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Taxonomy of respiratory function in patients with idiopathic chronic neck pain
A cluster analysis

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Ταξινόμηση της αναπνευστικής λειτουργίας σε ασθενείς με ιδιοπαθή χρόνιο αυχενικό πόνο: Μια ανάλυση συστάδων

Περίληψη στο τέλος του άρθρου

Key words: Chronic neck pain, Respiratory function, Respiratory measures

Chronic neck pain (CNP), which is one of the commonest musculoskeletal complaints, has drawn considerable research interest the last decades. Patients with CNP present a number of accompanying clinical manifestations, including changes in the muscle efficiency of their cervical muscles,[1] postural changes,[2] restricted range of movement,[3] impaired sensorimotor control,[4] psychological compromise,[5] and respiratory dysfunction.[6]

Some years ago, a hypothesis was proposed that describes the development of respiratory dysfunction in patients with CNP.[7] Since then, a number of studies have confirmed this initial hypothesis, leading to the conclusion that patients with CNP may present manifestations of respiratory dysfunction, including reduced respiratory strength, reduced partial pressure of arterial carbon dioxide, reduced respiratory flow and volume, and changes in chest biomechanics.[6]

Although there is now sufficient evidence that this clinical population has respiratory dysfunction, there is no documentation concerning the possible patterns of this dysfunction. The classification of patients into patterns of respiratory function could give further opportunities for improved understanding, prognosis and clinical management of this problem.

The aim of this study was to perform a cluster analysis of currently available data, in order to describe the respiratory function patterns of patients with CNP.

MATERIAL AND METHOD

A secondary analysis was conducted of data that had been obtained for the needs of other published studies[8–10] on 45 patients with idiopathic CNP (>6 months, at least one episode per week). The eligibility criteria have been previously described,[8] and all the participants had provided their written informed consent. The study was approved by the Ethics Committee of the University of Manchester (Manchester, UK) and the Ethics Committee of the Technological Educational Institute (TEI) of Lamia (Lamia, Greece).

The respiratory outcome measures used in this study were: (a) The partial pressure of arterial carbon dioxide ($P_{tc}CO_2$), which had been recorded with the TCM40 (Radiometer, Copenhagen, Analis, Belgium), (b) the vital capacity (VC), the forced expiratory volume in one second (FEV_1), the forced vital capacity (FVC), the peak expiratory flow (PEF), the forced expiratory flow from 25% to 75% of forced expiration ($FEF_{25-75\%}$), the FEF at 25% of forced expiration ($FEF_{25\%}$), the FEF at 50% of forced expiration ($FEF_{50\%}$), the FEF at 75% of forced expiration ($FEF_{75\%}$) and the maximum voluntary ventilation (MVV), all of which had been recorded with an electronic spirometer (Spirolab II, SDI Diagnostics Inc, USA), and (c) the maximal inspiratory pressure (MIP) and the maximal expiratory pressure (MEP), which had been recorded with a mouth pressure meter (microRPM, Medical Limited, Rochester, Kent, England).

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The psychological outcome measures were anxiety and depression, which had been assessed using the Hospital Anxiety and Depression Scale (HADS), kinesiophobia, which had been assessed with the Tampa Scale for Kinesiophobia (TSK), and pain catastrophizing, which had been assessed with the Pain Catastrophizing Scale (PCS).

Pain intensity had been assessed with a Visual Analog Scale (VAS) and neck pain-induced disability with the Neck Disability Index (NDI). The detailed procedures for all the measurements are provided in previously published studies.[8–10]

Taxonomy of respiratory function of the 45 patients with idiopathic CNP was performed by hierarchical cluster analysis, according to the distant neighbor method. The variables that were included were the z-scores of $P_{tc}CO_2$, MIP % predicted, MEP % predicted, VC % predicted, FEV1 % predicted, FVC % predicted, PEF % predicted, $FEF_{25-75\%}$ % predicted, and MVV % predicted. Pearson correlation coefficients were used as a measure of similarity. Decisions about the clusters were taken based on the dendrogram that was constructed.[11]

Following recognition of the clusters, their demographics and respiratory function parameters were described, using mean and standard deviation (SD) as measures of central tendency and dispersion, respectively. The anthropometric characteristics, the psychological status and the respiratory function parameters were then compared among clusters, using one-way ANOVA, and their z-scores were visually presented in box-plots. The significance level was set at p=0.05.[12]

All data analysis was performed using the Statistical Package for Social Sciences (SPSS), version 20.0.

RESULTS AND DISCUSSION

Based on the constructed dendrogram, it was decided that the data could be divided into three separate clusters. The anthropometric and pain characteristics, and the respiratory functions in the clusters are presented in table 1 and table 2, respectively. The reference values were those used by the previously published studies that used the same sample of patients.[8–10] The respiratory functions of the clusters is presented visually in figure 1.

The analysis revealed three separate clusters. The respiratory function of each cluster is described in the following paragraphs.

Cluster 1 (hypocapnic): Eight patients were classified into this cluster, the main respiratory function characteristic of which is reduced $P_{tc}CO_2$. $P_{tc}CO_2$ was not only found to be

Table 1. Respiratory function in chronic neck pain. Demographic characteristics for each of the three clusters.*

Variables	Cluster 1	Cluster 2	Cluster 3	p value	$CNP_{reference\ values}$	$Healthy_{reference\ values}$
Participants (n)	8	19	18	–	45	45
Gender (m/f)	1/7	2/17	10/8	0.006	13/32	13/32
Age (years)	35.25±11.61	37.0±15.71	35.11±14.95	0.92	35.9±14.5	35.4±14
Height (cm)‡	165.06±5.69	161.97±8.83	170.14±9.38	0.02	165.8±9.2	167.1±8.7
Weight (kg)	66.45±12.56	68.37±11.65	77.20±19.79	0.15	71.6±16.0	72.3±15.2
BMI (kg/m^2)	24.32±3.76	26.07±4.22	26.40±5.17	0.55	25.9±4.5	25.8±4.4
BQHPA (/15)	8.36±1.44	7.73±0.87	7.95±1.62	0.64	7.9±1.3	7.6±1.4
VAS_{pain} (mm)‡	57.5±14.59	47.05±18.30	38.50±18.67	0.049	45.49±18.78	–
Pain duration (months)	75.88±60.94	76.00±57.29	60.28±58.91	0.69	69.55±57.75	–
NDI (/50)	9.75±3.50	12.16±4.80	9.33±5.92	0.23	10.60±5,17	–
HADS anxiety	8.88±5.52	9.21±4.76	8.06±3.86	0.74	8.7±4.5	7.4±3.5
HADS depression	4.00±3.89	5.42±2.59	4.89±4.75	0.68	5.0±3.8	4.0±3.4
TSK	36.25±8.48	35.11±6.60	31.5±6.09	0.16	33.9±6.9	–
PCS	20.63±13.02	23.63±12.02	19.39±11.82	0.56	21.4±12.0	–

*Cluster 1: Hypocapnic, Cluster 2: Weak, Cluster 3: Flow restricted

m/f: Masculine/feminine, BMI: Body mass index, BQHPA: Baecke Questionnaire of Habitual Physical Activity, VAS_{pain}: Visual Analog Scale (pain), NDI: Neck Disability Index, HADS: Hospital Anxiety and Depression Scale, TSK: Tampa Scale for Kinesiophobia, PCS: Pain Catastrophizing Scale

Statistically significant differences were found

†Between clusters 1 and 2

‡Between clusters 1 and 3 or

§Between clusters 2 and 3

Descriptives are reported as mean±SD. Reference values were provided from the studies of Dimitriadis et al[8–10]

Table 2. Respiratory function in chronic neck pain. Descriptives of respiratory function for each of the three clusters.*

Variables	Cluster 1	Cluster 2	Cluster 3	p value	$CNP_{reference\ values}$	$Healthy_{reference\ values}$
$P_{tc}CO_2$ (mmHg)‡,§	33.38±2,67	34.26±2.35	36.39±2.79	0.06	34.9±2.9	37.3±3.5
FEV_1%pre§	103.27±6.86	112.11±10.93	93.55±12.68	<0.001	103.1±13.8	106.6±15.7
FVC %pre†,§	98.84±8.75	110.65±9.56	97.83±11.37	0.001	103.4±11.8	110.0±16.7
FIV_1/FVC %pre‡,§	109.66±3.17	105.34±4.68	98.92±4.90	<0.001	103.5±6.1	101.5±6.8
PEF %pre	96.79±10.89	99.64±15.95	97.13±18.01	0.87	98.1±15.8	102.7±17.9
$FEF_{25-75\%}$%pre‡,§	108.89±8.24	100.58±16.75	76.33±17.72	<0.001	92.4±20.8	92.0±23.3
$FEF_{25\%}$%pre	98.38±17.33	99.73±14.97	87.34±21.29	0.11	94.4±18.5	100.6±20.6
$FEF_{50\%}$%pre‡,§	108.29±15.37	97.99±18.05	76.15±18.90	<0.001	91.1±21.8	90.2±25.3
$FEF_{75\%}$%pre†,‡,§	108.55±34.33	86.52±15.14	61.34±14.77	<0.001	80.4±26.0	79.1±26.6
VC %pre	89.51±7.13	102.44±15.83	92.15±14.02	0.04	96.0±14.8	103.4±15.0
MVV %pre	84.9±11.39	91.96±20.20	97.16±24.36	0.38	92.2±20.7	104.4±21.7
MIP %pre	106.39±20.19	83.71±18.43	100.57±38.18	0.10	86.9±31.2	100.8±34.5
MEP %pre	100.42±30.53	91.22±23.44	98.85±40.12	0.71	107.36±43.3	126.9±43.1
MIP/MEP	0.93±0.20	0.81±0.19	0.85±0.26	0.41	0.85±0.22	0.81±0.17

*Cluster 1: Hypocapnic, Cluster 2: Weak, Cluster 3: Flow restricted

Statistically significant differences were found

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Descriptives are reported as mean±SD. Reference values were provided from the studies of Dimitriadis et al[8–10]

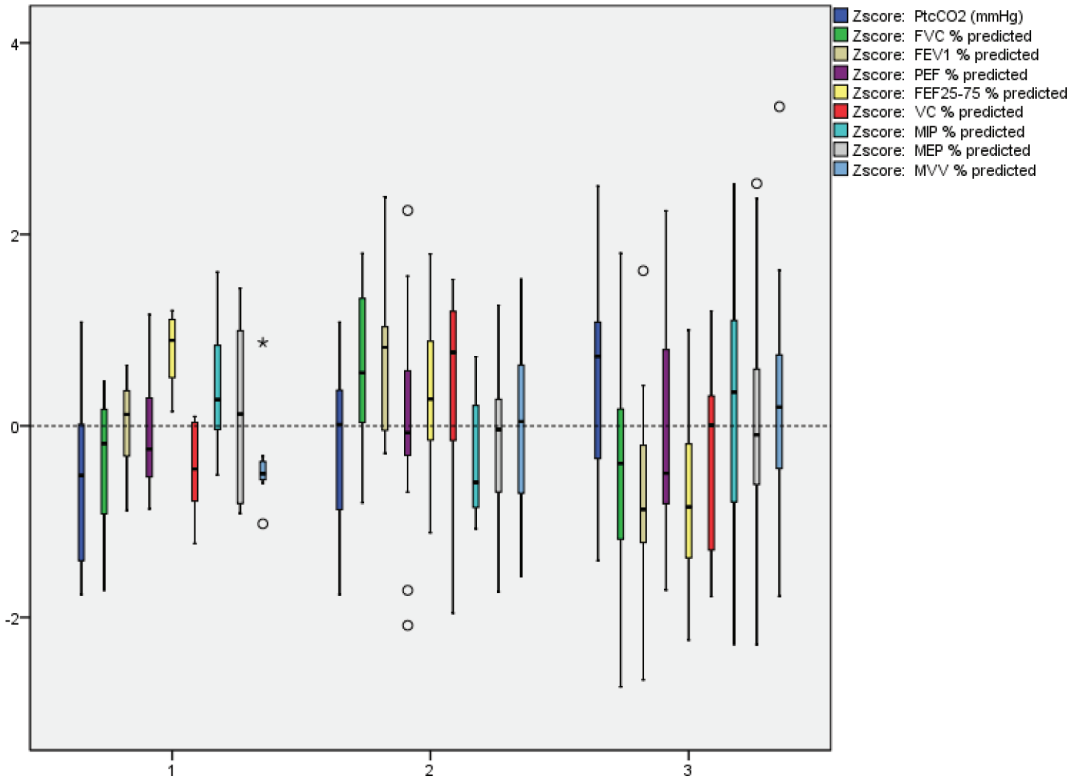

Figure 1. Respiratory function in chronic neck pain. Box-plots of the z-scores of the main respiratory parameters for each of the three clusters (cluster 1: Hypocapnic, cluster 2: Weak, cluster 3: Flow restricted).

one of the indices most severely affected, but was also significantly reduced in comparison with the other two clusters. MVV was also one of the most impaired respiratory function parameters of the cluster, and lower in comparison with the other two clusters. VC and FVC were also found to be at lower levels, in comparison with the other respiratory variables, and in comparison with the second cluster. Respiratory flow measurements, with the exception of the more strength-dependent PEF, were found be among the higher respiratory indices of the group, and higher than in the other clusters. Lastly, the MIP/MEP ratio was found to be the highest among the three clusters.

Cluster 2 (weak): Nineteen patients were classified into cluster 2, the main respiratory function characteristic of which was the reduced strength of respiratory muscles, although the difference between the clusters was not significant. The MIP/MEP ratio was normal. The spirometric indices of cluster 2 were normal, except for the $FEF_{75\%}$. The $P_{tc}CO_2$ of cluster 2 was better than that of cluster 1, but worse than that of cluster 3. The MVV of cluster 2 was also better than that of cluster 1, but worse than that of cluster 3, although the differences were not significant.

Cluster 3 (flow-affected): Eighteen patients were classified into cluster 3. The most prominent characteristic of respiratory function of this cluster was the impaired spirometric indices. Specifically, FEV_1, FVC, FEV_1/FVC, and all the respiratory flow measurements, apart from PEF, were the worst among the clusters. Although VC and FVC were reduced in comparison to healthy controls, they were not the indices most affected among the clusters, as both were similarly affected in cluster 1. Respiratory strength was better than in cluster 2, but worse than in cluster 1. However, MIP was near the normal values, but MEP was reduced in comparison to healthy controls, and the $P_{tc}CO_2$ of cluster 3 was normal.

It is of note that cluster 1 was the cluster with the highest pain intensity level, and therefore it could be stipulated that pain is the determining factor for this pattern of respiratory dysfunction. This notion is further strengthened by the close relationship of pain with hyperventilation.[13] Cluster 2 presented the most pronounced respiratory weakness. This group of patients had similar anthropometric characteristics with those in cluster 1. Cluster 3 patients recorded the lowest pain intensity, but the highest restriction in respiratory flow. The patients in cluster 3 had considerably higher height and weight than the other clusters, which may be partially attributed to the fact that mostly male patients were classified into this cluster. These anthropometric differences would not be expected to influence the pulmonary function parameters, however, since the % predicted values were used for both analysis and interpretation.

The possible mechanisms for the observed respiratory dysfunction in patients with CNP have been described analytically in previous publications.[8–10] This study adds to the existing knowledge the observation that the respiratory dysfunction of these patients does not follow one specific pattern, but may show different combinations among patients. Their respiratory dysfunction can be grossly classified into three specific patterns, or clusters. Each of these patterns may reveal a higher compromise in $P_{tc}CO_2$, respiratory flows or strength of respiratory muscles. The preferred methods for the management of their respiratory dysfunction may be different, depending on the cluster, as the clinical priorities change.

It is important to point out that the classification of a patient into a cluster neither constitutes a diagnosis nor describes with detail his(her) respiratory pattern. The terms hypocapnic, weak and flow-restricted were designated to offer a better understanding of the respiratory patterns, and this does not necessarily mean that each individual belonging to a specific cluster may have a specific respiratory condition. The classification of each patient into a pattern was performed with statistical criteria, and the actual respiratory function may be much more complicated, as can be partially demonstrated by the large SDs and the long whiskers of the most of the box-plots. This classification into clusters, however, helps significantly in the interpretation and understanding of the respiratory dysfunction in CNP and contributes the generation of hypotheses regarding its management.

ΠΕΡΙΛΗΨΗ

Ταξινόμηση της αναπνευστικής λειτουργίας σε ασθενείς με ιδιοπαθή χρόνιο αυχενικό πόνο: Μια ανάλυση συστάδων

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Πραγματοποίηση μιας ανάλυσης συστάδων υπαρχόντων δεδομένων για την περιγραφή των προτύπων αναπνευστικής λειτουργίας σε ασθενείς με χρόνιο αυχενικό πόνο. Ανα-

λύθηκαν δεδομένα 45 ασθενών με χρόνιο αυχενικό πόνο. Η αναπνευστική λειτουργία, οι μέγιστες αναπνευστικές πιέσεις και η μερική πίεση του αρτηριακού διοξειδίου του άνθρακα είχαν αξιολογηθεί σε αυτούς τους ασθενείς χρησιμοποιώντας ένα ηλεκτρονικό σπιρόμετρο, μια συσκευή καταγραφής στοματικών πιέσεων και μια συσκευή διαδερμικής καταγραφής των αερίων αίματος. Στα δεδομένα διενεργήθηκε ανάλυση συστάδων για την ταξινόμηση της αναπνευστικής λειτουργίας των ασθενών σε πρότυπα. Μετά την ανάλυση του αντίστοιχου δενδρογράμματος, οι ασθενείς ταξινομήθηκαν σε τρεις διαφορετικές ομάδες που αντιστοιχούσαν σε διαφορετικά αναπνευστικά πρότυπα. Στην πρώτη ομάδα ταξινομήθηκαν 8 ασθενείς και κύριο χαρακτηριστικό ήταν η μειωμένη μερική πίεση του αρτηριακού διοξειδίου του άνθρακα. Στη δεύτερη ομάδα ταξινομήθηκαν 19 ασθενείς και κύριο χαρακτηριστικό ήταν η μειωμένη δύναμη των αναπνευστικών μυών. Στην τρίτη ομάδα ταξινομήθηκαν 18 ασθενείς και κύριο χαρακτηριστικό ήταν οι μειωμένες αναπνευστικές ροές. Συμπερασματικά, η κλινική παρουσίαση της αναπνευστικής λειτουργίας των ασθενών με χρόνιο αυχενικό πόνο μπορεί να ποικίλλει. Αυτή η ποικιλομορφία καθιστά αναγκαία την εξατομικευμένη αξιολόγηση της αναπνευστικής τους λειτουργίας και τον ανάλογο σχεδιασμό της θεραπείας.

Λέξεις ευρετηρίου: Αέρια αίματος, Αναπνευστική δύναμη, Αναπνευστικό πρότυπο, Αυχενικός πόνος, Σπιρομέτρηση

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