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THE COMPREHENSIVE SYSTEMATIC REVIEW OF RECURRENT EPISTAXIS

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ABSTRACT

Background: *Epistaxis affects roughly 60% of adults at some point in their lives, yet only about 10% necessitate medical intervention. Recurrent epistaxis remains a frequent reason for emergency department visits and involves multiple risk factors. This study aims to systematically review the literatures on recurrent epistaxis in the last 10 years.*

Methods: *This systematic review adhered to the PRISMA 2020 standards and included full-text English literature published between 2014 and 2024. Exclusion criteria involved editorials, review articles from the same journal, and submissions lacking a DOI. Literature was gathered from online sources such as PubMed and SagePub.* ***Result:*** *Our search in PubMed yielded 76 articles, while SagePub produced 2415 articles. Focusing on the last 10 years (2014-2024), PubMed had 57 articles and SagePub had 712 articles. Ultimately we selected 6 papers that met our criteria, 3 from PubMed and 3 from SagePub.*

Conclusion: *Managing recurrent epistaxis requires detailed examination on risk factors and underlying etiologies. The risk factors for recurrent epistaxis were unidentified bleeding point, blood parameters, the use of antithrombotic agent, and hereditary diseases. The current treatment of recurrent epistaxist can be done with bipolar cauterization and microwave ablation on bleeding points.*

Keyword: *Epistaxis, recurrent epistaxis, anterior epistaxis, posterior epistaxis*

INTRODUCTION

Epistaxis, commonly known as nosebleeds, affects roughly 60% of adults at some point in their lives, yet only about 10% necessitate medical intervention. Surgical procedures are seldom required, although there are instances where persistent epistaxis do not respond to standard treatments. Consequently, epistaxis is frequently cited as a cause for hospital admissions in otolaryngology departments.[1]

The causes and risk factors associated with epistaxis are categorized into local factors (such as trauma, medication usage, infections, inflammation, and tumors), systemic factors (including blood disorders, leukemia, atherosclerosis, hypertension, and heart failure), or idiopathic origins. Recurrent epistaxis can serve as potential indicators of underlying systemic or local neoplastic conditions. Hereditary hemorrhagic telangiectasia (HHT), an inherited vascular disorder, often manifests with spontaneous epistaxis and can significantly impact both functional abilities and social interactions.[2]

The nose has a rich blood supply from arteries branching off the internal and external carotid arteries. Most epistaxis (80-90%) occur in the front part of the nasal cavity, primarily from an area called Little's area on the anteroinferior septum, where the Kiesselbach plexus is located. This plexus represents a dense network of vessels derived from both the internal carotid (specifically the anterior ethmoidal artery) and external carotid arteries (including branches like the sphenopalatine, greater palatine, and superior labial arteries). These anterior epistaxis are typically easy to manage and pose minimal risk. Posterior epistaxis, comprising 10-20% of cases, arise from branches of different arteries and are harder to control. They occur mainly on the posterior septum, lateral nasal wall, or nasal floor and carry a higher risk of complications like airway compromise or aspiration.[2]

Most cases of epistaxis resolve without medical intervention, and only a minority of patients seek professional help. However, some individuals experience recurrent epistaxis. Factors contributing to single episodes of epistaxis include facial injury, irritation, allergic rhinitis, infections, nasal tumors, and environmental factors such as temperature and humidity. Additionally, certain medications, herbal supplements, blood disorders like thrombocytopenia or von Willebrand disease, kidney failure, alcohol consumption, and liver disease can increase susceptibility to epistaxis. Frequent epistaxis are also common in individuals with inherited conditions like hereditary hemorrhagic telangiectasia (HHT). Furthermore, medication usage, particularly antiplatelet drugs like aspirin and clopidogrel for heart attack and stroke prevention, is associated with an elevated risk of epistaxis.[3]

In most cases, epistaxis resolve on their own and typically only cause mild anxiety and discomfort. However, larger bleeds can result in hemodynamic instability, particularly in elderly individuals with underlying cardiovascular conditions. Complications such as angina and heart attacks have been reported due to excessive blood loss. Frequent but less severe epistaxis, while not immediately life-threatening, can still affect a patient's quality of life. They have been associated with premature cessation of antiplatelet medications and an elevated risk of heart attacks due to blood clot formation in stents. This study aims to systematically review the literatures on recurrent epistaxis in the last 10 years.

METHODS

Protocol

The author followed the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 to ensure that this study adhered to the requirements. This method was chosen to guarantee the accuracy of the conclusions drawn from the inquiry.

Criteria for Eligibility

This systematic review was done by assessing evidence on on recurrent epistaxis in the last 10 years. Evidence was compiled and analyzed thoroughly to provide an explanation and enhance the handling of patients' treatments. The primary objective of this paper is to demonstrate the relevance of the identified main points as a whole.

The inclusion criteria for this study are as follows: 1) The paper must be written in English, and 2) The studied papers include several that were published between 2014 and 2024. The exclusion criteria for this study are: 1) Editorials; 2) Submissions without a DOI; 3) Review articles that have already been published; and 4) Identical entries in published journals.

Search Strategy

We used “epistaxis”, “recurrent epistaxis”, “posterior epistaxis” and “anterior epistaxis” as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: *("epistaxis"[MeSH Terms] OR "epistaxis"[All Fields] OR (("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields]) AND ("epistaxis"[MeSH*

Terms] OR "epistaxis"[All Fields])) OR (("posterior"[All Fields] OR "posteriors"[All Fields]) AND ("epistaxis"[MeSH Terms] OR "epistaxis"[All Fields])) OR (("anterior"[All Fields] OR "anteriores"[All Fields] OR "anteriorization"[All Fields] OR "anteriorized"[All Fields] OR "anteriors"[All Fields]) AND ("epistaxis"[MeSH Terms] OR "epistaxis"[All Fields]))) AND ((ffrft[Filter]) AND (randomizedcontrolledtrial[Filter]) AND (fft[Filter]) AND (2014:2024[pdat])).

Data retrieval

The authors assessed studies by reviewing their abstracts and titles to determine their eligibility. We selected relevant studies based on their inclusion criteria, focusing on research that aligned with their article's objectives. A consistent trend across multiple studies led to a conclusive finding. The selected submissions were required to be in English and previously unpublished.

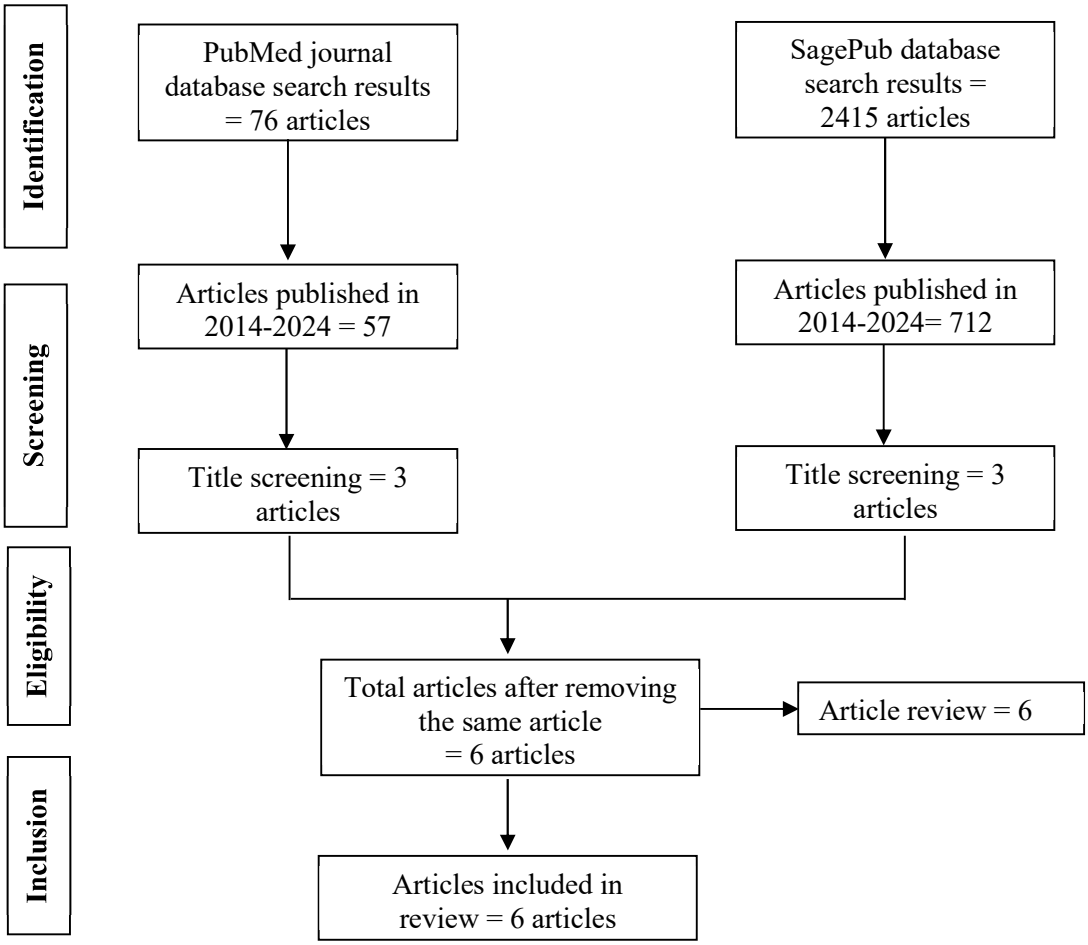

Figure 1. Article search flowchart

This systematic review only considered literatures that met all inclusion criteria and relevance to the topic. Studies not meeting these criteria were excluded, and their conclusions were not considered. The subsequent analysis delved into various details uncovered during the research inquiry, including names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author individually examined the research mentioned in the publication's title and abstract before deciding which publications to explore further. The next step involves evaluating all articles that meet the criteria set for inclusion in the review. Based on the uncovered findings, decisions will be made regarding which articles to include in the review. This criteria streamlines the process of selecting papers for further assessment, discussing the earlier investigations conducted and the elements that make them suitable for inclusion in the review.

RESULT

In our search on the PubMed database, we found 76 articles, while on SagePub, the search yielded 2415 articles. Specicifally, ten years filter (2014-2024) search on PubMed produced 57 articles and SagePub produced 712 articles. Ultimately, we selected a total of 5 papers, with 3 from PubMed and 3 from SagePub. The study includes six literatures that met the criteria, and Table 1 displays the literature included in this analysis.

Table 1. The literature included in this study

Author	Origin	Method	Sample	Result
Ando, et al.[1] (2014)	Tokyo, Japan	Retrospective study	299 patients	Recurrent epistaxis occurred in 32 cases, accounting for 10.7% of the total. An unidentified bleeding point was associated with a significantly higher risk of recurrent epistaxis (adjusted odds ratio 5.67, 95% confidence interval 1.83–17.55, p = 0.003), while the use of electrocautery during treatment was linked to a reduced risk of recurrence (adjusted odds ratio 0.07, 95% confidence interval 0.03–0.17, p = 0.000). Regarding initial treatment for posterior epistaxis, patients who received electrocautery had a significantly lower rate of recurrent epistaxis compared to those who did not (6.4% vs. 40.7%, p < 0.01). Conversely, patients who underwent endoscopic gauze packing had a significantly higher rate of recurrent epistaxis compared to those who did not (39.5% vs. 15.9%, p < 0.01).
Cohen, et al.[4] (2017)	Rehovot, Israel	Retrospective study	653 patients	The study examined the medical records of patients hospitalized for epistaxis between 1999 and 2015, with a three-year follow-up period after admission. Recurrent epistaxis events (REAs) were divided into two categories: early (within 30 days) and late (31 days to 3 years) occurrences. Logistic regression was employed to identify

				potential predictors of REAs. Out of 653 patients studied, 86 (14%) experienced REAs, with 48 (7.5%) classified as early and 38 (6.5%) as late occurrences. Both early and late REAs exhibited nonlinear incidence patterns. Logistic regression analysis revealed prior nasal surgery and anemia as independent risk factors for early REAs, while thrombocytopenia was significantly associated with late REAs according to multivariate analysis.
Ekber Karabulut, et al.[5] (2018)	Keçioren, Turkey	Retrospective case control study	306 patients	This study involved 136 patients with recurrent epistaxis and 170 healthy individuals as controls. They recorded demographic details, vital signs, and complete blood count results, excluding patients with conditions potentially influencing mean platelet volume (MPV) or red cell distribution width (RDW). MPV and RDW levels were compared between the two groups, revealing significantly lower median MPV levels (7.6 fL vs. 8.2 fL, $p < 0.001$) and higher median RDW levels (15.4% vs. 14.3%, $p < 0.001$) in the patient group. Multivariate analyses included variables like systolic blood pressure, leukocyte count, age, sex, RDW, and MPV levels with p values <0.2. Elevated RDW levels were associated with increased nosebleed risk ($p < 0.001$; odds ratio [OR]: 1.89 [95% confidence interval (CI): 1.53–2.33]), while higher MPV levels were linked

				to reduced risk ($p < 0.001$; OR: 0.54 [95% CI: 0.39–0.72]).
Abrich, et al.[3] (2014)	Arizona, USA	Retrospective cohort study	461 patients	This study retrospectively analyzed patients diagnosed with epistaxis in the Marshfield Clinic system from January 1, 1991, to January 1, 2011. It included 461 cases with at least two occurrences of spontaneous epistaxis within three years, compared to 912 controls with only one episode during the same period. Over 50 potential risk factors were examined, spanning demographic details, substance use, nasal abnormalities, infectious and inflammatory conditions, medical comorbidities, medications, and laboratory findings. Hazard ratios for recurrent epistaxis were calculated using Cox proportional hazards regression modeling. Findings revealed that traditional risk factors like nasal perforation, septum deviation, rhinitis, sinusitis, and upper respiratory infections did not heighten the risk of recurrence. However, significant risk factors for recurrent epistaxis included congestive heart failure, diabetes mellitus, hypertension, and a history of anemia. The use of warfarin was associated with an increased risk of recurrence, regardless of the international normalized ratio, whereas aspirin and clopidogrel did not pose a heightened risk. Few major adverse cardiovascular events

				occurred within 30 days of the initial nosebleed episode.
Lou and Jin[6], (2019)	Zhejiang, China	Prospective randomized control study	110 patients	One hundred and ten patients with unexplained recurrent epistaxis were divided randomly into two groups: those undergoing microwave ablation (MWA) and those undergoing bipolar electrocautery. The main objectives were to determine the percentage of patients in each group whose bleeding stopped within 24 hours post-treatment and the time it took to achieve successful hemostasis. Secondary goals included assessing rebleeding rates at different intervals and identifying any complications. Results showed that all patients experienced immediate cessation of bleeding. The MWA group achieved successful hemostasis significantly faster (2.13 ± 1.04 minutes) than the bipolar electrocautery group (6.60 ± 2.68 minutes). Recurrent bleeding rates did not differ significantly between the two groups. However, secondary crusting was more common in the bipolar electrocautery group, while pseudomembrane formation was more prevalent in the MWA group. No severe postoperative complications, such as septal perforation or orbital or brain complications, were reported in either group during the 6-month follow-up period.
McWilliams, et al.[7] (2022)	Los Angeles, USA	Randomized control trial	22 patients	A single-center study conducted between December 2017 and July 2020 involved 22

				eligible patients randomized into two groups: one receiving doxycycline followed by placebo, and the other vice versa. The primary objective was to assess differences in epistaxis severity between treatments, with secondary endpoints including changes in quality of life, bleeding laboratory markers, and frequency of blood transfusions or iron infusions. Post hoc analyses evaluated additional parameters such as dripping and gushing epistaxis frequency. While doxycycline was found to be safe and well tolerated, it did not significantly reduce nosebleed frequency, duration, or severity score compared to placebo. Quality of life, hemoglobin levels, and transfusion rates were similar between groups. However, post hoc analysis indicated a potential reduction in gushing episodes with doxycycline, although the clinical significance was uncertain.

Ando, et al.[1] (2014) highlighted that unidentified bleeding points were significant risk factors for recurrent epistaxis, emphasizing the importance of identifying and cauterizing these points to prevent recurrence. Electrocautery was shown to be effective in reducing the risk of recurrence. Additionally, the study suggested that gauze packing as initial treatment for posterior bleeding might have led to a higher rate of recurrent epistaxis. Therefore, electrocautery was recommended as the preferred treatment for all bleeding points of epistaxis, while gauze packing was deemed potentially inadvisable for posterior bleeding due to its potential for pain and higher recurrence rates.

Cohen, et al.[4] (2017) identified different risk factors for early and late recurrent epistaxis admissions (REA). Understanding these risk factors can aid in stratifying risk for this patient group, enabling tailored preventive measures. Patients deemed at risk for early REA may benefit from a more proactive approach to management and prevention.

Ekber Karabulut, et al.[5] (2018) showed that low mean platelet volume (MPV) and high red blood cell distribution width (RDW) levels are associated with an increased tendency to bleed in patients with recurrent epistaxis. Mean platelet volume (MPV) is a significant parameter determining platelet function, with higher MPV values linked to shorter bleeding periods. Red blood cell distribution width (RDW) measures the variability in the erythrocyte population.

Abrich, et al.[3] (2014) identified congestive heart failure as a lesser-known risk factor for recurrent epistaxis. Both hypertension and diabetes mellitus can cause atherosclerotic changes in nasal vessels, making them fragile and more prone to bleeding. Recurrent epistaxis may also predispose patients to anemia.

Lou and Jin[6], (2019) identified electrocautery and microwave ablation (MWA) to treat reccurent epistaxis. Both bipolar electrocautery and MWA yielded similar results in managing recurrent epistaxis in adult patients. However, MWA offered faster hemostasis, reduced local nasal discomfort, and less crusting compared to bipolar electrocautery. Therefore, MWA may be a more favorable treatment choice for individuals with unexplained recurrent epistaxis.

McWilliams, et al.[7] (2022) suggested a decline in epistaxis frequency and duration over time with doxycycline treatment. Despite these post hoc findings, caution is advised due to the overall negative results of the study regarding doxycycline's efficacy in treating epistaxis.

DISCUSSION

Epistaxis affects roughly 60% of adults at some point in their lives, yet only about 10% necessitate medical intervention. However, it remains a frequent reason for emergency department visits, accounting for around 0.5% of all ED visits and up to 33% of otolaryngology-related visits. About 6% of epistaxis ED visits result in hospital admission, with associated costs ranging from $6,282 to $22,347, particularly when arterial embolization is required.[4]

Several factors have been suggested as potential risks for adult epistaxis. Epistaxis is thought to be more prevalent among individuals aged 45 to 65, initially affecting men more than women but becoming equally common in both sexes after age 49, possibly implicating estrogen. The use of antithrombotic agents, particularly warfarin, is considered a significant risk factor, although whether discontinuing these medications is necessary remains controversial. While some studies suggest no need for discontinuation, others report that a substantial portion of patients taking antithrombotic agents experience epistaxis annually. Evidence regarding aspirin's association with epistaxis is inconclusive, with some studies finding no difference in aspirin usage between habitual nose bleeders and controls, while others suggest a positive correlation. The link between hypertension and epistaxis is uncertain, some studies suggest that longstanding hypertension may elevate the risk of epistaxis and others argue that while hypertension does not directly cause epistaxis, it may prolong bleeding episodes.[1]

Cohen, et al.[4] (2017) identified different risk factors for early and late recurrent epistaxis admissions (REA). Early recurrent bleeding after initial treatment may result from unresolved active bleeding sources. Prior sinonasal surgery and anemia are associated with such early episodes, suggesting potential iatrogenic causes or prolonged bleeding patterns. Anemia at presentation may indicate a resistant bleeding source or reflect the severity and origin of the bleed. Older age, anemia, and thrombocytopenia were associated with late REA initially, but after adjusting for confounding factors, only thrombocytopenia remained significantly associated. Studies have indicated that only a minority of patients with chronic thrombocytopenia experience epistaxis, suggesting a complex relationship between thrombocytopenia and recurrent epistaxis.[4]

Recent studies have investigated potential connections between epistaxis and different blood parameters, particularly mean platelet volume (MPV) and red blood cell distribution width (RDW). Platelets, originating from megakaryocytes, are essential for blood clotting and have a disc-shaped structure. MPV is a critical factor determining platelet function, with higher levels associated with reduced bleeding duration. Elevated MPV levels have also been linked to conditions like acute myocardial infarction (AMI), acute cerebral ischemia, and transient ischemic attacks. RDW measures the variability in erythrocyte population. Increased RDW can indicate various diseases where immature reticulocytes are prematurely released into circulation. Apart from diagnosing anemia, elevated RDW levels have been associated with conditions such as heart failure, cardiovascular events, celiac disease, inflammatory bowel disease, and increased inflammatory markers. Ekber Karabulut, et al.[5] (2018) showed that low mean platelet volume (MPV) and high red blood cell distribution width (RDW) levels are associated with an increased tendency to bleed in patients with recurrent epistaxis [5]

Various cardiovascular risk factors were examined to understand their impact on recurrent epistaxis, particularly in relation to atherosclerosis of nasal blood vessels. Hypertension and diabetes mellitus were identified as minor contributors to recurrence, likely due to their role in promoting systemic atherosclerosis. However, conditions such as coronary artery disease, cerebrovascular disease, and peripheral vascular disease were not associated with recurrent epistaxis, as they are outcomes rather than causes of atherosclerosis. Notably, congestive heart failure (CHF) showed a strong association with recurrent epistaxis, possibly due to increased venous pressure in nasal vessels. This suggests that individuals with a history of CHF may have a higher risk of recurrent epistaxis originating from venous sources in the nasal septum.[3]

The standard approach to treat recurrent epistaxis involves initial resuscitation, followed by nasal packing if the bleeding source cannot be identified. Bipolar cautery or suction monopolar cauterization are commonly used methods, along with arterial ligation or embolization. However, the success rates of procedures like sphenopalatine artery (SPA) ligation are limited. Microwave ablation (MWA) is typically used to achieving hemostasis during surgery and it has shown promising results in reducing blood loss. Recent studies have explored the use of MWA for epistaxis treatment, reporting favorable outcomes. Both bipolar electrocautery and MWA yielded similar results in managing recurrent epistaxis in adult patients.

However, MWA offered faster hemostasis, reduced local nasal discomfort, and less crusting compared to bipolar electrocautery.[6]

Other etiologies of recurrent epistaxis like Hereditary Hemorrhagic Telangiectasia (HHT) are genetic disorders marked by abnormal blood vessel formation, leading to symptoms such as frequent epistaxis and abnormal blood vessel clusters in the skin and internal organs. Epistaxis in HHT can significantly impact patients' lives, sometimes requiring blood transfusions. The fragile blood vessel clusters, especially in the nasal passages, are prone to spontaneous rupture, resulting in recurrent epistaxis. Although several treatments targeting abnormal blood vessel formation have been investigated for managing HHT-related bleeding, their cost and adverse effects pose limitations. Doxycycline is an affordable antibiotic that shows promise as an alternative treatment due to its ability to inhibit matrix metalloproteinases (MMPs), thereby reducing abnormal blood vessel growth. Theuse of doxycycline shoewd a decline in epistaxis frequency and duration over time. However, caution is advised due to the overall negative results of the study regarding doxycycline's efficacy in treating epistaxis.[7]

CONCLUSION

Managing recurrent epistaxis requires detailed examination on risk factors and underlying etiologies. The risk factors for recurrent epistaxis were unidentified bleeding point, blood parameters, the use of antithrombotic agent, and hereditary diseases. The current treatment of recurrent epistaxist can be done with bipolar cauterization and microwave ablation on bleeding points. poses an ongoing challenge for dermatologists.

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