Epidemiological, clinical and endoscopic features of epistaxis severity and quality of life in Hereditary haemorrhagic telangiectasia: a cross-sectional study*

Fabio Pagella[1,2], Eugenia Maiorano[2], Sara Ugolini[2], Roberta Lizzio[2], Fabio Sovardi[2], Rosolino Mirabella[1,2], Ludovica Nanfitò[1,2], Carmine Tinelli[3], Annalisa De Silvestri[3], Carla Olivieri[4], Giuseppe Spinozzi[2], Elina Matti[2]

[1] Department of Otorhinolaryngology, University of Pavia, Pavia, Italy

[2] Department of Otorhinolaryngology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

[3] Clinical Epidemiology and Biometry Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

[4] Molecular Medicine Department, General Biology and Medical Genetics Unit, University of Pavia, Italy

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Abstract

Background: Epistaxis is the main complaint in patients with Hereditary haemorrhagic telangiectasia (HHT). Even though the role of epistaxis in affecting the quality of life (QoL) is well-known, little is known about epidemiological and clinical factors contributing to epistaxis severity and QoL.

Methodology: This is a cross-sectional study, including adult patients with HHT with epistaxis. All patients underwent an oto-laryngological evaluation with nasal endoscopy. Epistaxis severity was graded using the FID score, and QoL was evaluated with the Short-Form Health Survey (SF-36). Descriptive statistics were produced for demographic characteristics; the Shapiro-Wilk test was used to test the normal distribution of quantitative variables. Correlation between the quantitative variables was evaluated with Pearson's correlation coefficient. Both univariate and multivariate linear regression models were fitted to find associations between demographic or clinical factors and the FID score or SF-36.

Results: A total of 234 patients with HHT were included in the study. The univariate analysis highlighted the association between high blood pressure, septal perforation, nocturnal epistaxis, surgery, blood transfusion, hormonal therapy and both FID score and QoL. Sex, allergic rhinitis and nasal polyposis were neither related to epistaxis severity nor perceived health.

Conclusions: Epistaxis severity and QoL in patients with HHT are influenced by several clinical factors both dependent and independent from HHT. Some of the results are consistent with those already published, but for the first time, we extended the analysis to different clinical parameters, such as endoscopic findings, never assessed before.

Key words: epistaxis, FID score, HHT, quality of life, SF-36

Introduction

Hereditary Haemorrhagic telangiectasia (HHT) is a rare autosomal dominant genetic disease, which is characterized by vascular dysplasia leading to visceral and mucocutaneous arteriovenous malformations (AVMs) [1,2]. HHT has a highly variable phenotype and an almost complete age-related penetrance [3,4]. Mucocutaneous telangiectases are most frequently found on the nasal and oral mucosa and on the face and skin of the fingers. Visceral AVMs may affect the lungs, liver, central nervous system and gastrointestinal tract [5]. The clinical spectrum of HHT is very heterogeneous, ranging between minimal anomalies to life-threatening manifestations [3,6]. Approximately 80% of patients with HHT develop gastric or intestinal telangiectases throughout their lifetime, but gastrointestinal (GI) bleeding is present in only 30% of cases.

Pulmonary AVMs (PAVMs) are present in 15-50% of patients with

HHT. These may cause both neurologic complications, related to the right-left shunt and the consequent paradoxical embolization, and haemorrhagic complications due to the rupture of AVMs [3]. Liver vascular malformations are reported in 32-78% of patients, being most frequently asymptomatic, but occasionally producing portal hypertension, high output heart failure and biliary necrosis [3]. Cerebral vascular malformations are reported in 10% of patients with HHT; they may be asymptomatic or associated with headache and epilepsy due to bleeding [1].
Epistaxis is the most common symptom at presentation and is reported by 95% of patients, with the mean age of 12 years old at onset. The recurrence and severity of epistaxis frequently leads to iron deficiency anaemia, multiple blood transfusions and nasal surgery. Epistaxis is the main complaint of patients and represents the most common cause of disability and social impairment. Its severity has been associated with a lower quality of life (QoL)[7,8], and in the absence of definitive treatment, this explains why, nowadays, there is a tendency to address the treatment toward improving the QoL of patients [9,10]. Even if the relationship between epistaxis severity and perceived health is well-known, a detailed study of the contributing factors is missing. Therefore, the present study was designed in order to analyse epistaxis severity and QoL in a cohort of adult patients with HHT, stratifying the results according to clinical findings typical of the disease or even not directly associated with HHT.

Materials and methods

The present observational cross-sectional study was conducted at the Otolaryngology Department of our institution (Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), after being approved by the Internal Review Board and Ethics Committee (reference number 1-29/1/14). To ensure high-quality presentation, the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines were followed [11]. Furthermore, the present research project was designed and conducted following the principles stated by the Declaration of Helsinki and by the guidelines for Good Clinical Practice.

Study population

Patients with HHT consecutively referred to our department between November 2014 and February 2018 were recruited. Inclusion criteria were as follows: clinical diagnosis of HHT according to Curaçao diagnostic criteria or positivity at genetic testing [12,13], spontaneous and recurrent epistaxis and age ≥ 18 years. Written informed consent was obtained from all study participants.
All patients underwent nasal endoscopy and a general physical examination, including inspection for telangiectases, particularly on the face, oral cavity, oropharynx and fingers. All nasal endoscopies were performed bilaterally with a 0° endoscope using an IMAGE1 S™system (Karl Storz GmbH & Co., Tuttlingen, Germany). Two expert rhinologists (FP and EM) assessed the presence of telangiectases, septal perforation, allergic rhinitis, nasal polyposis and other eventual nasal pathologies [14].
Transthoracic contrast echocardiography, high-resolution chest computed tomography and abdominal ultrasound to screen for pulmonary and hepatic AVMs were proposed to all participants. Genetic counselling and tests were proposed for the index case of the family and relatives.

Epistaxis severity and quality of life measurement

Every patient filled in the Frequency, Intensity and Duration (FID) score questionnaire and the Italian version of the Short Form Health Survey (SF-36).
The FID score is a precise and quick validated grading system for evaluating HHT-related epistaxis [15]. It is based on the average frequency, intensity and duration of epistaxis in the last 3 months and is calculated as the sum of the scores (1, 2 or 3) for each value. Epistaxis severity is considered low if the sum is 3, mild if 4-6 and severe if 7-9.
The SF-36 questionnaire is an internationally recognized tool to assess a patient's level of health and corresponding QoL. It has been validated by Ware et al. and consists of 36 questions regarding the following eight aspects of health: physical functioning (PF), role limitations because of physical health problems (RP), bodily pain (BP), social functioning (SF), general mental health (psychological distress and psychological wellbeing) (MH), role limitations because of emotional problems (RE), vitality (VT) and general health perceptions (GH), and it also includes a single-item measure of health transition or change [16,17]. SF-36 scores on these dimensions may also be summarized to obtain a physical component score (PCS) and a mental component score (MCS). The PCS averaged the results for the following items: PF, RP, BP and GH. Similarly, the MCS averaged the results for VT, SF, RE and MH.
The score ranges from 0 to 100, with 0 indicating the worst condition and 100 representing the best condition.

Statistical analysis

Descriptive statistics were produced for demographic characteristics for this study sample of patients. The Shapiro-Wilk test was used to test the normal distribution of quantitative variables. When quantitative variables were normally distributed, the results were expressed as the mean value and standard deviation (SD). Otherwise, the median and interquartile range (IQR; 25th-75th percentile) were reported. Qualitative variables were summarized as counts and percentages.
Correlation between the quantitative variables was evaluated with Pearson's correlation coefficient.
Both univariate and multivariate linear regression models were fitted to find associations between demographic or clinical factors (independent variables) and the FID or SF-36 scores

Table 1. Patients' clinical features (n° 234).

	N (%)
Sex	
Males	125 (53.4)
Female	109 (46.6)
Comorbidities and therapies	
High blood pressure	66 (28.5)
Allergic rhinitis	75 (32.2)
Nasal polyposis	10 (4.3)
Septal perforation	37 (16.2)
Hormonal therapy	18 (12.1)
Anticoagulant / antiplatelet therapy	34 (14.7)
AVM	
Pulmonary AVM	56[a] (28.7)
Hepatic AVM	60[b] (29.9)
Surgery for epistaxis	
Yes	119 (51.7)
No	115 (48.3)
Age at first nosebleed	
< 10 years	79 (33.9)
10-20 years	81 (34.8)
20-30 years	33 (14.2)
30-40 years	18 (7.7)
> 40 years	22 (9.4)
Nocturnal epistaxis	
Rare	113 (49.3)
Frequent	92 (40.2)
No	24 (10.5)
Blood transfusions	
Yes	91 (39.7)
No	143 (60.3)
Age at first transfusion	
< 10 years	3 (3.4)
10-20 years	6 (6.8)
20-30 years	4 (4.6)
30-40 years	6 (6.8)
> 40 years	69 (78.4)
Number of transfusions	
< 5	39 (42.8)
5-10	10 (11.0)
>10	42 (46.2)

AVM = arteriovenous malformations; [a] = data on 195 patients; [b] = data on 201 patients

(dependent variables). Results are expressed as coefficients with their 95% confidence intervals (CIs) and presented with term specific p-values; the coefficient represents the mean variation of outcomes for unit change of quantitative predictors or between levels of categorical or ordinal predictors. $p < 0.05$ was considered statistically significant. All tests were two-sided. The data analysis was performed with the STATA statistical package (release 14.0, 2015, Stata Corporation, College Station, TX, USA).

Results

A total of 234 patients were included in the study (109 females and 125 males). The mean age of patients was 54 years (SD 15.4), ranging between 18 and 83 years. Table 1 summarizes the clinical features of patients. The mean FID score was 5.0 (SD 2.5), with 51.7% of patients requiring surgery for epistaxis and 39.7% requiring transfusion during their lifetime.

Epistaxis severity

As shown in Table 2, patients with high blood pressure, septal perforation, nocturnal epistaxis and those who needed surgery or blood transfusion had significantly higher FID scores ($p < 0.05$). Age also appeared to play an essential role in determining epistaxis severity, with FID values statistically higher with advancing age. Sex, allergic rhinitis, nasal polyposis, anticoagulant or antiplatelet therapy and the presence of hepatic AVMs were not related to a significant difference in epistaxis severity. Women receiving hormonal therapy had significantly lower epistaxis scores ($p = 0.039$). Multivariate regression analysis confirmed the association between the FID score and nocturnal epistaxis ($p = 0.016$ and $p = 0.001$ for rare and frequent nocturnal epistaxis, respectively).

Quality of life

Concerning the QoL, our sample demonstrated lower scores in every SF-36 result, with a maximum difference in physical role limitation (Δ of -34.8%) and emotional role limitation (Δ of -32.7%), compared to a healthy Italian population (Table 3) [17]. Epistaxis severity is negatively correlated with PCS (-0.38; $p < 0.01$) and MCS (-0.31; $p < 0.01$). In particular, among the components of the FID score, the strongest correlation was found between epistaxis duration and PCS (-0.43; $p < 0.01$) and epistaxis frequency and MCS (-0.30; $p < 0.01$).

Table 4 reports the results of the SF-36 evaluation in the study sample, analysing PCS and MCS, as well as highlighting the specific dimension of health when statistically significant.

Both physical and mental dimensions were negatively influenced by high blood pressure, nocturnal epistaxis and blood transfusion, in particular the number of blood transfusions needed over a lifetime. The need for nasal surgery was associated with a significantly worst PCS, while MCS was not significantly lower. The presence of septal perforation did not affect only the PCS but also two subscales of MCS, while the mental dimension altogether/globally seemed not significantly worsened.

Table 2. FID score for epistaxis severity according to patients' characteristics – Univariate analysis.

	FID score	
	Mean (SD)	p
Sex		
Male	5.9 (1.9)	0.084
Female	5.5 (1.8)	
Age		
< 30 years	4.7 (1.46)	*0.03
30-39 years	5.1 (1.93)	
40-49 years	5.6 (1.77)	
50-59 years	5.9 (1.88)	
60-69 years	6.1 (1.96)	
> 70 years	6.0 (2.05)	
High blood pressure		
Yes	6.4 (2.0)	*0.002
No	5.5 (1.9)	
Allergic rhinitis		
Yes	5.8 (1.9)	0.847
No	5.7 (1.9)	
Nasal polyposis		
Yes	6.2 (1.8)	0.459
No	5.7 (1.9)	
Septal perforation		
Yes	6.4 (2.0)	*0.015
No	5.6 (1.8)	
Hormonal therapy (female only)		
Yes	4.5 (1.6)	*0.039
No	5.7 (2.0)	
Anticoagulant / antiplatelet therapy		
Yes	6.0 (2.1)	0.424
No	5.7 (1.9)	
Pulmonary AVM		
Yes	5.4 (1.9)	*0.044
No	6.0 (1.8)	
Hepatic AVM		
Yes	6.0 (2.0)	0.304
No	5.7 (1.9)	
Surgery for epistaxis		
Yes	6.4 (1.9)	*< 0.001
No	5.2 (1.7)	
Age at first nosebleed		
< 10 years	5.6 (2.0)	0.767
10-20 years	5.9 (1.9)	
20-30 years	6.0 (1.8)	
30-40 years	5.6 (1.8)	
> 40 years	5.8 (1.7)	
Nocturnal epistaxis		
No	4.1 (1.4)	*< 0.001
Rare	5.5 (1.9)	
Frequent	6.5 (1.8)	
Blood transfusions		
Yes	6.4 (2.0)	*< 0.001
No	5.4 (1.8)	
Age of first transfusion		
< 10 years	5.0 (2.6)	0.104
10-20 years	6.5 (2.3)	
20-30 years	6.8 (1.3)	
30-40 years	8.3 (1.2)	
> 40 years	6.2 (2.0)	
Number of transfusions		
< 5	5.4 (2.0)	*< 0.001
5-10	6.1 (1.6)	
> 10	7.4 (1.6)	

FID score = Frequency-Intensity-Duration score; AVM = arteriovenous malformation.

No significant differences associated with allergic rhinitis, nasal polyposis, age at first nosebleed and anticoagulant/antiplatelet consumption were reported.

The multivariate regression analysis confirmed that frequent nocturnal epistaxis ($p = 0.008$) and need for blood transfusion ($p < 0.001$) played important roles in determining the QoL in patients with HHT.

Discussion

Epistaxis is the most commonly reported symptom of HHT. Recurrent and spontaneous epistaxis generally appears before the age of 20 years and affects 95% of all adult patients with HHT (3). The frequency of episodes ranges between a few per year and several per day and intensity ranges between slight stains on the handkerchief and gushing.

Epistaxis is extremely frequent, even in people without HHT, as nearly 60% of the population experience a nosebleed at least once in their lifetime. Also, according to a recent study, nosebleeds account for 0.32% of all emergency department visits [18]. Several studies have analysed the possible causes of epistaxis in the general population, evaluating the role of systemic diseases, such as haematologic, hepatic, cardiovascular and renal pathologies. The association between hypertension and epistaxis is well-known, with a prevalence varying from 24% to 64% [19]. An-

Table 3. Comparison of SF-36 results between HHT patients and normal Italian population.

	HHT (n° 234)	Normal Italian population (n° 2031)	Difference between population	
	Mean (SD)	Mean (SD)	Δ abs	Δ %
Physical functioning - PF	76.5 (24.0)	84.5 (23.2)	-7.93	-9.4%
Physical role limitation - RP	51.0 (42.0)	78.2 (35.9)	-27.23	-34.8%
Bodily pain – BP	70.7 (31.2)	73.7 (27.7)	-3.02	-4.1%
General health – GH	52.6 (22.8)	65.2 (22.2)	-12.64	-19.4%
Vitality – VT	52.7 (22.3)	61.9 (20.7)	-9.19	-14.8%
Social functioning – SF	62.3 (28.3)	77.4 (23.3)	-15.15	-19.6%
Emotional role limitation - RE	51.2 (43.1)	76.2 (37.3)	-24.93	-32.7%
Mental health - MH	63.0 (21.5)	66.6 (20.9)	-3.57	-5.4%

ticoagulant agents may increase the risk of epistaxis [20]. The use of aspirin has a controversial role in determining epistaxis. Tay and colleagues [21] found a positive correlation between epistaxis and aspirin use, while Beran and collaborators [22] did not find differences between aspirin users and controls in habitual nose bleeders. There is no reported increased risk associated with other nonsteroidal anti-inflammatory drugs [21].

As far as patients with HHT are concerned, the factors specifically involved in epistaxis severity are still a matter of debate.

The first report of an extensive series of patients with HHT receiving anticoagulant therapy was published in 2012 [23]. Authors reported that the majority of patients with HHT could tolerate anticoagulant/antiplatelet therapy without significant haemorrhage, with 46% having a worsening of epistaxis and 3% with a new development of epistaxis [23]. Another study published in 2013 revealed that 40% of patients with HHT who received antiplatelet or anticoagulant therapy reported no change in their nosebleeds, while 2% of patients reported an improvement, with a lower number of episodes [24]. A recent retrospective audit conducted by the European Reference Network for Rare Multisystemic Vascular Diseases analysed the use of the newer direct oral anticoagulants, finding a similar HHT bleeding profile to existing anticoagulants for apixaban [25]. Our results align with published data, with an epistaxis severity not significantly affected by antiplatelet/anticoagulant agents.

With regards to hormonal therapy, in our study sample, it was significantly associated with a reduced FID score. This finding confirms previous reports by other authors in which oestrogen, oestrogen plus testosterone, oestrogen plus progesterone, progesterone and tamoxifen may reduce bleeding in patients with symptomatic HHT [26,27].

Interestingly, comorbidities characterized by sinonasal inflammation, such as nasal polyposis and allergic rhinitis, did not appear significantly associated with epistaxis severity. In particular, the 75 patients with allergic rhinitis, despite underlying inflammation of the nasal mucosa, did not report significantly worse epistaxis scores compared to others. Similarly, in the 10 patients with nasal polyposis, there was no relationship between epistaxis severity and the underlying pathology, but this finding may be affected by the small number of patients.

The association between high blood pressure and epistaxis severity found in our sample is, as we have seen, already known in the literature [19]. On the contrary, concerning epistaxis severity in patients with HHT with previous nasal surgery and septal perforation, there is only one report [28]. In 2005, Folz and colleagues analysed questionnaires from 49 patients with HHT, and those reporting the presence of septal perforation had to be admitted for inpatient epistaxis treatment more frequently than patients with an intact nasal septum [28]. Our data, with the support of the endoscopic investigation, confirmed that patients with a history of nasal surgery for epistaxis have a greater epistaxis severity. A possible explanation is that patients with severe epistaxis are more inclined to ask for surgical help. Therefore, epistaxis severity might be higher, even before surgery. However, it is essential to emphasize the relevance of careful planning of the surgical intervention both in the acute phase and prevention to avoid a worsening of epistaxis severity.

Epistaxis often significantly interferes with the life routines of patients with HHT because of the frequent need for medical attention. The first study about QoL in patients with HHT was published in 2004 by Pasculli et al. and compared the SF-36 score of a cohort of 50 patients with HHT with the values reported in a healthy Italian population [29]. They found a significant reduction in all scales, except for BP; furthermore, females showed significantly lower PF scores, RP, RE, and PCS [29]. In 2005, Lennox et al. compared the results of the SF-36 questionnaire of 38 patients with HHT with healthy patients. In all dimensions, except for BP, patient groups demonstrated lower scores, and they found no correlation between the SF-36 score and number of blood

Table 4. SF-36 results according to patients' characteristics - Univariate analysis.

	PCS		MCS		Subscales
	Mean (SD)	p	Mean (SD)	p	
Sex					BP (F = 65.3 vs M = 75.2; p = 0.016)
Male	46.2 (10.7)	0.253	42.1 (10.9)	0.646	
Female	44.6 (10.1)		41.4 (12.0)		
High blood pressure					/
Yes	43.0 (10.6)	*0.020	38.8 (11.7)	*0.010	
No	46.6 (10.2)		43.1 (11.2)		
Allergic rhinitis					/
Yes	46.4 (9.8)	0.393	41.8 (11.8)	0.992	
No	45.1 (10.7)		41.8 (11.4)		
Nasal polyposis					/
Yes	42.2 (11.9)	0.301	40.2 (11.5)	0.651	
No	45.7 (10.3)		41.9 (11.5)		
Septal perforation					RE (Yes=32.4 vs No=54.8; p = 0.004), SF (Yes = 52.1 vs No = 64.7; p = 0.013)
Yes	41.0 (9.3)	*0.003	39.5 (11.5)	0.193	
No	46.6 (10.2)		42.3 (11.4)		
Hormonal therapy					
Yes	50.0 (8.5)	*0.055	45.9 (10.0)	*0.119	
No	43.9 (10.7)		40.8 (11.1)		
Anticoagulant / antiplatelet therapy					GH (Yes = 42.7 vs No = 54.6; p = 0.004) MH (Yes = 54.1 vs No = 64.5; p = 0.022)
Yes	42.8	0.0851	38.8 (13.3)	0.099	
No	46.1		42.4 (11.1)		
Pulmonary AVMs					RE (Yes = 62.3 vs No = 47.5; p = 0.029)
Yes	46.1 (9.9)	0.794	44.2 (11.9)	0.900	
No	45.7 (10.6)		41.0 (11.1)		
Hepatic AVMs					GH (Yes = 46.3 vs No = 55.5; p = 0.009)
Yes	43.5 (10.7)	0.079	41.5 (11.6)	0.900	
No	46.4 (10.2)		41.7 (11.3)		
Surgery for epistaxis					SF (Yes=56.5 vs No = 68.5; p < 0.001)
Yes	43.6 (9.5)	*0.003	40.9 (11.5)	0.248	
No	47.8 (10.8)		42.7 (11.6)		
Age at first nosebleed					/
< 10 years	45.2 (9.6)	0.072	40.0 (11.2)	0.158	
10-20 years	45.6 (10.9)		43.0 (11.79		
20-30 years	47.9 (11.0)		45.1 (11.0)		
30-40 years	48.6 (7.2)		38.7 (10.2)		
>40 years	40.4 (11.3)		40.6 (12.0)		
Nocturnal epistaxis					/
No	51.5	*< 0.001	46.6 (10.4)	*< 0.001	
Rare	46.6		43.5 (11.3)		
Frequent	42.5		38.5 (11.1)		
Blood transfusion					/
Yes	41.1	*< 0.001	39.6 (11.3)	*0.025	
No	48.2		43.2 (11.5)		

	PCS		MCS		Subscales
	Mean (SD)	p	Mean (SD)	p	
Age of first transfusion					SF (30-40 years = 20.8 vs >40 years = 58.5; p = 0.028)
< 10 years	43.0	*0.018	41.2 (13.6)	0.080	
10-20 years	40.2		39.3 (5.9)		
20-30 years	35.8		27.2 (10.2)		
30-40 years	28.5		31.8 (8.5)		
> 40 years	42.4		40.5 (11.3)		
Number of transfusions					/
< 5	45.5	*< 0.001	43.1 (11.9)	*0.028	
5-10	42.7		37.8 (11.1)		
> 10	36.6		36.3 (10.1)		

AVMs = Arteriovenous malformations, PCS = physical component score; MCS = mental component score; BP = bodily pain; RE = emotional role limitation; SF = social functioning; GH = general health perceptions; MH = general mental health.

transfusions required [30]. In 2007, Geisthoff et al. analysed a cohort of 77 patients. They revealed that the duration of epistaxis, liver involvement, gastrointestinal bleeding, and the number of visible telangiectases significantly influenced the HR-QoL in HHT. In contrast, the epistaxis frequency seemed to play a minor role [31]. In 2011, Ingrand et al. were the first to consider preventive treatment. In their cohort of 109 patients, the duration of epistaxis, comorbidities, visceral involvement, transfusions and the need for prophylactic treatment were associated with several dimensions of the SF-36 [32]. In 2012, Geirdal et al. studied 66 Norwegian patients and stated the correlation between the intensity and frequency of epistaxis and the SF-36; except for BP, no significant differences were found between genders [33]. In 2014, Merlo et al. published the most extensive QoL study on patients with HHT. In a total of 604 patients, they demonstrated a linear association between epistaxis severity and the physical and mental well-being of patients [7]. Some other studies did not use the SF-36 questionnaire or analysed only specific aspects of the QoL; however, they still reported worse scores in patients with HHT compared to a normal population [34–36].

In our study sample, the SF-36 results in patients with HHT were significantly lower compared with a normal Italian population. High blood pressure, nocturnal epistaxis and the need for blood transfusion are associated with a lower QoL. Interestingly, previous surgery for epistaxis and the presence of septal perforation significantly affected the physical scores of the SF-36, while only some subscales of mental scores were involved. Concerning hormonal therapy, both PCS and MCS appeared improved.

In particular, multivariate analysis showed that frequent nocturnal epistaxis and the need for blood transfusion have the higher impact in determining a lower level of physical and mental well-being.

Our study has some limitations, indeed. The study is cross-sectional and does not allow for casual inferences. All patients with HHT included in the study have epistaxis and were referred to our department; therefore, it is possible that their epistaxis severity may not be representative of a larger population of patients with HHT.

Conclusion

Despite these possible limitations, the present research project adds interesting new insights into the field of HHT. It is the first study in Europe involving such a large number of patients and considering so many variables, both dependent and independent from HHT. Besides, the endoscopic evaluation made it possible, for the first time, to correlate nasal pathologies with nosebleed severity and QoL in patients with HHT.

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Authorship contribution

FP, EM and GS study design, data interpretation and manuscript review; EM literature search, data collection, interpretation and writing of the manuscript. CT and ADS data analysis.

Conflict of interest

The authors declare that they have no conflict of interest.

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Eugenia Maiorano
Department of Otorhinolaryngology
Fondazione IRCCS Policlinico San Matteo
Piazzale Golgi 19
27100 Pavia
Italy

Tel: +39-3342613552
E-mail: eugenia_maiorano@libero.it
ORCID ID 0000-0001-7876-0489