Unveiling Vocal Phenotypes of Dysphonia with Unsupervised Learning

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Keywords: Dysphonia, Acoustic Analysis, Unsupervised Learning, k-means.

Abstract: Dysphonia is a voice disorder caused by morphological and neurological alterations. This work proposes a clustering analysis on vocal properties of patients diagnosed with benign lesions of the vocal folds (BLVF) and unilateral vocal fold paralysis (UVFP) to identify if they constitute separate vocal subtypes of dysphonia and to understand whether misclustered data depend on a specific diagnosis and age. Two hundred seventy-five patients uttered a sustained vowel /a/, from which acoustic features were extracted and transformed. Two conditions were tested separately for each gender: the unaware and the aware approach, where statistical analysis was performed to select the significantly different parameters between BLVF and UVFP. The best clustering results were obtained for the aware condition, with a silhouette score of 0.70 for both genders; accuracies were 0.67 and 0.70 for the female and male patients. A single component was retained for both genders: phonation and articulation parameters presented high weights for female and male patients, respectively. Misclustered observations analysis showed that feature transformation and reduction improved the UVFP voices clusterability. The clustering error outcome did not depend on age, voice disorder types, or subtypes. These findings may contribute to a better understanding of voice disorders' properties, reducing misdiagnoses and supporting their follow-up.

1 INTRODUCTION

The acoustic analysis represents an automatic, objective, computer-based approach to study and characterize a wide variety of digitalized human sounds, such as snoring, neonatal cry, voice and speech (Sebastian et al., 2021; Manfredi et al., 2018; Frassineti et al., 2023). Usually, acoustic analysis implements specific models of sound production to compute a set of parameters capable of describing certain properties of these biomedical signals, e.g., frequency perturbation, noise level or nonlinear dynamics (Brockmann-Bauser and Drinnan, 2011). With the recent advancements in artificial intelligence (AI) methods and applications, such metrics are increasingly used as features to train AI frameworks to develop automatic tools that aim at supporting clinicians' work to differential diagnosis and severity assessment of vocal pathologies. Indeed, several studies have demonstrated how machine learning (ML) algorithms can carry out exploratory analysis to identify vocal subtypes (Desjardins et al., 2022; Shembel et al., 2023), to recognize and classify voice disorders (Hu et al., 2021; Verde et al., 2021) and to predict perceptual assessments ratings (Jalali-Najafabadi et al., 2021). These results are achieved by applying two different AI strategies: unsupervised learning techniques are performed for exploratory analyses, whereas classification and regression tasks are typically carried out with supervised methods. The main difference between these two relies on the type of data used. Supervised learning uses labelled data, which means that models, when trained, are provided with a baseline understanding of what the correct output should be. On the contrary, unsupervised learning or clustering

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Calà, F., Correnti, F., Frassineti, L., Cantarella, G., Buccichini, G., Battilocchi, L. and Lanatà, A.
Unveiling Vocal Phenotypes of Dysphonia with Unsupervised Learning.
DOI: 10.5220/0013132200003911

In *Proceedings of the 18th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2025) - Volume 1*, pages 860-867
ISBN: 978-989-758-731-3; ISSN: 2184-4305

works with unlabelled data. Therefore, it analyzes the inherent structure of data without any specific instruction to identify hidden groups by considering proximity or dissimilarity rules (Xu and Wunsch, 2005; Saxena et al., 2017). Clustering in acoustic analysis has been used firstly as a feature weighting technique, i.e., to estimate and rank the relevance of extracted features to better highlight an underlying pattern in data and improve classification performance (Niño-Adan et al., 2021). The k-means algorithm, one of the most used clustering techniques, was used to transform nonlinearly separable features to linearly separable ones that, by gathering data with similar features, proved to determine an increase in the discrimination ability of ML algorithms. This has allowed obtaining better accuracy, sensitivity and specificity to detect the presence of voice pathology up to 10 percentage points for some models (Hariharan et al., 2014) and to boost the diagnostic power of a voice-based automatic Parkinson's disease classifier (Gürüler, 2017). Moreover, clustering is particularly indicated in case of highly heterogeneous diseases that are characterized by complex and large pathophysiology to refine the phenotype of a given disease. This allows highlighting novel clusters of patients to make and plan better precision medicine procedures. Indeed, such an approach could identify that patients grouped by specific properties present a unique symptom requiring separate assessments and therapies to make them more effective. For this latter task, the k-means algorithm was implemented to characterize the degree of speech impairments and find speech subtypes in Huntington's (Diehl et al., 2019) and Parkinson's disease (Rusz et al., 2021). There is no accepted guideline to define such subgroups, and several factors can be considered as motor, cognitive and speech disorders and symptoms. Therefore, these evaluations may suffer from clinicians' experience and expertise, as well as intra-subject variability (Tsanas and Arora, 2022). A data-driven approach helped to define more compact speech disorder subtypes to better understand the underlying mechanism of speech production and to find possible explanations of contradictory effects in applying specific treatments in both Huntington's and Parkinson's diseases. Dysphonia is another type of voice disorder, typically characterized by a higher irregular pitch and lower vocal intensity (Gómez-García et al., 2019). The combination of acoustic analysis and supervised AI techniques proved that distinct voice pathologies can be recognized with good accuracies, usually around 85% (Za'im et al., 2023; Calà et al., 2023). However, the underlying patterns that supervised learning can detect between data and labels may be difficult to explain and interpret to clinicians unless specific precautions are taken. In this study, it will be investigated whether unsupervised learning can detect subtypes of dysphonia in a newly recorded Italian database of pathological voices. Specifically, as an exploratory analysis, two main disorders will be considered: unilateral vocal fold paralysis (UVFP) and benign lesions of the vocal folds (i.e., nodules, polyps, cysts, hereinafter abbreviated with BLVF). They were chosen because they present a straightforward difference in vocal fold motor dynamics that can be assessed with visual inspection by means of high-resolution endoscopy. However, this device may not always be available, especially in decentralized ambulatories, and its invasiveness hinders patients' tolerability (Hamdan et al., 2023). Moreover, it requires the patients' physical presence in a medical care setting. On the other hand, acoustic analysis is a contactless and cost-effective procedure. Nevertheless, the distinction of dysphonia subtypes is not trivial with acoustic measures only. Moreover, it will be explored if clustering can further recognize the subtypes of the BLVF class to understand whether acoustic parameters may support their differential diagnosis. Finally, an evaluation of misclustered observations will be performed to understand the role of two confounding factors. Firstly, it will be investigated if cluster errors are biased by a specific pathological group, including their subtypes (i.e., unilateral left or right vocal fold paralysis or cysts rather than nodules and polyps). Additionally, the implicit role of age will be addressed to develop an effective tool that can detect voice pathologies even in the ageing population.

This approach could be helpful for otolaryngologists to support voice perceptual assessment, and reduce the impact of confounding factors in mis- and underdiagnosis of voice pathologies.

2 MATERIALS AND METHODS

The pipeline of this work comprises three main steps: after data collection and organization, features were preprocessed as explained in subsection 2.2. Then, two clustering problems based on the k-mean algorithm were implemented to understand whether and how selecting acoustic features that are statistically different between pathological classes (aware analysis, subsection 2.5) enhances clustering performance with respect to using uncorrelated features only (unaware analysis, subsection 2.4).

2.1 Dataset

A total of 287 patients (183 females F, mean age = 44.6±4.6 years, 104 males M, mean age = 42.6±9.4 years) was recruited at the Ospedale Maggiore Policlincio Milano (Milan, Italy). Dysphonia and related voice pathology were diagnosed with both perceptual evaluation of voice with the GRB scale (Hirano, 1981) and video-laryngostroboscopic assessment. However, in this study, only acoustic features were considered in the unsupervised learning experiments.

Commonly, UVFP patients present a higher mean age with respect to BLVF (Herrington-Hall et al., 1988). In our database, female patients diagnosed with BLVF have a mean age of 44 years (minimum-maximum range: 19-68), whereas the ones diagnosed with UVFP present a mean age of 50 years (min-max range: 21-72). For male patients, the mean age for BLVF is 42 years (min-max range: 19-78), whereas the mean age of UVFP subjects is 51 years (min-max range: 26-80).

Table 1 displays their distribution, expliciting BLVF subtypes, i.e., nodules, polyps and cysts.

Table 1: Patients distribution divided by gender and voice pathology.

Pathology	Female patients	Male patients
Nodules	15	2
Polyps	56	38
Cysts	34	6
UVFP	78	58

For the acoustic analysis, patients were asked to utter a sustained /a/ for at least 3s at a comfortable pitch and loudness. Audio samples were recorded through a C1000S dynamic microphone (AKG, Vienna, Austria), with a sampling frequency of 44.1kHz and a fixed distance of 5cm from the patient's mouth during phonation.

2.2 Feature Extraction, Transformation and Selection

Acoustic parameters were extracted with the open-source BioVoice software (Morelli et al., 2021). After selecting age, gender and the type of vocal emission, this tool automatically selects the proper frequency range to identify and compute the fundamental frequency F0 and, subsequently, a set of features encompassing both time and frequency domains. Specifically, BioVoice calculates a perturbation measure (the local jitter), a noise measure (the Adaptive Normalize Noise Energy, NNE), first, second and third formants (F1, F2, F3, respectively), the number and duration of voiced and unvoiced parts of the recordings. Additionally, the median, standard deviation, minimum and maximum values of these metrics are computed.

Two preprocessing methods have also been implemented to enhance the clusterability of the data: logarithm and cube-root transform. They are both used to reduce the skewness of a distribution with the cube-root transform being less effective but suitable for both positive and negative values than the logarithm one. Finally, to reduce the problem's dimensionality and extract a subset of acoustic features containing the most valuable information, Principal Component Analysis (PCA) and correlation analysis were applied.

2.3 Clustering

A clustering problem assumes that an event space E, described by an observation matrix $n \times p$ comes from k different underlying divisible clusters (sometimes referred to as the clusterability assumption and aims to find each of the clusters. Several methods have been proposed, with the k-means algorithm being one of the most commonly used.

This algorithm initializes by selecting k values from the event space as candidate cluster centers. It then iteratively follows two steps:

- Assign: Each point in the event space is assigned to the nearest candidate cluster center, resulting in k different clusters.
- Update: Each cluster center is recalculated as the mean of the coordinates of all points in the cluster, yielding centroids.

The algorithm repeats these steps iteratively until convergence, where the cluster centers no longer change. Lloyd's algorithm is esteemed for its optimal results, particularly when the event space consists of data sampled from k independent normally distributed clusters with diagonal covariance matrices (Bock, 1996). Clustering efficiency was evaluated by considering the silhouette score, a value ranging between -1 and 1 that compares inter-cluster distances with intra-cluster ones. Moreover, accuracy was taken into account after performing manual diagnosis assignment, given that clustering is an unsupervised learning approach.

2.4 Unaware Analysis

A first clustering problem investigates whether the k-means algorithm can separate data into two separate groups, corresponding to the BLVF and UVFP

classes, for each gender. On the other hand, a second clustering problem explores the possibility of separating data into four groups, i.e., the BLVF subclasses (nodules, polyps, cysts) and UVFP. This experiment was performed for the F dataset only due to the low nodules numerosity of the M dataset.
The three approaches follow:

- **Vanilla:** No preprocessing is involved. It serves as a reference point for comparison.
- **PCA:** Outlier removal based on the Interquartile Range (IQR) is performed. Depending on data normality, features are also scaled and centred accordingly. PCA is then applied: the number of principal components m was chosen according to the k-means clustering performance.
- **Unskew + PCA:** Before applying the PCA pipeline, skewed data are cube-root or log-transformed.

2.5 Aware Analysis

To improve the identification of clustered structures in the analyzed groups, all available information should be leveraged to filter out irrelevant features. Hence, to identify an optimal subset, statistical tests were employed to determine which parameters present significant differences between groups. An analogous pipeline to the one presented in subsection 2.4 was implemented.

2.6 Misclustered Observations Analysis

To provide interpretable results for clinicians, this study also proposes an analysis over misclustered data for the best unsupervised learning pipeline. Specifically, by implementing cross-tabulation and chi-square statistics, it was investigated whether the clustering outcome depends on two factors: the pathology and the age of patients. Moreover, since both the considered diseases present subtypes, it was explored whether errors are related to BLVF subtypes, i.e., nodules, polyps and cysts, and UVFP subtypes, i.e., right and left vocal fold paralysis.

3 RESULTS

This section presents the results of both the unaware and aware analyses in subsection 3.1 and 3.2, respectively. In turn, each subsection displays the outcome of the 2- and 4-groups cluster analysis separately. For all experiments, the best results were obtained with one single principal component ($m = 1$). Figure 1 displays how the observations are distributed along the principal component.

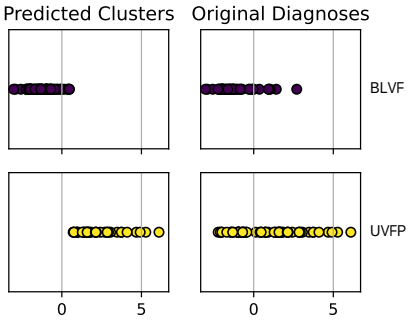


Figure 1: Graphical representation of the distribution of the observations along the principal component axis in the original dataset (right) and the predicted clusters (left).

3.1 Unaware Analysis

3.1.1 2 Clusters

Table 2 shows the results of the three pipelines for the 2-groups unaware cluster analysis, divided by gender. S_n is the silhouette score computed for each pathological group, where $n = 1$ refers to the BLVF class, whereas $n = 2$ refers to the ULVF one; on the other hand, S corresponds to the average silhouette score. The abbreviation A refers to accuracy. Finally, σ shows the percentage of variance explained by the single PCA component.

Table 2: Results of $k = 2$ clusters analysis on the males and females datasets. S = silhouette score, A = accuracy, σ = retained variance percentage.

F - Unaware	**S_1**	**S_2**	**S**	**A**	**σ**
Vanilla	0.47	0.37	0.42	0.54	1.00
PCA	0.68	0.62	0.65	0.55	0.19
Unskew + PCA	0.70	0.59	0.64	0.616	0.21
M - Unaware					
Vanilla	0.61	0.51	0.56	0.52	1.00
PCA	0.79	0.62	0.70	0.68	0.26
Unskew + PCA	0.77	0.64	0.70	0.69	0.28

3.1.2 4 Clusters

Table 3 displays the results of the three pipelines for the 4-groups unaware cluster analysis. S_n is the silhouette score computed for each pathological group, where $n = 1$ refers to the nodules, $n = 2$ refers to polyps, $n = 3$ to cysts, whereas $n = 4$ to UVFP. This experiment was not performed for the male dataset due to nodules low numerosity.

Table 3: Results of $k = 4$ clusters analysis on the females datasets. S = silhouette score, A = accuracy, σ = retained variance percentage.

F - Unaware	S_1	S_2	S_3	S_4	S	A	σ
Vanilla	0.21	0.28	0.18	0.17	0.21	0.34	1.00
PCA	0.63	0.59	0.61	0.55	0.60	0.30	0.19
Unskew + PCA	0.57	0.67	0.66	0.6	0.62	0.34	0.21

3.2 Aware Analysis

3.2.1 2 Clusters

Table 4 shows the results of the three pipelines for the 2-groups aware cluster analysis, divided by gender.

Table 4: Results of k = 2 clusters analysis on the males and females datasets, after only retaining statistically significant features.

F - Aware	S_1	S_2	S	A	σ
Vanilla	0.47	0.37	0.42	0.54	1.00
PCA	0.71	0.65	0.68	0.69	0.34
Unskew + PCA	0.68	0.72	0.70	0.665	0.35
M - Aware					
Vanilla	0.61	0.51	0.56	0.52	1.00
PCA	0.79	0.61	0.70	0.69	0.43
Unskew + PCA	0.77	0.64	0.70	0.70	0.42

3.2.2 4 Clusters

Table 5 shows the results of the three pipelines for the 4-groups aware cluster analysis for the female dataset only.

Table 5: Results of k = 4 clusters on females dataset, after only retaining statistically significant features.

F - Aware	S_1	S_2	S_3	S_4	S	A	σ
Vanilla	0.21	0.28	0.18	0.17	0.21	0.34	1.00
PCA	0.52	0.56	0.54	0.60	0.58	0.33	0.43
Unskew + PCA	0.56	0.53	0.56	0.60	0.58	0.34	0.43

3.3 PCA Weights Analysis

Figure 2 shows the barplot explaining which acoustic features, after checking for their statistically significant difference between BLVF and UVFP, contributed the most to the PCA component before (left) and after (right) unskewing the original data. Blue bars refer to male patients, whereas red bars to female ones. An unskewed feature is marked with a green dotted line.

3.4 Misclustered Observation Analysis

Figure 3 shows the percentage of misclustered observations for each voice disorder divided by pipeline and gender for the unaware condition.

Figure 4 displays the percentage of misclustered observation for each voice disorder, divided per pipeline and gender, for the aware condition.

The best clustering results were obtained for the aware condition and the Unskew + PCA pipeline, for both genders. Therefore, the relationship between clustering outcome and pathology and age was performed for these models only.

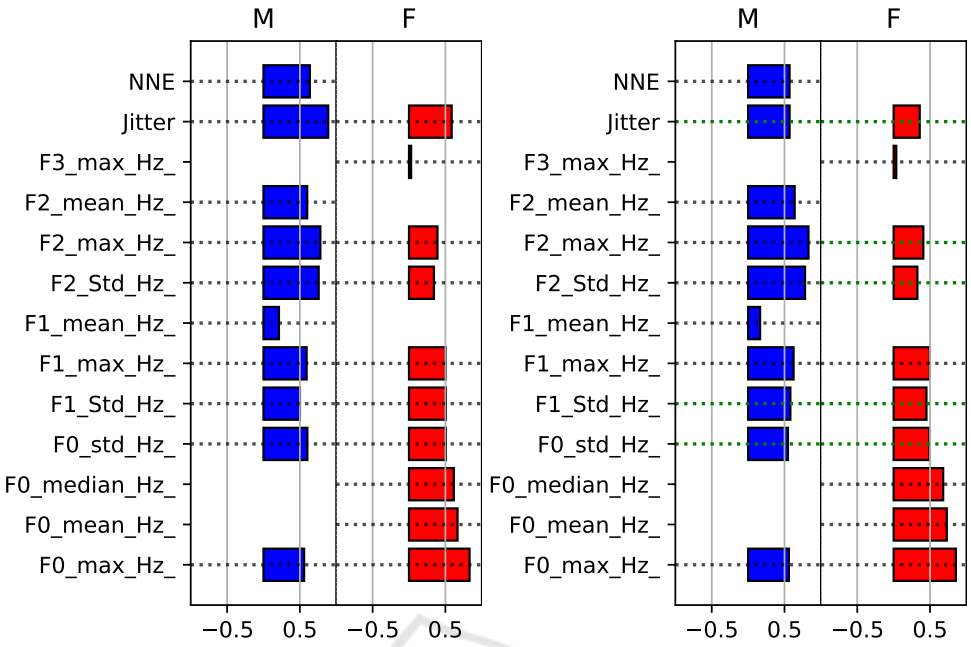
For the female dataset, the clustering outcome did not depend on the general voice pathology ($p = 0.91$). Specifically, when considering the BLVF subtypes, a close to significant ($p = 0.08$) relationship was found with the clustering outcome. The incorrectly clustered observations mostly belonged to patients diagnosed with polyps. Similarly, separating right and left vocal fold paralysis had no significant result ($p = 0.41$). As far as age is concerned, the clusterization outcome did not depend on patients' age ($p = 0.51$), and this result was also confirmed when separating the female cohort in the BLVF ($p = 0.06$) and UVFP classes ($p = 0.37$).

Similar results were found for the male dataset. Clustering error did not relate to patients' pathology, neither in general terms (BLVF vs UVFP, $p = 0.34$) nor considering their respective subtypes (nodules vs polyps vs cysts, $p = 0.32$, and left vs right vocal fold paralysis, $p = 0.79$). Moreover, age and clustering outcome did not relate significantly ($p = 0.58$ considering pathologies altogether, 0.59 considering BLVF only, $p = 0.63$ considering UVFP only).

4 DISCUSSION

This study proposes an unsupervised learning approach to explore the clusterability of patients diagnosed with benign lesions of the vocal folds and unilateral vocal fold paralysis based on uncorrelated acoustic features (unaware condition) and significantly different features between BLVF and UVFP (aware condition).

When considering the two groups classification problem, the best results for both genders were achieved using the aware condition. Indeed, for the female dataset, the average silhouette score and accuracy for the best pipeline (i.e., the Unskew + PCA one) are 0.70 and 0.67, respectively, compared to the unaware condition where $S = 0.64$ and $A = 0.62$. On the other hand, for the male dataset, the aware condition obtained similar results of those concerning the unaware condition. In fact, both experiments present $S = 0.70$ and a slightly higher accuracy for the aware condition ($A = 0.70$ vs $A = 0.69$). Interestingly, the preprocessing procedure helped improving



(a) Vanilla (b) Unskewed

Figure 2: Barplot of features weights in the first principal component after retaining only features that show statistical difference. PCA is performed before (a) and after (b) unskewing. The skewed, transformed features, are marked with a dotted green line.

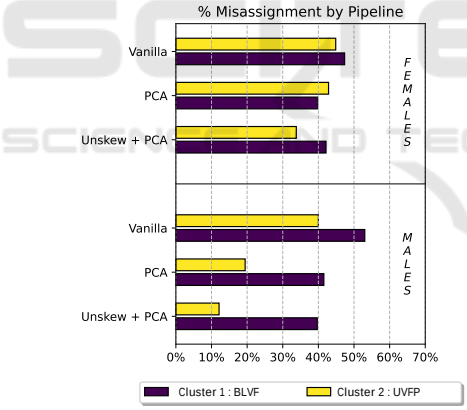


Figure 3: Barplot of the percentage of misassignments in each cluster found by the unaware condition in the three pipelines.

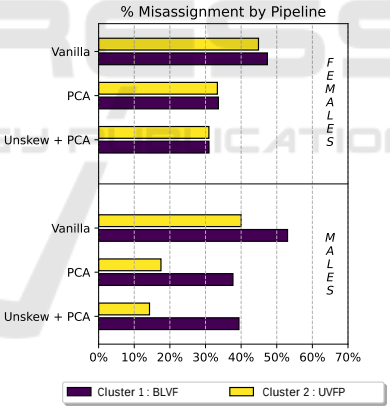


Figure 4: Barplot of the percentage of misassignments in each cluster found by the aware condition in the three pipelines.

the silhouette score for the UVFP class, especially for the female dataset. Indeed, clustering went from the $S_2 = 0.37$ of the Vanilla pipeline to the $S_2 = 0.72$ of the Unskew + PCA one. A model with such a property could be helpful in clinical practice because it better recognizes the most severe of the considered pathologies, possibly reducing its misdiagnosis (Low et al., 2024). An analogous result was obtained for the male dataset, for which feature transformation allowed to obtain a $S_2 = 0.64$, starting from the Vanilla pipeline value of $S_2 = 0.51$.

The benefits of feature preprocessing is also supported by Figure 4, as indeed the upper panel concerning female patients shows a monotonical decrease of the number of misassignments from the vanilla to the Unskew + PCA pipelines and, for this latter one, a balance between misclustered BLVF and UVFP observations. Moreover, Figure 2 highlights that the largest contributions for the principal component derive from parameters describing phonation characteristics only, specifically the mean and maximum of the fundamental frequency. This outcome suggests that

parameters related to the vibratory dynamics of the vocal folds may be sufficient to distinguish the pathological classes, possibly simplifying recording protocols and the subsequent objective analysis of audio acquisitions (Robotti et al., 2021).

For the male dataset, the lower panel of Figure 4 highlights a similar beneficial effect. However, it also displays a close number of misassignments for both pathologies to the one showed in Figure 3. A smaller sample size might cause this similarity, therefore, more data from a male population should be collected to validate such an outcome. Oppositely to the female dataset, articulation parameters weighted the most to the principal component (right panel of Figure 2). Specifically, the maximum and standard deviation of the second formant, as well as the standard deviation of the first formant, show the largest contribution. This may mean that the UVFP negatively affect the constriction degree and motility of the supraglottic area and the tongue, consequently altering vocal properties differently from BLVF. This could suggest clinicians using non-invasive tools, e.g., ultrasound imaging, to assess their movements as additional methods to monitor UVFP (Saigusa et al., 2006; Wang et al., 2012).

A chi-squared test of associations ($\alpha = 0.05$) proved that the number of errors in the clustering did not depend on the pathology. Furthermore, even if UVFP usually presents a later onset with respect to BLVF, age was not a significant factor when comparing correctly and incorrectly clustered data ($p = 0.51$). Such a result suggests the feasibility of the proposed approach to better define a vocal phenotype for the involved pathologies that can be effectively used in elder care. Similarly to the female dataset, the chi-squared test of associations ($\alpha = 0.05$) proved that the number of errors in the clustering did not depend on the pathology and age ($p = 0.58$), even when considering subtypes. Regarding the four groups classification experiment, the usage of the optimal subset of significantly different features between BLVF and UVFP did not produce a better outcome. In fact, the best average silhouette score of $S = 0.62$ was obtained for the unaware condition. Analogously to the two group problem, feature selection and transformation allowed to improve all evaluation metrics.

Finally, the right panel of Figure 1 shows that, even if the proposed approach achieves a good separation of the two considered pathologies, the original data distribution of UVFP observations seem to be more dispersed than BLVF ones. This could result from the severity degree of vocal fold paralysis, which should be considered in future studies as a confounding factor.

5 CONCLUSION

This study has developed an automatic and robust framework that, based on unsupervised learning methods, can distinguish between two voice disorders provoking dysphonia with acoustic features only. Therefore, clinicians could use it to support differential diagnosis. The results from the male dataset remain similar between the unaware and aware conditions, whereas the female data clusterability benefits the most from the identification of significantly different parameters between BLVF and UVFP. In both genders, misclustered observations seem not to depend on a specific pathology (and its subtypes) and age. Moreover, through the PCA weight analysis, this study highlighted that phonation parameters were the most contributive ones for the female dataset, whereas articulation feature were the most relevant for the male dataset.

ACKNOWLEDGEMENTS

The research leading to these results has received funding from the project PE8-AGE-IT “A NOVEL PUBLICPRIVATE ALLIANCE TO GENERATE SOCIOECONOMIC, BIOMEDICAL AND TECHNOLOGICAL SOLUTIONS FOR AN INCLUSIVE ITALIAN AGEING SOCIETY”, Codice MIUR: PE 00000015, CUP: B83C22004800006.

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