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# CAN HYPERCOAGULABILITY STATUS HAVE AN IMPACT ON THE RECOVERY OF AUDITORY THRESHOLDS? SUDDEN NEUROSSENSORIAL HEARING LOSS

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#### ARTICLE INFO

### ABSTRACT

Article History: Received 10 <sup>th</sup> April, 2018 Received in revised form 18 <sup>th</sup> May, 2018 Accepted 26 <sup>th</sup> June, 2018 Published online 28 <sup>th</sup> July, 2018	<b>Introduction:</b> Sudden sensorineural hearing loss (SSHL) is a clinical diagnosis, characterized by decrease in hearing of $\geq 30$ decibel (dB) affecting at least three consecutive frequencies, occurring over a 72 hour period. Since some theories advocate blood viscosity phenomena as a probable aetiology for SSHL, in our study we attempted to understand the impact of "hypercoagulability state" (atrial fibrillation / active oncologic disease) on the recovery of audiometric thresholds. <b>Materials and Methods:</b> Retrospective study of all cases of SSHL diagnosed on a two and
Key words:	a half year period at the Ear, Nose and Throat (ENT) Department in a tertiary referral center. The purpose of this study was to demonstrate the impact of comorbidities on the
Sudden sensorineural hearing loss; oncology disease; auricular fibrillation	recovery of hearing thresholds. <b>Results:</b> The mean age at diagnosis was 58 years, with 59% of cases being males. Twenty four % had "hypercoagulability state" (atrial fibrillation / active oncologic disease). Regarding management, 76% were treated with systemic corticosteroid therapy. The mean tonal threshold at the time of diagnosis was 81 dB and the mean threshold value after at least 6 months was 59 dB, [statistical significance ( $p < 0.05$ )]. In patients without a "hypercoagulable state", the improvement of auditory thresholds was higher compared to those with that comorbidity ( $p < 0.05$ ) <b>Conclusions:</b> We concluded that patients with "hypercoagulable state" have worse hearing thresholds recovery and therefore, it should be considered as a risk factor for recovery of SSHL.

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# **INTRODUCTION**

Sudden hearing loss is defined as a rapid onset, occurring over a 72 hour period, of a subjective sensation of hearing impairment in one or both ears. Sudden sensorineural hearing loss is a sub-set of sudden hearing loss (representing any abnormality of the cochlea, auditory nerve or higher aspects of central auditory perception or processing). The following audiometric criteria need to be fulfilled: decrease in hearing of  $\geq$  30 decibels (dB) affecting at least three consecutive frequencies. Since generally premorbid audiometry is unavailable, hearing loss is defined as related to the opposite ear's thresholds.<sup>1</sup>

Sudden hearing loss is a relatively common complaint of ENT daily practice with an incidence of  $5-20 / 100,000.^2$ .

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Department of Otorhinolaryngology, Head and Neck Surgery, Centro Hospitalar Vila Nova de Gaia/Espinho Rua Conceição Fernandes, s/n, 4434-502, Vila Nova de Gaia, Portugal It was first described in 1944 as a sudden unilateral episode with loss  $\geq$ 30 dB in at least 3 contiguous audiometric frequencies, in a period of less than 72 hours.<sup>3</sup> Spontaneous recovery rates of auditory thresholds are reported in 32-65% of the cases, which suggests that many patients could have this pathology without seeking for medical care.<sup>4-5</sup> Thus, in this context, its true incidence may be much higher than that currently reported. Several theories have been proposed in order to understand which mechanisms are in the genesis of SSHL, including vascular disorders (thromboembolic events, vasoconstriction phenomena, hypertension and blood viscosity), viral infections, autoimmune diseases, metabolic cochlear damage and ototoxicity.<sup>5-8</sup> In a meta-analysis of 23 studies on sudden sensorineural hearing loss, the most frequently identified causes were infectious (13%), otologic (5%), traumatic (4%), vascular or haematological (3%), neoplastic (2%) and others (2%).

In fact, in addition to the uncertainty about the aetiology and true incidence of this pathology, there is also some controversy regarding to the necessity of treatment. In fact, 45-65% of patients present spontaneous resolution without any

treatment.<sup>2,5,7</sup> Several treatments and agents have been investigated including anti-inflammatories, antimicrobials, calcium channel blockers, vitamins, vasodilators, diuretics and hyperbaric oxygen therapy.<sup>10</sup> However, in the United States, 98% of Ear Nose and Throat (ENT) physicians treat their patients with systemic corticosteroids; Additionally, 8% report the use of intra-tympanic corticosteroid therapy.<sup>11</sup> The concept of corticosteroids therapy is based on the fact that it can reduce inflammation and edema in the inner ear. Despite all the research devoted to this matter, much controversy remains. Regardless of aetiology, the recovery of auditory thresholds after an episode of sudden sensorineural hearing loss may not occur, be partial or even complete.<sup>12</sup>Among the factors involved in the recovery of auditory thresholds are age at diagnosis of SSHL, severity of hearing loss, presence of vertigo and time between the onset of symptoms and medical treatment.

Since some theories advocate blood viscosity as a probable aetiology of SSHL, in our analysis we have also attempted to understand the impact of "hypercoagulability state" (atrial fibrillation / active oncologic disease) on recovery of auditory thresholds.

## **MATERIALS AND METHODS**

The authors conducted a retrospective analysis of all clinical data with different diagnostic codes: "hearing loss", "unspecified deafness", "sensorineural deafness", "central deafness", "sensorial deafness" in the period between January 2013 and June 2015. As inclusion criteria we considered patients with hearing loss decrease of  $\geq$  30dB, affecting at least three consecutive frequencies, occurring over a 72 hour period. All patients with an evolution of more than 72 hours were excluded. Thus, of a total of 216 analysed clinical data, only 46 patients fulfilled the inclusion criteria and were included in statistical analysis. Several variables were analysed, including age, gender, comorbidities, auditory thresholds at diagnosis, auditory thresholds at least 6 months after diagnosis, and treatment approach. Statistical analysis was performed with Statistical Package for Social Sciences (SPSS), version 24 software. To test normality of continuous variables, the "asymmetry and kurtosis tests" and Kolmorog-Sminov test were used. Student's T-test was used to analyse statistical significance in means of different groups. Qui-square test was usedto compare categorical variables. The ANOVA test was used to analyse the impact of different treatments on auditory threshold recovery. To understand the impact of the different variables, namely the impact of "state of hypercoagulability" on recovery of auditory thresholds, a simple linear logistic and multiple linear logistic regression model were performed, controlled for factors such as age and sex. p<0,05 was considered statistically significant.

### RESULTS

46 patients had a diagnosis of SSHL, 27 of whom were male and 19 female. The mean age was 59 years, with a standard deviation (SD) of 15. The mean value of the initial auditory thresholds obtained by the mean at frequencies 500, 1000, 2000 and 4000 Hz was 81 dB, with a standard deviation of 21 dB.The mean auditory threshold value obtained over a period of 6 months after the first audiogram was 59 dB, with a SD of 28 dB. Table 1 shows the characteristics of the study population.

Gender27 (59)Male27 (59)Female19 (41)Age – Mean [±Standard Deviation (DP)]59 [±15]Initial hearing thresholds – Mean (DP)81 (±21)Mean Hearing thresholds <55 dB5 (11)Final hearing thresholds <255 dB41 (89)Mean hearing thresholds recovery (DP)21 (±18)Diabetes Mellitustype II10 (22)Dyslipidemia20 (44)Arterial Hypertension19 (41)Head Trauma0 (0)Accoustic trauma1 (2)Chronicotitis media5 (11)Hypercoagulabilitystate11 (24)Tinnitus35 (76)Vertigo14 (30)Internment3 (7)Initial treatment55 (76)	Table 1 Population study data	Patients Number - N (%)			
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Internment 3 (7) Initial treatment Systemic corticotherapy 35 (76)	Tinnitus	35 (76)			
Initial treatment Systemic corticotherapy 35 (76)	Vertigo	14 (30)			
Systemic corticotherapy 35 (76)	Internment	3 (7)			
	Initial treatment				
Intra tympanic corticotherapy $2(4)$	Systemic corticotherapy	35 (76)			
	Intra-tympanic corticotherapy	2 (4)			
Systemic + intra-tympanic corticotherapy 5 (11)	Systemic + intra-tympanic corticotherapy	5 (11)			
Hyperbaricoxy gentherapy 3 (7)	Hyperbaricoxy gentherapy	3 (7)			
None 1 (2)	None	1 (2)			

The most frequent comorbidity was dyslipidemia (44%)and "hypercoagulability state" was present in 24 % of patients. The variable "auditory thresholds improvement" had amean value of 21 dB, with a SD of 18 dB.

In order to determine if the severity of the initial hearing loss was correlated with improvement on final hearing thresholds, the patients were divided in two groups depending on the initial severity of hearing loss: - one group with initial hearing thresholds  $\leq$ 55 dB and one with hearing thresholds  $\geq$ 56 dB. The first group presented a mean hearing thresholds improvement of 26 dB while the second group had a mean improvement value of 21 dB (*p value* = 0.54).

Regarding the treatment performed, 76% of the patients were treated with systemic corticosteroid therapy, 11% with systemic and intra-tympanic corticosteroid therapy, 4% only with intra-tympanic corticosteroid and 7% with hyperbaric oxygen therapy. Since the majority of patients were treated with systemic corticosteroid therapy, it was not possible to compare the impact of different therapeutic approaches on the improvement of auditory thresholds. In 2% of the cases, no treatment was performed due to patients' refusal.

*Student's T* test was used to ascertain if the mean values of variable "Improvement of auditory thresholds" were significantly different in the different variables, as evidenced in table 2.

Table 2 Association of different factors on hearing threshold recovery	<i>p</i> value
Gender (Male)	0,53
Age (DP) - 59 (±15)	0,88
Initialhearingthresholds<55dB	0,54
Diabetes Mellitustype II	0,37
Dyslipidemia	0,72
Arterial hypertension	0,38
Tinnitus	0,99
Vertigo	0,59
Hypercoagulabilitystate	0,027

After testing the normal distribution, a statistically significant difference was found in "Auditory thresholds improvement" between the patients with "hypercoagulable state" versus patients with "no hypercoagulable state". Thus, patients with active oncologic disease / atrial fibrillation had an improvement of 11.36 dB, compared to much better improvement of 24.57 dB in patients without these comorbidities (p = 0.027). Subsequently, we performed a multiple linear regression analysis to identify the impact "Hypercoagulable state" on the "Hearing thresholds improvement", adjusted for confounding variables. In table 3 is exposed a regression model.

Table 3 Regression Model - Impact on hearing thresholds

Independentvariables	b coeficient	Standardize d error B	ß	t	Sig. t	95% Confidence interval of b	
						Inferior	Superior
						limit	limit
Hypercoagulability State	14,23	6,08	0,35	2,34	0,024	1,96	26,49
Gender (Male)	-2,59	5,09	-0,07	-0,51	0,61	-12,86	7,69
Age	0,13	0,17	0,11	0,74	0,47	-0,22	0,47

The model explains the variability of 12% in the mean value of "Hearing thresholds improvement", and the most preponderant variable was the presence of the factor "State of hypercoagulability", with a statistically significant p value (p = 0.027). Adding variables to the model, such as gender and age, we can see a statistically significant association between the variable "Hypercoagulability state" and variable "Improvement of hearing thresholds".

### DISCUSSION

The aetiology of most cases of sudden sensorineural hearing loss is uncertain <sup>9</sup>, However, viral cochlea phenomena, microvascular events and autoimmune diseases may justify some cases of idiopathic sudden sensorineural hearing loss.<sup>13-</sup> <sup>15</sup>Since several theories have been proposed to explain the pathophysiology of SSHL, including vascular disorders (thromboembolic events, vasoconstriction phenomena, hypertension and blood viscosity), we have attempted to understand the impact of certain comorbidities on recovery of auditory thresholds. Of the various comorbidities, including dyslipidemia, type II diabetes mellitus, arterial hypertension, otologic disease and hypercoagulability state, we only have concluded that hypercoagulable state had a statistically significant impact on the improvement of hearing thresholds. In this retrospective analysis, the age at diagnosis and presence of vertigo at diagnosis did not have a statistically significant association with the recovery of auditory thresholds, in contrast with the literature.<sup>12</sup> This can be explained by the small population sample. The severity of initial hearing loss is usually considered a prognostic factor in the recovery of auditory thresholds. That is in line with our study, where we also found that patients with greater hearing loss had less auditory recovery. Since phenomena of blood viscosity and thromboembolic events may be at the origin of SSHL<sup>5-8</sup>, it makes sense to think that diseases such as atrial fibrillation / active oncologic disease, which indeed are pro-coagulability states, may be related to either episodes of SSHL or lower probability of hearing threshold recovery.

In this study, we demonstrated that patients who present atrial fibrillation / oncologic disease had a mean hearing threshold improvement of only 11.36 dB, significantly lower compared to the group of patients without these comorbidities, in which hearing improvement was 24.57 dB(statistically significant p = 0.027). With this multiple linear regression model we found that this variable explains 13% of the hearing improvement.

Thus, oncologic disease / atrial fibrillation may be variables to be taken into account in future prospective studies, so that their involvement may be clearer in the aetiology of SSHL and evaluation of long-term prognosis.

The therapeutic approach of our study population is consistent with that described in the guidelines of the American Academy of Otolaryngology - Head and Neck Surgery <sup>1</sup>. In the vast majority of our patients, initial treatment was systemic corticosteroid therapy.

Although being retrospective and associated with some methodological limitations, we believe that our study can set an innovative concept that, if supported by further studies may strengthenthe association between hypercoagulability and prognosis in the recovery of auditory thresholds.

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#### **Conflict of interest**

We declare that no conflict of interest

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