliated with the University of Utah's Department of Otolaryngology - Head and Neck Surgery. Upon contact, the authors confirmed there was significant but unquantifiable overlap of patients between studies. Despite this, each study reported distinct outcomes and conclusions, so have been included in the review.

Synthesis of results

This review included a total of 192 patients who underwent nasal closure (107 males, 85 females). The mean patient age ranged from 50.0 to 65.3 years. In the single case-control study, there were five 'cases' who underwent nasal closure and eight 'controls' who did not.

In total, 164 patients underwent bilateral closure, while 28 patients underwent unilateral closure. Seven of those who initially underwent unilateral closure subsequently requested closure of the other nostril. Nasal closure was performed using the three-flap technique in 177 patients, and a two-flap technique in 15 patients. Among papers specifying follow up duration, mean follow up ranged from 19 to 70 months.

All patients had severe epistaxis secondary to HHT which was refractory to conventional medical and surgical management; this was the indication for surgery in all cases.

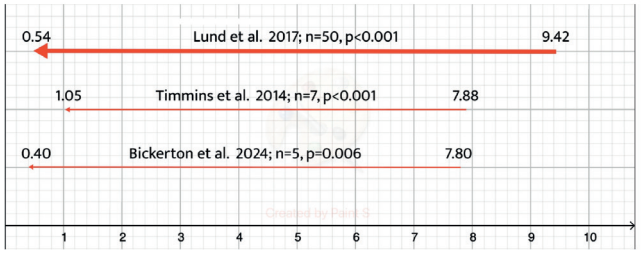

Figure 4. Improvement in epistaxis severity scores (ESS) post-operatively. Note that Lund et al. used a different grading score proposed by Al-Deen and Bachmann-Harildstad, which is also graded from 0 – 10.

Major findings from data synthesis are summarised below, and outcomes are summarised in Table 2.

1. Surgery generally resulted in improved quality of life post-operatively.

Quality of life was most frequently assessed using the GBI score, derived from 18 questions reflecting post-operative health-related quality of life [25]. Scores range between -100 (maximum negative) and +100 (maximum positive). Pooled analysis from 95 patients across five studies who had post-operative GBI scores found a mean GBI score of +50.267 (range 38.5 - 62.8). Only one of these patients was reported to return a GBI with a negative score.

Two patients out of 192 experienced intolerable symptoms of nasal obstruction following surgery and requested reversal of the closure [26,27]. One of these patients subsequently suffered severe epistaxis, requiring weekly transfusions, and underwent re-closure two months later [28]. No other patients requested re-opening for reasons related to quality of life.

2. Modified nasal closure reduces frequency and severity of epistaxis, often resulting in complete cessation of epistaxis.

Epistaxis severity score (ESS) is a validated tool which provides a standardised and objective way to measure the severity and frequency of epistaxis [28]. Two papers found a significant reduction in ESS following surgery, and another found a significant reduction in objective epistaxis severity using an alternative score proposed by Al-Deen and Bachmann-Harildstad, which is also graded from 0 – 10 [29]. These were statistically significant reductions in each study (Figure 4).

All studies reported that most patients who underwent nasal closure experienced complete cessation of epistaxis post-operatively. Lund et al. report that 8 of 87 patients (9%) who underwent bilateral closure continued to experience any bleeding from the nose in the long term. Otherwise, no other studies quantified the proportion of patients who continued to experience epistaxis [31].

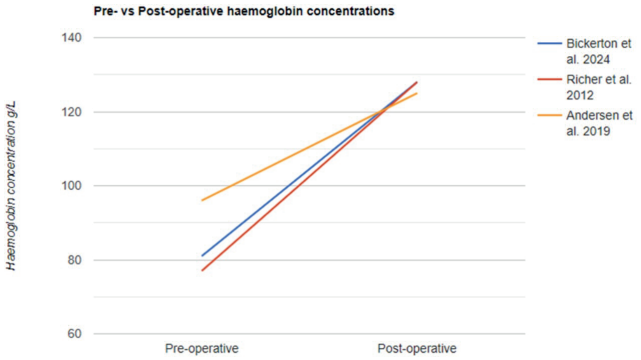

Figure 5. Improvement in haemoglobin concentration post-operatively.

One study [30] reported on three patients who suffered profound post-nasal bleeding in the months following surgery despite complete closure. One requested reversal of the procedure, and another required emergent reversal with immediate reclosure after successful treatment of epistaxis. Another study [31] noted four patients with moderate post-nasal bleeding following surgery, all due to partial dehiscence, none requiring transfusion. These patients underwent successful revision surgery. Three who had continued bleeding despite full closure were treated with systemic tranexamic acid, tamoxifen or bevacizumab to good effect.

3. Surgery resulted in increased post-operative haemoglobin levels.
Three studies compared pre-operative with post-operative haemoglobin levels, finding increases in all cases. Mean pre-operative haemoglobin ranged from 77 – 95g/L, and mean post-operative haemoglobin ranged from 125 – 128g/L (Figure 5). In the five studies which reported post-operative transfusion requirements, no patients who underwent nasal closure required transfusion for anaemia secondary to HHT-related epistaxis.

4. Closure of the nasal airway results in unavoidable symptoms, but patients would prefer to manage these inevitable side effects over their pre-operative epistaxis.
Frequently reported post-operative symptoms from patients who underwent nasal closure included loss of taste and smell, sleep disturbance, xerostomia, voice change and ear fullness. Of 76 patients across three papers [31–33] who were asked if they would undergo the procedure again, all said yes, preferring to manage these symptoms over the pre-operative epistaxis.

Thompson et al. assessed sleep and severity of obstructive symptoms using the Pittsburg Sleep Quality Index (PSQI) and Nasal Obstruction Symptom Evaluation (NOSE) scores [34], in those who underwent nasal closure with controls. They found no significant difference in scores between the two groups, although this finding is caveated with a small sample size and a therefore underpowered study.

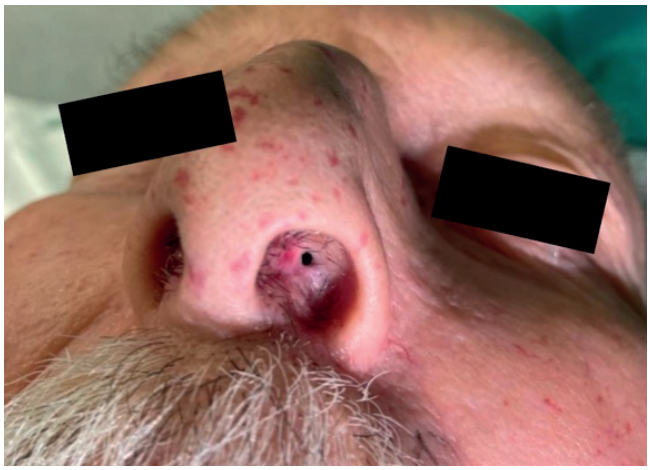

Figure 6. Partial dehiscence of nasal closure, reproduced with the permission of the authors Bickerton et. al. 2024.

5. Partial dehiscence is a frequently reported complication.
Seven of nine papers reported partial dehiscence of nasal closures (Figure 6). Pooled analysis of 181 patients with recorded complications found that 42 patients (23.2%) experienced partial dehiscence post-operatively. This was typically treated with revision surgery involving primary closure, nasolabial flaps, or occasionally occluded with petroleum jelly [35] or adhesive tape [36]. It is unclear at which stage post-operatively dehiscence usually occurs, but Timmins et al. report a mean time to revision surgery of 21.5 months with a range of 1.8 - 59.4 months, suggesting that breakdown can occur in the months to years following surgery. Revision surgery was successful in the first instance for 22 of 30 (73.3%) patients across five studies which reported their success rates.

Discussion

In our systematic review assessing nasal closure as a treatment for severe, refractory HHT-related epistaxis, we found unanimous advocation for this intervention across all included studies. Surgery generally resulted in improved post-operative quality of life, with a significant reduction in the frequency and severity of epistaxis, often leading to its complete cessation. Although the procedure results in lifelong obligate mouth-breathing, and potentially associated xerostomia, reduced taste, anosmia and altered sleep, these were considered preferable by patients to the severe, often life-threatening epistaxis experienced pre-operatively. Surgical complications include partial dehiscence of the closure, which is important to consent for, and posterior epistaxis, which appears to be rare and may require systemic treatment or very rarely re-opening of the nostril in the acute setting.

We believe the presented evidence is sufficient to recommend modified nasal closure as a conventional treatment option

Table 3. Quality assessment of included studies.

Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Quality (total score)
Lund et al. 2017	×	✓	✓				✓	✓	Good - 4/5
Anderson et al. 2020	×	✓	✓				✓	×	Fair - 3/5
Thompson et al. 2018	×	✓	×				✓	✓	Fair - 3/5
Richer et al. 2012	×	✓	×				✓	✓	Fair - 3/5
Ichimura et al. 2011	×	✓	✓				✓	✓	Good - 4/5
Timmins et al. 2014	✓	✓	✓				×	×	Fair - 3/5
Gluckman and Portugal 1994	×	✓	×				✓	×	Poor - 2/5
Esteves et al. 2015	✓	✓	×				×	✓	Fair - 3/5
Bickerton et al. 2024	×	✓	✓				✓	✓	Good - 4/5
Hosni and Innes 1994	×	✓	×				✓	×	Fair - 3/5

Q1: Do the patients represent the whole experience of the centre, or is the selection method unclear to the extent that other patients with similar presentation may not have been reported?; Q2: Was the exposure adequately ascertained?; Q3: Was the outcome adequately ascertained?; Q4: Were other alternative causes that may explain the observation ruled out?; Q5: Was there a challenge/rechallenge phenomenon?; Q6: Was there a dose–response effect?; Q7: Was follow-up long enough for outcomes to occur?; Q8: Are the cases described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice? Please note that Q4, Q5 and Q6 reflect quality assessment for pharmacological interventions and are mostly related to adverse drug events, hence why they are not assessed for included papers.

for the most severe, refractory cases of HHT-related epistaxis. Criteria for surgery should include patients with severe epistaxis (which can be quantified using an ESS of 7 or above) requiring frequent blood transfusions for whom medical and ablative surgical treatment has failed to improve, or with contraindications to medical therapies such as bevacizumab. These criteria reflect the patients in whom this procedure has been demonstrated to be successful.

Patient selection

The decision for nasal closure should involve careful consideration by both patient and clinician. While the procedure can dramatically improve or eliminate epistaxis, it results in the inevitable consequence of obligate mouth-breathing and impairment of taste and smell. Thus, robust pre-operative counselling for patients is imperative, with the decision for surgery taking place over multiple clinical contacts. Several centres [27,31,32] offer prospective patients contact with others who have undergone the procedure to ensure patients are thoroughly informed and adequately prepared for the physical consequences of surgery. Two centres [27,35] provide patients with nasal obturators to help them become accustomed to mouth-breathing prior to closure. Additionally, there are reports of the use of silastic obturators as an alternative to nasal closure for patients reluctant to commit to surgical closure [37,38].

Special considerations

Patients with severe HHT-related epistaxis often require frequent surgical ablation of telangiectasia. For high-risk patients with severe comorbidities, each general anaesthetic represents a significant risk to life. These patients may benefit from nasal closure earlier than others given that this procedure is usually a definitive treatment with no further interventions needed. This was the indication for surgery in a patient reported by Bickerton et al., whose severe pulmonary hypertension required specialist intensive care support for a general anaesthetic. As such, following extensive patient discussion, the decision was made to perform nasal closure to avoid recurrent procedures under general anaesthetic.

Furthermore, patients having frequent transfusions for anaemia secondary to HHT-related epistaxis may develop alloantibodies, which can increase risk of transfusion reactions, complicate future pregnancies and cause difficulty in finding compatible red cell units [39]. Nasal closure could be used in this circumstance to reduce the transfusion burden and minimise risk of transfusion reactions in this subset of patients.

Patients with HHT-related epistaxis who require systemic anticoagulation for conditions such as venous thromboembolism (VTE), shown to occur more readily in HHT patients [40,41], present a challenging dilemma in management. Richer et al. suggest

considering nasal closure in this cohort as it generally results in complete cessation of epistaxis, therefore reducing the risk of systemic anticoagulation. In this context, nasal closure could serve as a temporary measure to enable a period of anticoagulation, and then be reversed once anticoagulation is no longer required.

Nasal closure is not a feasible management option for patients requiring long term oxygen via nasal cannula, and again this indicates careful weighing of benefits over risks. There is a risk, however, of uncontrolled epistaxis due to drying of the nasal mucosa from nasal oxygen therapy, therefore alternative methods for oxygen administration should be considered.

Management of posterior epistaxis following nasal closure is challenging; the conventional methods for controlling epistaxis are no longer available. Life-threatening posterior epistaxis associated with nasal closure, although rare, can occur and may necessitate aggressive management, including systemic therapies, blood transfusions, embolisation, and possibly reversal of the procedure to allow for treatment [30]. One case report [42], which details such a complication, advocates for surgeons to address all potential or active bleeding points before or during surgical closure to minimise the risk of ongoing epistaxis. It is important to discuss the risk of posterior epistaxis following the procedure with prospective surgical candidates, including the small possibility of the need to reopen the closure to allow control of bleeding.

Limitations

Overall, the included case series exhibited varying degrees of bias as assessed by the tool proposed by Murad et al. [24], with scores for each paper demonstrated in Table 3. The evidence is generally confined to case series, each with relatively small sample sizes given the rarity of both HHT and nasal closure. Between publications, there was a variable standard of reporting on patients' medical backgrounds and treatments prior to nasal closure. Furthermore, the reported outcome measures were extremely varied within the included studies; two did not describe quantitative outcomes [20,34] and 3 did not report any validated patient-reported outcome measures (PROMS) [20,26,33]. Within the included publications which reported PROMS, three reported epistaxis severity scores [27,34,35], two used an alternative score to grade epistaxis severity [31,36], and five reported GBI [27, 30–32,35]. The small sample sizes and heterogeneity between publications confounded our ability to perform a meta-analysis as the recommended gold-standard measure of effect and necessitated a narrative synthesis with pooled analysis where appropriate. Finally, a notable limitation of this review is the inclusion of three studies with overlapping patient populations, as confirmed by the authors affiliated with the University of Utah. While the extent of this overlap could not be quantified, the only pooled analysis affected is the rate of partial dehiscence, and each studys distinct outcomes and conclusions provided valuable contributions to the overall analysis.

Some outcome measures used by studies can be confounded by other factors. Haemoglobin concentration, for instance, can fluctuate due to varying epistaxis pre-operatively, and may fall for myriad other reasons post-operatively such as gastrointestinal bleeding or anaemia of chronic disease. One study used epistaxis severity scales as a proxy for quality of life, which is not a valid extrapolation of effect [34]. However, the limitations of individual outcome measures are mitigated in this review by synthesising multiple outcomes across several studies.

Further research

Given that the Young's procedure is mostly used a 'last resort' management option, some may not consider it ethical to conduct controlled studies assessing its efficacy against conventional treatment options. Therefore, the evidence is likely to remain confined to case series. Additionally, due to the rarity of HHT, it may be difficult to adequately power such a study. Consequently, it is important to establish a reporting standard for future studies evaluating the efficacy of nasal closure.

We believe that the most important outcome measure is post-operative patient reported quality of life. The procedure effectively controls epistaxis in almost all cases, but the significant trade-off of losing nasal airflow makes it crucial to assess quality of life when determining whether surgery was appropriate. We would recommend measuring this using the Glasgow Benefit Inventory. The GBI is extensively validated and used in the literature, therefore it will also facilitate comparison of outcomes with previously published research [23]. Epistaxis severity should be measured using the epistaxis severity scale where possible, with pre- and post-operative ESS reporting for each patient undergoing nasal closure.

It would be useful for studies to assess how patient-related factors – such as age, comorbidity, medications, smoking - affect the rate of success of nasal closure. Centres should also ideally continue to assess outcomes over a prolonged follow-up duration for their patients who have undergone nasal closure, as demonstrated by Lund et al.. This is particularly important given the relatively high rates of partial dehiscence, which can possibly occur several months to years following surgery, and potential deterioration of epistaxis despite initial treatment success. Extended follow up also helps assess the long-term tolerability of symptoms related to complete nasal obstruction, therefore allowing clinicians to evaluate whether an initially improved quality of life is sustained over time.

Conclusion

Our systematic review suggests that modified nasal closure is an effective and viable treatment option for patients with severe, refractory epistaxis secondary to hereditary haemorrhagic telangiectasia. The reviewed studies generally demonstrate significant improvements in quality of life post-operatively with marked reductions in epistaxis severity, and in many cases, complete cessation of bleeding. Despite the inevitable consequences of nasal closure, such as obligate mouth-breathing and impairment of taste and smell, patients are willing to tolerate these over the debilitating effects of persistent epistaxis. Careful patient selection and pre-operative counselling is crucial to ensure improved quality of life post-operatively for this challenging patient population.

Authors' contributions

RB: acquisition, analysis, interpretation of data; drafts and revisions during the writing process. RG: acquisition, analysis, interpretation of data; drafts and revisions during the writing process. TR: drafts and revisions during the writing process. CR: drafts and revisions during the writing process; final approval of the article before submission to Rhinology.

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Conflicts of interest

The authors declare no conflict of interest.

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SUPPLEMENTARY MATERIAL

Appendix 1. Review protocol as registered in the PROSPERO database.

https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=511489

Appendix 2. Full search strategy.

The literature search was performed in February 2024 across Cochrane Library (CENTRAL), EMBASE, PubMed and clinical trial registers.
We were prepared to include case reports or series, observational studies, case-control/cohort and randomised controlled studies. Non-English language papers were excluded. There were no limitations on the date of publication.
PICO framework:

- Population: any age, sex, ethnicity or nationality patient with HHT and persistent severe epistaxis despite conventional management
- Intervention: modified nasal closure
- Comparator: patients with severe epistaxis who did not undergo nasal closure
- Outcomes:
  - Efficacy of the procedure in controlling epistaxis
    - Changes in pre- and post-operative haemoglobin concentrations
    - Transfusion frequency
    - Epistaxis severity scores (ESS).
  - Patient reported outcome measures related to quality of life
    - Glasgow Benefit Inventory (GBI)
  - Post-operative complications

Search string:

1. Hereditary haemorrhagic telangiectasia
2. HHT
3. Osler-Weber-Rendu
4. 1 or 2 or 3
5. Nasal closure
6. Young's procedure
7. Modified nasal closure
8. Modified Young's procedure
9. 5 or 6 or 7 or 8
10. 4 and 9