MAYO CLINIC

# Risk Factors for Recurrent Spontaneous Epistaxis

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## Abstract

**Objective:** To identify risk factors associated with spontaneous recurrent epistaxis.

**Patients and Methods:** This was a retrospective cohort study assessing patients in the Marshfield Clinic system diagnosed as having epistaxis between January 1, 1991, and January 1, 2011. There were 461 cases with at least 2 episodes of spontaneous epistaxis within 3 years and 912 controls with only 1 episode in the same time frame. More than 50 potential risk factors were investigated, including demographic features, substance use, nasal anatomical abnormalities, nasal infectious and inflammatory processes, medical comorbidities, medications, and laboratory values. A Cox proportional hazards regression modeling approach was used to calculate hazard ratios of epistaxis recurrence.

**Results:** Traditional risk factors for epistaxis, including nasal perforation, nasal septum deviation, rhinitis, sinusitis, and upper respiratory tract infection, did not increase the risk of recurrence. Significant risk factors for recurrent epistaxis included congestive heart failure, diabetes mellitus, hypertension, and a history of anemia. Warfarin use increased the risk of recurrence, independent of international normalized ratio. Aspirin and clopidogrel were not found to increase the risk of recurrence. Few major adverse cardiovascular events were observed within 30 days of the first epistaxis event.

**Conclusion:** Congestive heart failure is an underappreciated risk factor for recurrent epistaxis. Hypertension and diabetes mellitus may induce atherosclerotic changes in the nasal vessels, making them friable and more at risk for bleeding. Patients with recurrent epistaxis may also be more susceptible to developing anemia. Physicians should promote antiplatelet and antithrombotic medication adherence despite an increased propensity for recurrent epistaxis to prevent major adverse cardiovascular events.


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Epistaxis is a common otolaryngologic condition, accounting for approximately 1 in 200 emergency department visits in the United States.[1] Most episodes of epistaxis are self-limited,[2] and few patients seek medical attention.[3] However, a subset of patients with epistaxis will experience frequent recurrent episodes.[4] Many putative risk factors for single epistaxis events have been described, including facial injury, physical and chemical irritation, allergic rhinitis, viral and bacterial rhinosinusitis, nasal tumors, temperature, and humidity.[5] Patients may be predisposed to epistaxis as a result of impaired hemostasis caused by antithrombotic and antiplatelet medications, certain herbal supplements, thrombocytopenia, uremia,[6] alcohol use,[7] or deficiency in the production of clotting factors in liver disease.[8] Frequent epistaxis may also be observed in patients with inherited coagulopathies, such as von Willebrand disease, and genetic abnormalities, such as hereditary hemorrhagic telangiectasia (HHT). Epistaxis can also occur as a result of medication exposure and is associated with the use of antiplatelet medications for the secondary prevention of heart attack and stroke, including aspirin and clopidogrel.

In addition to the known risk factors for epistaxis described previously herein, other potential risk factors have been described, but causality has not been demonstrated. Nasal septum abnormalities have often been implicated, although their association is unclear.[9] Elevated blood pressure characteristic of uncontrolled hypertension is also thought to precipitate epistaxis; however, anxiety in the context of an epistaxis episode may explain such findings. Long-term, uncontrolled hypertension is also believed to predispose patients to epistaxis through the development of atherosclerosis in vessels of the nasal mucosa.[5] Postmortem studies have reported greater nasal vascular damage marked by degenerative fibrotic changes in the tunica media of individuals with epistaxis who had chronic hypertension compared with individuals with epistaxis



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alone.[10] These friable vessels may increase the severity of bleeding during an acute episode of epistaxis.[11]

In most patients, epistaxis is self-limiting and causes, at worst, anxiety and discomfort. However, larger bleeds can lead to hemodynamic instability,[2] especially in elderly patients with coexisting cardiovascular disease.[9] Complications from blood loss, including angina and myocardial infarction, have also been described.[12] Frequent nuisance bleeding, although not as immediately dangerous, may also have an impact on patient quality of life and has been linked to premature discontinuation of antiplatelet medications and increased risk of myocardial infarction from in-stent thrombosis.[13]

Although many risk factors for individual episodes of epistaxis are known, risk factors that predispose patients to recurrent episodes of epistaxis have not yet been described. The goal of this study was to identify risk factors specific to recurrence.

## PATIENTS AND METHODS

This was a retrospective cohort study assessing patients in the Marshfield Clinic system (Marshfield, Wisconsin) diagnosed as having epistaxis between January 1, 1991, and January 1, 2011. Cases were defined as having at least 2 episodes of epistaxis requiring medical care separated by a minimum of 3 months within a 36-month period, whereas controls had only 1 episode in the same time frame. An episode of epistaxis consisted of a cluster of nontraumatic nosebleeds, including the incident event, subsequent care, and follow-up. Manual adjudication of epistaxis episodes in the electronic medical record led to the identification of 461 cases of recurrent epistaxis for study inclusion. A total of 912 manually adjudicated controls were 2:1 frequency matched to cases. Time to recurrence was incorporated into the matching process as follows: the 3 years after a control's epistaxis event were divided into 3-month intervals. A control was eligible to be matched to a case if he or she had a clinic visit occurring during a 3-month interval corresponding to the time elapsed from a case's first episode to his or her second episode, ie, time to recurrence (Figure). Two controls were matched to every case in this manner for 451 cases, with the remaining 10 cases matched to 1 control owing to a limitation in the number of eligible controls.

Patients were eligible for study inclusion if they were aged 18 years or older, had sought medical attention for epistaxis in the Marshfield Clinic system during each episode, and had been seen for follow-up. Only patients who obtained most of their health care through the Marshfield Clinic were included in the study to ensure that longitudinal follow-up data were available. Patients had to have been seen by a primary care provider at least once within a 6-year window surrounding the incident event (up to 3 years before or after the event). They also had to be seen at least once by a primary care provider for follow-up within 3 years after the incident event. Patients were excluded if they had a history of blunt trauma or digital trauma to the nose, a history of nasal or sinus surgery, a known bleeding disorder (eg, von Willebrand disease), or a genetic predisposition to nosebleeds (eg, HHT). Data regarding demographic characteristics, substance use, treatment, comorbidities, medications, laboratory values, and adverse outcomes were electronically and manually abstracted for each epistaxis event. For controls, the second point of data collection was taken from the 3-month interval corresponding to a case's second epistaxis episode as a substitute for epistaxis recurrence. Additional data related to adverse

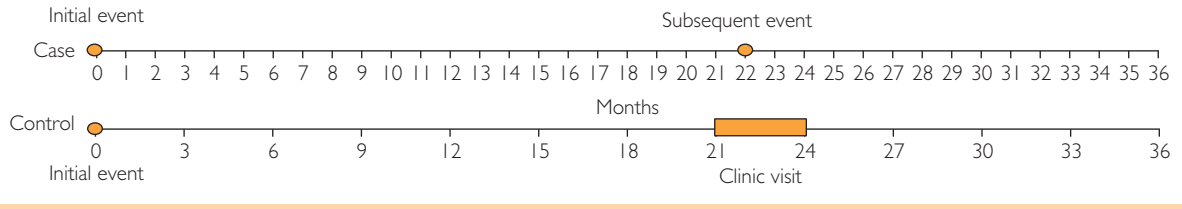


**FIGURE.** Matching a control to a case based on time to recurrence.