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Severe spontaneous epistaxis: retrospective study in a tertiary ENT centre

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Abstract

Purpose To investigate the clinical profile and outcomes of different treatment strategies in patients hospitalized for spontaneous severe epistaxis.

Methods This is a retrospective descriptive study of a case series of patients hospitalized for epistaxis in the University Hospital of Ghent between 2005 and 2012.

Results 124 patients with, respectively, 132 episodes were included. 64% were male. The mean age was 65 years. 73% had comorbidities of which arterial hypertension was the most common. 61% were taking one or more antithrombotics and in 25.7% a recent change in the medication schedule took place. 47% of the episodes necessitated a vascular intervention. The most performed surgery was endoscopic sphenopalatine artery ligation. The 1-year success rate of conservative treatment was 47% and of vascular intervention 81%. No significant difference between the recurrence rates and need for vascular intervention of the different comorbidities and medications was detected using Pearson chi-squared and Fisher's exact testing. The overall 5-year survival rate was 83.6%.

Conclusions The typical pattern of a patient presenting with severe epistaxis was a patient in the sixth decade, male, suffering from comorbidities and taking one or more antithrombotic agents. Based on the above-mentioned success rates of the different treatment options, we think all centres treating epistaxis should apply a well-defined protocol to guide the decision when to proceed with surgery. Furthermore, prospective research needs to precisely investigate the role played by comorbidities and their treatment in the occurrence of epistaxis and to test the effectiveness of proposed algorithms.

Keywords Comorbidity · Epistaxis · Mortality · Treatment outcome · Anticoagulants

Introduction

Epistaxis, active bleeding from the nose, is a common emergency in the general population and affects approximately 60% of the population at some stage in their lives [1].

Nasal haemorrhage occurs most commonly anterior, at the level of Little's area, an anastomotic network of vessels originating from the anterior and posterior ethmoidal arteries, the sphenopalatine artery, the greater palatine artery and the superior labial artery on the anterior portion of the nasal septum [2]. Anterior bleeding may also originate anterior to the inferior turbinate [3]. Severe epistaxis is usually posterior in origin. Posterior bleedings arise from the sphenopalatine artery, greater palatine artery and/or occasionally the posterior ethmoidal artery [2].

Epistaxis has a number of local and systemic etiological factors, but 85% of the cases are said to be idiopathic [1]. Local factors include trauma, infections and neoplasms [2, 3]. In the systemic group hypertension, disorders of the haemostasis and many different drugs have been implicated [2, 3]. The most common listed drugs are warfarin, aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) [1].

The clinical approach to epistaxis is patient dependent and can include conservative treatment options such as adjustment of anticoagulant therapy, cauterisation, anterior or posterior nasal packing or more invasive treatments such as endoscopic sphenopalatine artery ligation (ESPAL) or embolization. Severe epistaxis sometimes necessitates blood transfusion. Conservative measures usually manage to handle nosebleeds; yet, approximately 1% of the patients require surgical intervention to manage epistaxis [4].

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Although epistaxis is a very important cause for emergency admission to the ear, nose, and throat (ENT) clinic, investigation profiles and treatment preferences vary across different centres [5]. Considering the heavy caseload of this pathology and the associated morbidity, it is absolutely necessary to follow a well-defined protocol in the approach to these patients. When managed correctly not only the potential morbidity of epistaxis can be significantly reduced, but also the cost–benefit equation can be modified and hence decrease the burden of epistaxis [6].

The aim of this retrospective study was to investigate the clinical profile of epistaxis patients and to analyze the outcomes of conservative treatment and vascular interventions applied to treat patients hospitalized for severe epistaxis in the Ghent University hospital between 2005 and 2012.

Materials and methods

Data sources

All files of patients with spontaneous severe epistaxis hospitalized in the University hospital of Ghent between 2005 and 2012 were analyzed with attention to the circumstances of the epistaxis, the epidemiological profile of the patients, the use of drugs, possible interactions between drugs mutually, comorbidities, biological parameters, the applied therapy and the outcome of this therapy.

A questionnaire inquiring on the medication the patients were taking before and at the moment of the epistaxis and possible adjustments in the medication schedule short before the epistaxis was sent to the general practitioners. To the patients themselves, an informed consent was sent together with a letter explaining the study. All patients included in the study gave their written informed consent. The ethics committee of the Ghent University Hospital approved this study.

Study selection and protocol

In our study, spontaneous severe epistaxis was defined as all cases of epistaxis in which a hospitalization, posterior tamponade, surgical intervention or blood transfusion was required. Patients with Osler–Weber–Rendu disease, facial trauma, facial surgery and external or endoscopic surgery at the level of the upper airway system or skull base were excluded from the study. In addition, all patients with benign or malign tumours, or patients with a recent history of radio- and/or chemotherapy were also excluded from the study.

When the information on medication, comorbidities and others was missing in the patient record or questionnaire, the patient was excluded for the specific subgroup analysis.

We extracted information on the survival status out of the patient records and questionnaires as well.

Any new bleeding within 1 month after the previous episode was considered as a recurrence of the previous bleeding. A new admission more than 1 month after the previous hospitalization was considered as a new episode.

Analysis

The extracted data were entered into an SPSS work sheet. For the statistical analysis, we used measurements of central tendency and dispersion for quantitative variables (age, length of hospital stay and age at death) and absolute and relative frequencies for qualitative variables (gender, laterality of epistaxis, source of bleeding, moment of bleeding, medication intake, recent change of medication, comorbidities, referral, applied therapy, transfusion, recurrence, recidivism and survival).

Survival analysis was performed using Kaplan–Meier survival estimate.

All this was done using the programme SPSS 25. Categorical variables between groups were compared using Pearson chi-squared and Fisher's exact testing. Bonferroni correction was applied.

Results

Population (Tables 1, 2)

We included 124 patients, with 132 episodes in our database.

The mean length of hospitalization was 3.6 days (0–22) (SD 2.8). The mean age of the patients in the study population was 65 years (25–95) (SD 14.4). There was a higher proportion of males in the study group, with 63.7% males and 36.3% females. 66.7% of the epistaxis occurred between 4 and 8 a.m. in the morning. There was a fairly equal distribution in nosebleeds occurring from the left and right sides (47% and 48%) and in 5.9% of the cases the epistaxis was found to be bilateral. In 17.4%, the epistaxis was found to have an anterior source, in 73.9% a posterior source and in

Table 1 Comorbidity of the study population

	Count	Percentage of patients
Hypertension	62	56.4
Ischaemic heart disease	31	28.2
Arrhythmias	26	23.6
Diabetes mellitus	18	16.4
Valvulopathy	14	12.7
Coagulopathy	6	5.5
Renal failure	9	8.2

Amount of missing data: 14 on 124 patients

Table 2 Medication use of the study population

	Count	Percentage of episodes
Antihypertensives	67	59.8
Aspirin	42	37.8
Other antiaggregants	17	15.3
VKAs	29	26.1
NOACs	0	0.0
Heparin	2	1.8

Amount of missing data: 20 on 132 episodes

8.7% the epistaxis was located both anteriorly and posteriorly. We found mean systolic and diastolic blood pressure rates of, respectively, 153.0 (SD 27.4) and 84.2 (SD 10.4) in the emergency room (ER).

73% of our patients had comorbidities of which arterial hypertension (treated) (56.4%) was the most common one, followed by ischaemic coronary disease (28.2%).

61% of the patients were taking medication affecting the coagulation at the moment of the epistaxis and in 25.7% of the episodes a change in the medication schedule took place within the 2 weeks before the onset of epistaxis. Aspirin (37.8%) was the most frequently used anti-thrombotic, followed by vitamin K antagonists (VKAs) (26.1%).

Therapy (Tables 3, 4)

43.9% of the nosebleeds were referred to our centre, of which 5.3% by the general practitioner and 34.8% by an ENT specialist (remaining 3.8% of referrals was unfortunately not specified). In 6.9% of the episodes, the patient already underwent a cauterisation under local anaesthesia prior to the referral, in 18.9% the patient had an anterior packing in situ and in 6% a posterior packing. 3% already underwent surgery and 0.8% had an embolization performed prior to admission in our unit.

Table 3 Conservative management—packing

	Count	Percentages of episodes
No packing	18	14.8
Small Merocel, surgicel, vaseline gauze	27	22.1
Large Merocel	19	15.6
Rapid Rhino balloon/Epistat balloon	35	28.7
Foley catheter/Bellocq tamponade	8	6.6
Nasal packing—type not specified	1	0.8
Previously inserted packing left in situ	14	11.5

Amount of missing data: 10 on 132 episodes

Table 4 Vascular interventions

	Count	Percentage of vascular interventions
ESPAL	43	69.4
Internal maxillary artery ligation	2	3.2
Cautery of ethmoidal artery(-ies)	15	24.2
Cautery of mucosal bleedings	15	24.2
Embolization	2	3.2
Argon plasma coagulation	5	8.1
Vascular intervention—type not specified	1	1.6

No missing data

In terms of ER treatment, in 11.5% previously inserted packing was left in place. In 26.2%, cauterisation was performed as an attempt to halt the bleeding. In cases where the bleeding source could not be seen or additionally to cauterisation when this failed, packing was used in 73.8%.

In 47% of the episodes, a vascular intervention under general anaesthesia was needed to halt the bleeding after failed conservative treatment.

All first vascular interventions were surgical. Embolization was only performed after failed surgery (3.2%). The most performed surgical technique was ESPAL (69.4%), followed by cautery of mucosal bleeding sources (24.2%), cautery of the ethmoidal artery(ies) (24.2%), argon plasma coagulation (8.1%) and endoscopic clipping/ligation of the maxillary artery (3.2%). Sometimes, a combination of several techniques was used [ESPAL + cautery of mucosal bleedings; ESPAL + cautery of the ethmoidal artery(ies); cautery of the ethmoidal artery(ies) + cautery of mucosal bleedings].

In 90.6% of the episodes requiring a vascular intervention, the bleeding had a posterior source.

In 6.8% of the episodes, one or more blood transfusions were required, and for 82% of these episodes, the bleeding had a posterior source.

Nobody had to be resuscitated.

Outcomes and correlations

In 14.5% of all patients, a recurrence within a month and/or a new episode within 1 year after hospitalization occurred.

88.8% of these new bleedings were recurrences within 1 month. The median time to recurrence of the bleedings occurring within a year was 12 days.

In two patients, a new episode took place more than 1 year after the last hospitalization.

When only conservative measures were applied, the epistaxis was controlled for at least 1 month and at least 1 year after treatment in 48% and 47%, respectively.

The success rate of conservative treatment for anterior epistaxis was found to be 70%. For posterior epistaxis this was found to be 33.7%.

In the case where a vascular intervention was applied, the bleeding was controlled for at least 1 month and at least 1 year in 82% and 81%, respectively.

The success rate of surgery for anterior epistaxis was 100% and for posterior epistaxis 79.5%.

The overall 5-year survival rate was 83.6%.

No significant difference between the recurrence rates and need for vascular intervention of the different comorbidities and medications were detected.

Discussion

Our study demonstrates that the typical pattern of patients being hospitalized for severe epistaxis in the ENT department of the University hospital of Ghent is male, middle to advanced age, displaying some underlying comorbidity, taking medication affecting the coagulation and presenting a posterior epistaxis that started between 4 and 8 a.m. A descriptive study of a case series of patients hospitalized for epistaxis in the ENT-department of a tertiary hospital in Alicante, Spain, showed the same clinical profile of patients [7].

An increased incidence of epistaxis in patients older than 50 exists which has been stated in literature [7, 8]. We can confirm this finding, with a mean age of 65 years and 86% of the patients being above 50 years of age.

Male predominance of epistaxis has already been stated in large case series [7, 9] and can also been confirmed by our case series.

The circadian variation in onset of epistaxis was already investigated by Mafredini et al. and showed a similar biphasic pattern of onset of epistaxis as in our case series, with a primary peak in the morning and a smaller secondary peak in the evening. This biphasic pattern is consistent with the physiological circadian variation of blood pressure, which suggests that blood pressure could trigger or be conducive to epistaxis [10].

Since many years, it has been suggested that hypertension contributes to epistaxis. 73% of our patient population suffered from significant comorbidities of which arterial hypertension (treated) (56.4%) was the most common one. In the previously mentioned case series conducted in Alicante, the study population showed a prevalence of hypertension of 56% as well [7]. The contribution of hypertension in epistaxis stays, however, controversial. Although some studies, including ours, report an elevated blood pressure during epistaxis, it remains unclear if this rise in blood pressure is the cause or result of the bleeding, as epistaxis can lead to hypertension caused by anxiety [11–13]. Furthermore, hypertension is age dependent and the prevalence amounts to 60–70% of the population above 60 years of age [14]. Herkner et al. found that patients with an elevated blood pressure during epistaxis and consequent sustained arterial hypertension had significantly more episodes of epistaxis compared with patients without sustained arterial hypertension [12]. We, however, could not find any statistically significant association between hypertension and the need for vascular intervention or recurrence.

Common among etiological factors of epistaxis are drugs having an influence on the coagulation. 61% of our patient population was taking medication affecting the coagulation at the time of the epistaxis of which aspirin was the most important one (37.8%). The use of aspirin has been clearly implicated in contributing to epistaxis [1]. A prospective cohort study of 2008 showed that the patient group taking aspirin required more surgical interventions, had a higher recurrence rate and required a larger number of treatment modalities in the treatment of epistaxis [15]. Another study found clopidogrel and aspirin to be associated with an increased risk of troublesome epistaxis, without any difference between these two drug groups [6, 16]. Bleeding is also known to be the most important complication of VKAs [17]. Our study is, however, not conclusive to confirm any association between the use of anti-thrombotics and need for vascular intervention or recurrence.

Novel anticoagulant drugs (NOACs) have been introduced in the past 10 years and one of the advantages of NOACs over VKAs is their lower incidence of major bleeding [18]. At the time of our study, none of our study patients was taking NOACs. This finding could confirm the lower bleeding incidence with NOACs. Nonetheless, we have to be careful concluding this since a significant lower number of patients were treated with NOACs compared to VKAs at the time of our study.

Current knowledge on pharmacokinetics and –dynamics, and interactions of drugs mutually is very extensive. Except for some case reports, no studies are published yet, which examine the pharmacological profile and possible drug interactions in patients with severe epistaxis [19–22]. In 25.7% of our population, a recent change in the medication schedule took place. To our opinion, our case series provides the largest study population in whom a medication change in the recent past before the epistaxis was examined. Unfortunately, the quality of these results is low considering the retrospective character and the great amount of missing data in this sub-analysis. Nevertheless, this finding seems an interesting future research topic.

53% of the episodes were exclusively treated by conservative treatment modalities. 48% of these episodes were controlled for 1 month or more and 47% of the patients who exclusively underwent conservative treatment were controlled for at least 1 year. A randomized clinical trial comparing Merocel and Rapid Rhino packing for anterior

epistaxis showed a success rate of approximately 70% for both packings [23]. In our study, we found a similar success rate of conservative treatment for anterior epistaxis. In literature, many authors evidenced a high failure rate with posterior nasal packing, ranging from 26 to 52% [24–26]. In our department, we also evidenced a high failure rate with posterior nasal packing (33.7%). More recent research of Soyka et al. showed that the successful treatment of posterior epistaxis in their department could be achieved in 62% by packing and in 97% by surgery [27].

The traditional approach of posterior nasal packing has nowadays been largely replaced by ESPAL and endovascular arterial embolization [28]. In 47% of the episodes, a vascular intervention under general anaesthesia was needed to halt the bleeding after failed conservative treatment and the most performed surgical technique was ESPAL (69.4%). With the widespread popularization of endoscopic sinus surgery and a greater understanding of local regional anatomy, ESPAL has become the preferred form of surgery [24]. Ligation of the ethmoidal artery(-ies) is a different surgical procedure performed in intractable anterior epistaxis, that is most often caused by trauma or iatrogenic injury [29]. Compared to ligation of the internal maxillary artery, ESPAL seems to have less severe peri- and post-operative complications and a shorter hospital stay [30].

Kumar et al. reviewed the evidence for the efficacy of ESPAL in epistaxis. Based on 11 studies with an average follow-up of 9.8 months, the efficacy of the operation was found to be between 92% and 100% [31, 32]. Nouraei et al. published a success rate of ESPAL of 92% at 9.8 months [31]. The success rate of surgery in our institution was roughly 10% lower than the above-mentioned results.

A prospective randomized trial showed that ESPAL enables a reduced inpatient stay, improved patient satisfaction and cost reductions compared to traditional packing techniques [33]. More recent research of Dedhia et al. confirmed that ESPAL is the most cost-effective strategy compared with posterior packing [28, 34] and in literature there is growing body of support for early intervention in epistaxis with ESPAL [35].

Five patients in our study population underwent an embolization, after one or more failed surgical interventions. The 1-year success rate of embolization in our institution was 60%.

Rudmik et al. stated that the success rates for both ESPAL and embolization are estimated to be greater than 90% [28]. Our results of embolization are significantly lower; nonetheless, this lower success rate might be explained by the fact this analysis only included five patients and that these patients already underwent one or more surgical interventions, which emphasize the severity of their epistaxis.

The above-mentioned findings emphasize the need to apply a well-defined therapeutic protocol with appropriate patient selection for early surgical intervention. Our data collection was executed until 2012 and at that time we were not using a well-defined protocol for epistaxis in our centre yet. Since 2013, we are using a protocol for epistaxis based on the 'Dundee protocol' in our department [36]. Further research to test the effectiveness of our therapeutic algorithm and to compare the outcomes seems promising.

In addition to local therapy, in 6.8% of the episodes one or more blood transfusions were given. Murer et al. investigated the common factors that may represent risk factors for blood transfusion in patients during their epistaxis treatment. Patients with severe nosebleeds, especially of posterior origin, who had several bleeding episodes over time before presenting at their institution, were at increased risk to undergo surgery and also to receive blood transfusions [37]. The posterior location as a risk factor for blood transfusion and need for vascular intervention was confirmed in our case series: for 88.9% of the blood transfusions and 93.5% of the episodes requiring a vascular intervention, the bleeding had a posterior source.

Eikelboom et al. stated that there is growing evidence that both minor and major bleeding are independently predictive of adverse clinical outcomes, including myocardial infarction, stroke, and death. Major bleeding was found to be associated with a two- to eightfold increase in the risk of death among patients with acute coronary syndromes [38–42]. The overall 5-year survival rate in our study was 83.6%, possibly confirming the presumption that severe epistaxis can be an independent predictive of adverse outcome. To our knowledge, we are the first authors publishing results on this topic. Unfortunately, there are some important limitations on these results considering the retrospective character of our study and the fact our study population only consists of 124 patients. Nevertheless, it seems prudent to conclude that a full cardiovascular workup is advised in patients presenting with severe spontaneous epistaxis. Future research should provide more clarity on this topic.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

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