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The role of liquid biopsy in early diagnosis of Lung Cancer in patients with Pulmonary Fibrosis

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Key words:
- Pulmonary fibrosis
- Lung cancer
- Liquid biopsy

Pulmonary fibrosis (PF) describes a condition in which the normal lung anatomy is replaced by a process of active remodeling, deposition of extracellular matrix and dramatic changes in the phenotype of both fibroblasts and alveolar epithelial cells, as a result of an abnormal wound healing process1-8. This condition can be idiopathic, as in idiopathic pulmonary fibrosis (IPF), or secondary to genetic disorders, lung parenchyma involvement in connective tissue disorders (CTDs), sarcoidosis9 or to exposure to environmental toxins or radiation. IPF is the most common idiopathic form of pulmonary fibrosis that affects approximately 5 million people worldwide, leading to death more than 100,000 patients each year, the same as breast cancer2. IPF, as well as other forms of progressive fibrotic lung disease, present with a median survival of 3-5 years from the time of diagnosis, evidence that makes them the non-cancer lung diseases with the gravest prognosis2-4-7.

Despite extensive research efforts pathogenesis of lung fibrosis remains elusive reflecting to a significant health burden and an unmet therapeutic need10-12. Recent FDA-approved anti-fibrotic compounds (pirfenidone and nintedanib) do not improve lung function and have shown minimal efficacy in affecting patients’ survival13-18. In addition, none of these compounds has been tested prospectively in the context of IPF coexisting with major comorbidities19 such as lung cancer20. Interestingly, it has been proposed that many of the hallmarks of aging and cancer including genomic instability, telomere attrition, epigenetic alterations, and mitochondrial dysfunction can be considered characteristic of the fibrotic lung21.

Recent epidemiologic evidence suggests that 3 to 22% of patients with IPF develop lung cancer with a nearly 5-fold increased risk compared with the general population22. Lung cancer has a severe impact on PF patients’ survival and quality of life. Despite abundant epidemiologic and mechanistic links between PF and lung cancer23-24, there is considerable lack of knowledge on the diagnostic and therapeutic management of these patients. Current ATS/ERS/JRS/ALAT guidelines (2011) do not address this crucial issue2.

The implementation of a minimally invasive diagnostic tool for the early identification and monitoring of patients with IPF and lung cancer development represents a major challenge. Liquid biopsies have been seminally developed for molecular profiling of tumors in a minimally invasive and less
time-consuming way. They are based on the principle that tumor cells and subsequently their DNA are released into the circulation and therefore circulating-free DNA (cfDNA) can be easily isolated and used for detection of mutations responsible for drug responsiveness or resistance. The first “liquid biopsies” were developed to detect circulating fetal DNA in blood of pregnant females in order to test for fetal aneuploidies, referred to as non-invasive prenatal testing (NIPT). These were rapidly evolved to frequently used tests capable of detecting trisomies with high specificity and sensitivity on mass scale. The development of liquid biopsies for applications in patients with cancer, though being more arduous, has recently received much of attention and currently being implemented as a novel diagnostic and prognostic tool.

The inability to perform molecular tumor profiling in almost 20% of patients with advanced stage lung cancer due to poor performance status, insufficient tissue and long turnaround time led to the implementation of the first PCR-based droplet-biopsy tests for BRAF (V600) and EGFR (T970M) mutations into clinical practice. Similarly, almost half of patients with fibrotic lung disease become symptomatic when fibrosis has significantly progressed leading to severe functional impairment and thus are unfit to undergo surgical lung interventions. Moreover, surgical lung interventions in patients with pulmonary fibrosis have been strongly associated with disease acute exacerbations and increased peri- and post-operative mortality.

Despite the amenable need for non-invasive diagnostic procedures that will allow clinicians to predict lung cancer development in high risk populations including patients with fibrotic lung diseases, the application status of liquid biopsies in this setting has significantly lagged behind. Our study group has spearheaded the field of molecular biomarkers that mirror disease progression and reflect treatment response in patients with IPF. We were the first group that implicated the role of circulating mitochondrial DNA as a biomarker of disease progression in patients with IPF. Moreover, we have recently conducted the largest, so far, biomarker study in the field of lung fibrosis and identified a 52-gene signature that correlated with disease clinical outcomes in 6 different cohorts of patients with IPF. Importantly, in a follow-up biomarker study, researchers identified an epithelial biomarker signature that was strongly correlated with disease mortality. Interestingly, among the most highly-enriched genes were CA-19-9 and CA-125 two cancer-related antigens that are commonly elevated in patients with specific types of cancer including pancreatic, ovarian and lung. The application of similar prediction tools comprising a panel of analytes that reflect both pathologies, lung fibrosis and cancer, may revolutionize current problematic diagnostic modalities and allow clinicians to timely apply personalized medicine therapeutic approaches.

REFERENCES


Chemotherapy in patients with lung cancer and interstitial lung disease

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Key words:
- IPF
- Lung cancer
- Chemotherapy

Interstitial lung disease (ILD) is frequently associated with lung cancer.1,2 Idiopathic pulmonary fibrosis (IPF) has been identified as an independent risk factor for the development of lung cancer and shares several pathogenic commonalities with tumorigenesis3. Patients with lung cancer and concomitant ILD have been excluded from the majority of clinical trials of chemotherapeutic regimens, considering the increased risk of acute exacerbations (AE) of preexisting ILD4,5. Thus, there is no consensus statement with regards to therapeutic approach of this specific subgroup of patients.

The past few years have seen the advent of novel discoveries in the pathogenesis of lung cancer leading to personalized medicine therapeutic approaches6. Current standard of treatment for advanced NSCLC consists of a doublet regimen of a platinum and a third generation agent. Molecular targeted therapies for tumors with driver mutations –EGFR mutation and ALK and ROS1 rearrangement- and immune checkpoint inhibitors for tumors with high expression of PD-L1 represent alternative options in specific subsets of patients7. Doublet regimen of platinum plus etoposide or platinum plus irinotecan represents the first-line standard of treatment for small cell lung cancer (SCLC).8

In light of the rapidly increasing incidence of concomitant ILD-LC and the emergence of the novel chemotherapeutic agents physicians have focused on addressing the following dilemmas: 1) Can we establish an optimal regimen for ILD-LC patients which is both efficacious and safe. 2) Can we identify a reliable biomarker to predict treatment response and disease progression on an individual basis? 3) Can we expect that delineation of common pathogenetic pathways between IPF and lung cancer will open new therapeutic revenues potentially through drug repurposing?

Regarding cytotoxic chemotherapy, a recent meta-analysis demonstrated that a platinum-based doublet presents with an acceptable efficacy profile as first-line therapy in ILD-NSCLC patients given that response rate, progression-free survival and overall survival are comparable to those of patients with NSCLC without ILD. Currently, carboplatin in combination with paclitaxel represents the gold-standard of safety and efficacy in patients with IPF and NSCLC. Carboplatin plus nanoparticle-albumin-bound-paclitaxel has also shown both safety and efficacy in a small cohort of ILD-NSCLC patients.9 The incidence of ILD-AE following first-line chemotherapy is highly variable mainly due to the lack of definitive diagnostic criteria.
for AE. The aforementioned meta-analysis estimated that incidence of AE after first-line chemotherapy was 8.47%. Limited data on second-line treatment with docetaxel or pemetrexed as monotherapy have shown increased risk for ILD-AE. With regards to SCLC, existing data suggests that standard treatment with platinum plus etoposide/irinotecan is relatively efficacious and safe in ILD-SCLC patients.

Data on the efficacy and safety of molecular-targeted therapies in ILD-NSCLC patients is still scarce and controversial. Gefitinib has been associated with ILD-AE and thus EGFR-TKIs are generally avoided in ILD-NSCLC patients. It’s also noteworthy that frequency of EGFR mutations is significantly lower in patients with ILD-NSCLC compared to non-ILD-NSCLC patients. Choi et al (2014) reported poor outcomes when EGFR-TKIs were used as second-line therapy in ILD-NSCLC patients, of whom the majority did not harbor a mutation of EGFR. Authors suggested that the use of EGFR-TKI should be restricted to those patients harboring specific EGFR mutations. Regarding safety and efficacy of ALK inhibitors as well as immune checkpoint inhibitors data is limited and deserves further investigation. Molecular profiling of this subset of NSCLC could be very useful for the application of personalized medicine approaches with minimal side-effects and optimal efficacy.

To this end, the identification of a reliable prognosticator to stratify patients at high risk for exacerbation following chemotherapy represents a major challenge. Small studies have identified smoking status, elevated CRP and decreased baseline FVC% predicted as independent risk factors for disease AE. Usual interstitial pneumonia (UIP) pattern on pre-treatment chest CT has been also shown to be associated with increased risk of ILD-AE.

IPF and lung cancer are two disease paradigms that share many epidemiologic and pathogenetic commonalities. Nintedanib, an FDA-approved agent for the treatment of IPF, has been originally identified as an anticancer drug in combination with docetaxel as second-line treatment for NSCLC. This evidence has raised the attention on exploiting the existing data of oncology research to IPF therapeutics. In particular, dysfunctional activity of the signal transduction pathway PI3/AKT is involved in both IPF and cancer pathogenesis and inhibition of PI3K which is currently being explored as anticancer treatment has also been suggested as a novel option in IPF therapeutics. Epigenetic modifications have been involved in both fibrogenesis and tumorigenesis and thus targeting the epigenome may hold therapeutic promise for both disease entities. Finally, in the case of patients with concomitant IPF-NSCLC it’s interesting to examine whether a combination of anti-fibrotic and anti-cancer drugs could present with synergistic action. A preclinical study demonstrated that pirfenidone in combination with cisplatin led to increased cell death of NSCLC cells and cancer-associated fibroblasts. In addition, perioperative treatment with pirfenidone of IPF-LC patients has been associated with fewer AE after lung cancer operation. Currently, a new, prospective, randomized study has been designed in order to compare nintedanib, combined with carboplatin plus nab-paclitaxel to carboplatin plus nab-paclitaxel alone in IPF-NSCLC patients.

In conclusion, patients with ILD and lung cancer present with increased risk for chemotherapy-induced ILD-AE. To this end, physicians should apply the Hippocratic premise “first do no harm”. Unfortunately, there is major lack of knowledge with regards to safety and efficacy profiles of the majority of conventional chemotherapeutic regimens as well as the novel immune-checkpoint inhibitors. Both disease paradigms present with considerable pathogenetic and phenotypic heterogeneity and thus randomized controlled clinical trials involving highly characterized enrolled patients are extremely difficult and challenging. The application of high-throughput screening strategies may help clinicians to stratify patients based on their risk profile and apply precision medicine approaches that will maximize therapeutic benefits and reduce chemotherapy-induced cytotoxicity.

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Smoking prevalence, compliance and attitudes towards smoking bans among School Teachers in Attica, Greece 2014

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SUMMARY
BACKGROUND: Non-compliance with smoking bans in Greece leave children exposed to secondhand smoke. The current study summarized teachers’ smoking prevalence, compliance and attitudes towards smoking bans. METHODS: A multi-stage sampling design collected data from teachers in Attica, Greece. A secondary source of national data to represent a matching sample of the general population (GP) was used for comparison. Teacher responses were compared by smoking status using logistic regression. To compare teachers and the GP, a binomial proportion test was used and a χ² and Fishers test between modalities, with p set to <0.05 for all results.

RESULTS: 647 educators and 1,678 respondents for the GP ages 25-67 years old residing in Attica, were included. Smoking prevalence among teachers was 26.4%, which was significantly lower than the GP prevalence at 39.7% (p<0.001). Daily smoking prevalence was significantly lower among teachers (p<0.001) compared to the GP. 25.8% of teachers reported complete compliance with smoke-free policies at their school. Teachers who smoked were less likely to report recently teaching their class about smoking (p=0.006) than nonsmokers. A majority of teachers agreed and would volunteer with educational programs aimed at reducing smoking among their students.

CONCLUSION: Prevalence of smoking among teachers in Attica was significantly lower than in the general population and their attitudes were proactive towards implementation of smoking bans in public places in Greece. Compliance with the smoking ban on school grounds could be improved by training teachers on the school policy and protocol regarding smoking on school grounds. Pneumon 2017, 30(4):227-235.

Key words:
- Smoking
- Prevalence
- Attitudes
- Teachers
- Smoke-free legislation
- School-based programs

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INTRODUCTION

Robust scientific evidence supports legislative implementation of smoking bans to improve health outcomes for the population through reduction of second hand smoke (SHS) exposure, namely, the reduction of hospital admissions and mortality from smoking-related diseases\(^1\). In Greece, since ratification of the Framework Convention for Tobacco Control (FCTC) in 2009\(^1\), smoking prevalence has decreased\(^4\). Despite the majority of the public supporting the indoor smoking bans\(^5\), there has yet to be a major change in the context of compliance with smoking bans in public places in Greece\(^6\) where 83% of the public are exposed to SHS when frequenting bars and restaurants\(^7\).

Even more concerning is that smoking bans are poorly enforced in schools, kindergartens, nurseries and playgrounds, leaving 37.2% of students exposed to SHS at school\(^8\). School-aged children are more often exposed to smoke at school than at home and public places; with teachers and peers smoking on school grounds being significantly associated with their daily exposure\(^8\). Knowing that teachers are role models to students and that onset of smoking typically begins at adolescence\(^9\), smoke-free schools play an important role in shaping a smoke-free generation. Properly enforced smoke-free policies in schools have been associated with reduced adolescent smoking uptake\(^10\), decreased smoking prevalence\(^11\) and increased support for the bans by students\(^12\).

In Greece, several school-based educational programs carried out by various non-governmental organizations and scientific societies, supervised by the Hellenic Ministries of Health and Education, have been implemented since 2009, with the aim to reduce smoking initiation through focusing on healthy lifestyles free from smoking among school-aged students\(^13\).

Therefore, the aim of the current study was to summarize teachers’ smoking prevalence and compliance as well as attitudes towards tobacco control policies on school premises in 2014; five years after implementation of these educational programs and the smoking ban law. The second aim was to compare their prevalence rates with the general population of Attica in order to further understand the smoking prevalence among teachers.

METHODS

Smoking prevalence, compliance and attitudes towards smoking bans among teachers in Attica, Greece were examined using a cross-sectional, descriptive study design. An epidemiological study on tobacco use and attitudes of Greek educators in Attica and Thessaloniki (Teacher Survey) within the frame of the National Strategic Reference Framework (NSRF) project, “I learn the Truth; I say no to cigarettes” in 2014, was used as the primary data source. Prevalence of smoking was summarized by total smokers including daily and occasional smokers. A further sub-analysis of attitudes towards smoking policies was completed by teachers’ smoking status. Smoking prevalence of teachers in Attica was also compared to the general population (GP) in Attica using the 2014 Hellenic Statistical Authority (ELSTAT) Health Interview Survey (HIS) data on smoking.

Teacher Survey

Sampling Design

A stratified geographically clustered sampling design was employed as the methodology for the Teachers’ survey. The three levels of stratification were city, regional directorate of secondary education and school. A complete list of all public and private middle or high schools in Attica and Thessaloniki were included, while schools of special education, such as music and vocational schools were excluded. Schools were selected with probability based on their size. A random selection of 852 teachers during the 2014 school year completed the survey.

Survey Questionnaire

The Teacher surveys were collected using an online administered questionnaire covering tobacco use, compliance and attitudes towards smoking bans. Created by the Biomedical Research Foundation Academy of Athens and approved by the Greek Ministry of Education (protocol approval No. 63377/G2/24-04-2014), the questionnaire took no longer than 15 minutes to complete and was collected from May to June 2014. Each respondent used a unique code, randomly distributed to ensure anonymity. Participants were informed of the study aims and anonymity of their participation prior to administration of the survey.

Variables

Socio-demographic information collected included age, gender, smoking status, and teaching grade. Age was grouped into categories 25-34, 35-44, 45-54, and 55-67 years old. Smoking status included never-smokers, ex-smokers, daily smokers and occasional smokers. For
logistic regression analysis and comparison with ELSTAT available data, “never” and “ex-smokers” were grouped into “nonsmokers”.

ELSTAT Survey

The ELSTAT HIS is a nationally representative survey with a multi-stage stratified sampling design conducted every five years in compliance with regulation (EC) No. 1338/2008 of the European Parliament and of the Council. The 2014 survey sampling design used surface area, household, followed by household member over 15 years of age as the sampling units. The questionnaire was administered by in-person interviews in Greek and gathered information on demographics, health status, health practices and services.

To match the geographical and age categories used in the Teacher survey, only respondents from Attica ages 25-67 years were used from the ELSTAT data. As of 2011 population census data, 3.8 million people resided in Attica, accounting for 35.4% of the Greek population.

Sample weighting was applied to the current analysis as provided by ELSTAT to represent the actual population. Variables used included age, gender, and smoking status and created into variables identical to the Teachers Survey for comparability.

Statistical Analysis

Frequencies and relative frequencies were calculated for all responses. For the Teacher survey, a χ² test was used to assess differences between gender and a Fisher’s exact test for the differences between age groups. Simple logistic regression was used to compare differences between teachers’ attitudes by smoking status. Difference in prevalence of smoking between the Teacher Survey and GP was performed using a two-sided binomial proportion test. Analyses were performed with the statistical package STATA 13.1, with a statistically significant threshold of p<0.05.

RESULTS

The current study of teachers included 647 educators with an even distribution of Gymnasium and Lyceum school grades, aged 25-67 years old, residing in Attica, Greece. A final un-weighted sample size of the GP included 1,678 respondents, representing approximately 2,313 149 people living in Attica. There were more female educators (60%) than males (40%), whereas gender in the GP was 52.8% and 47.2%, respectively. In regards to age of teachers, 17.7% were between ages 25-34, 46.3% between ages 35-44, 29.7% between ages 45-54 and 6.4% between 55-67 years of age with distribution of age groups among the GP being 18.1%, 24.2%, 29.0%, respectively.

Prevalence of Smoking

Prevalence of smoking among teachers was 26.4%, with 15% being daily and 11.4% occasional smokers. Smoking prevalence among the GP was 39.7%. As seen in Table 1, total and daily smoking prevalence of teachers was significantly lower than the GP by gender and age groups.
age groups \((p<0.002)\) with exception of “total smokers” among ages 55-67 years \((p=0.474)\). Prevalence of smoking among teachers who were occasional smokers was significantly higher than the GP for gender and age with the exception of ages 25-34 \((p=0.255)\).

**Characteristics of smoking among teachers**

Almost all teachers who smoked \((97.1\%)\) reported primary tobacco use with conventional or rolled cigarettes. Among daily smokers, 8.3\% reported having their first cigarette within 5 minutes, 52.1\% within the first 6-30 minutes of waking, 16.7\% within 31-60 minutes and 22.9\% having their first cigarette after an hour of waking. 83.7\% of smokers also reported being worried about the health effects of their smoking and 63.5\% of smokers believed their smoking has an influence on their students. Characteristics of teachers who smoked are summarized in Table 2.

**Compliance with smoking bans in schools**

Complete compliance with smoke-free policies reported by teachers in their schools was 25.8\%, with 63.8\% having reported people smoke on school grounds and 4.1\% that the smoking is permitted anywhere on school premises. A majority \((63.7\%)\) of teachers reported less than half their students smoke and 55.9\% of them smoke on school grounds. 72.3\% of teachers said they would inform their students of the harms of smoking if they were seen smoking; 69.1\% said they would reproach them; 53.6\% said they would inform the principal; 26.3\% would inform their family and 2.8\% said they would do nothing. Occasional smokers were significantly less likely than nonsmokers to report reproaching their students for smoking on school grounds \((p=0.014)\).

Of the teachers who smoked, 70\% reported smoking inside their home and 32\% stated they smoke inside nightclubs, cafes or bars. When asked if they smoked on school grounds, a majority \((69\%)\) stated they did where 10.8\% reported being reprimanded by their principal for violating the smoking ban and 6.6\% reported their principal did nothing when caught smoking on school grounds \((p=0.014)\). From the entire sample of teachers, 56.3\% reported having seen other teachers smoking on school grounds; 9.6\% inside classrooms, 37.4\% in open areas inside, and 9.3\% in both inside and outside the school grounds. Of daily teachers who smoked, 34.4\% and 27.7\% of occasional smokers reported feeling that the behaviors of colleagues had influenced their own.

**Attitudes and Support towards smoke-free schools**

More than 95\% of teachers were aware that nicotine is addictive and SHS is harmful to health and 86.9\% reported they had advised their students within the last 12 months on the benefits of a healthy diet and physical activity. When asked if they had spoken to their students about a life far from addictions and smoking in the past 12 months, 78.7\% of teachers reported they had. Logistic regression analysis of smoking status with their responses showed daily \((p=0.006)\) and occasional smokers \((p<0.05)\) were less related to reporting they had spoken to their students about a life far from smoking in the past 12 months as compared to nonsmokers.

The majority of teachers \((92.1\%)\) agreed with the enforcement of legislation to protect against passive smoking in indoor public places and 78.7\% reported being upset that it is not enforced. Moreover, most teachers \((92\%)\) believed that Greece should set the reduction of smoking prevalence as a national goal and almost all \((97.9\%)\) of teachers agreed with the systematic enforcement of school-based smoking programs in youth and the health education programs for smoking in schools. Over 75\% agreed with their participation in these school-based programs and would volunteer to participate in initiatives aimed at reducing smoking among youth. A simple logistic regression analysis comparing nonsmokers, daily and occasional smokers found that daily and occasional smokers were significantly less related to supporting the ban inside school grounds than nonsmokers \((p<0.01)\) and daily smokers were significantly less related \((p<0.001)\) to support the ban outside on school grounds than nonsmokers.

**DISCUSSION**

Teachers in Attica had a lower smoking prevalence than the general population, a generally lower addiction to smoking and high rate of cessation attempts, yet two-thirds were incompliant with smoking bans in schools. They were also highly aware of the risks associated with smoking, supportive of smoking bans and willing to participate in programs aimed at reducing smoking in schools. Current prevalence of smoking among teachers was in contrast to previous findings of Sichletidis et al in 2006, who found that teachers in Greece had the highest smoking prevalence of 46.4\% and lowest cessation attempts at 21.7\% as compared to the overall and subpopulations analyzed\(^1\). Noting that in the current study almost half of
TABLE 2. Characteristics and Addiction among School Teachers in Attica, Greece by Total, daily and occasional smoking status

<table>
<thead>
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<th>Occasional</th>
<th>Total</th>
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<td></td>
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<tr>
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<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>I would like to, but I don't think I can</td>
<td>10</td>
<td>10.3</td>
<td>18</td>
</tr>
<tr>
<td>I do not plan on quitting</td>
<td>42</td>
<td>43.3</td>
<td>25</td>
</tr>
<tr>
<td>Refused</td>
<td>42</td>
<td>43.3</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>74</td>
<td>171</td>
</tr>
</tbody>
</table>

Note: n- number

Smokers among teachers smoked less than 10 cigarettes per day could indicate that tobacco consumption has been declining among teachers in Greece.

Considering that complete smoking bans in public places and smoking prevention programs in schools aiming at students are currently in place in Greece, it is suggested that cumulatively, these two factors could have a possible beneficial effect among teachers.

Meta-analyses on prevention programs in schools have identified they have not had significant effects in reducing smoking initiation among adolescents. However, taking into account that the school community includes not only students but also adults (teachers), these studies had not examined the possible effect these programs may have had among adults. Therefore, it is suggested that, although aimed at students, these programs could
have an unexpected positive effect among teachers who were found to have low prevalence of smoking and high cessation attempts in the current study. In addition, the smoking ban law in schools has shown to reduce amount of smoking and prevalence rates among students which could also explain current findings of multiple cessation attempts among teachers and their significantly lower smoking prevalence than the general population. However, evaluative studies of school-based programs are needed to directly measure their effects in the entirety of the Greek school community including in children, parents and teachers.

The current study also identified smoke-free bans on school grounds are not enforced in Attica. Although there was a low prevalence of smoking, a majority of teachers and students who smoke did not comply with the smoking ban in public spaces. Furthermore, in the current study, teachers who smoked were found to be less related to supporting the bans or teaching their students about a life far from smoking and addictions as compared to non-smoking teachers. Teachers play a key part in curbing smoking among youth as previous studies have shown teachers’ smoking is associated with smoking status of students as well as a decrease in students’ support of smoking bans in schools. With this in mind, it is imperative the smoking ban be enforced in both indoor and outdoor school grounds to prevent the influence of teachers’ smoking habits on their students.

Previous studies have identified that barriers to adoption of smoking bans outdoors include socio-political,
school, individual and smoking ban characteristics. Firstly, if these factors are applied in the current Greek context, a vital consideration should be given to socio-political characteristics of the ban by addressing social norms in order to restore a healthy school environment for the physical health and psychological wellbeing of youth and school staff. Not limited to schools, the regular enforcement of Article 8 of the FCTC is important in reshaping social norms and creating supportive environments in all work and public places and promoting smoking prevention and cessation.

School characteristics include ratification by the director of the school and availability of educational resources. The current study results showed there is inconsistency with enforcement of the ban by principals. In the current study, only half of smokers who were non-compliant reported having been reprimanded for smoking on school grounds. It is important for principals to set the tone for the culture for smoking on school grounds and follow through with proper enforcement and expectations from their staff.

In terms of teachers’ individual characteristics as barriers to implementation, the current results showed teachers were very positive toward the smoking bans. Having high awareness of smoking-related harms and most reporting willing to voluntarily work towards a smoke-free environment for their students, highlighted their readiness and willingness to be involved in the process to prevent smoking among youth.

Teachers’ responses on how they would address a student or staff smoking on school grounds varied, implying they are not well-informed of their responsibilities regarding the school policy for smoking on school grounds. Furthermore, this implied that there is probably a gap in setting or implementing a common protocol and training of teachers on how to effectively address non-compliance with the ban with students and colleagues alike. Further research is needed to identify their understanding of smoking ban characteristics including guideline recommendations and outcome expectations in order to address possible issues with communication of implementation goals.

Limitations of the current study include a cross-sectional design to measure prevalence at one point in time. Results represented one urban area of Greece and cannot be inferred to the general population of teachers in Greece. Since results are drawn from a questionnaire, results are subject to recall bias. Lastly, the ELSTAT data on smoking was limited therefore the comparison was also limited to demographic characteristics only where comparison of level of addiction, cessation and attitudes would contribute to further understanding.

CONCLUSION

Teachers in Attica had lower total and daily smoking prevalence than the general public. Educational programs for prevention of smoking among students may have led to changes in smoking habits and attitudes in teachers, although this remains to be examined. Since teachers are willing to volunteer in programs aimed at reducing youth smoking, effectiveness of the smoking ban on school grounds could be improved by providing teachers with adequate training on the school policy and protocol regarding non-compliance.

FUNDING

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ΠΕΡΙΛΗΨΗ

Επιπλασμός του καπνίσματος, συμμόρφωση και στάσεις των εκπαιδευτικών της Αττικής απέναντι στην απαγόρευση του καπνίσματος στους Δημόσιους Χώρους, το 2014

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Εισαγωγή:
Η μη συμμόρφωση με την απαγόρευση του καπνίσματος στους εσωτερικούς Δημόσιους χώρους, έχει σαν αποτέλεσμα την έκθεση των παιδιών σε παθητικό κάπνισμα. Η παρούσα έρευνα επιχειρεί να συνοψίσει τον επιπολασμό του καπνίσματος στους Εκπαιδευτικούς δευτεροβάθμιας εκπαίδευσης της Αττικής, καθώς επίσης να εξετάσει τη συμμόρφωση και τη στάση τους απέναντι στον νόμο για την προστασία από το παθητικό κάπνισμα.

Μεθοδολογία:
Τα δεδομένα για τους εκπαιδευτικούς της Αττικής συλλέχθηκαν από ευρύτερη πολυσταδιακή δειγματοληψία με χρήση quota ως προς τη γεωγραφική κατανομή, ενώ αξιοπίπτωση τοπγενεσιακό πληθυσμό. Η σύγκριση των απαντήσεων των εκπαιδευτικών με το καπνιστικό τους ιστορικό έγινε με μοντέλο λογιστικής παλινδρόμησης. Για τη σύγκριση εκπαιδευτικών - γενικού πληθυσμού ως προς τον επιπολασμό του καπνίσματος χρησιμοποιήθηκε binomial proportion test, ενώ η σύγκριση για φύλλο και ηλικιακή κατηγορία έγινε με έλεγχο χ2 και Fishers. Η σημαντικότητα ορίσθηκε σε p<0.05 για όλα τα αποτελέσματα.

Αποτελέσματα:
Στην έρευνα συμμετείχαν 647 εκπαιδευτικοί απο την Αττική καθώς και 1678 άτομα γενικού πληθυσμού, ηλικίας 25-67 ετών, επίσης κάτοικοι Αττικής. Ο επιπολασμός του καπνίσματος στους εκπαιδευτικούς ήταν 26.4%, σημαντικά χαμηλότερο από το 39.7% του γενικού πληθυσμού (p<0.001). Η συχνότητα του καθημερινού καπνίσματος στους εκπαιδευτικούς ήταν σημαντικά χαμηλότερη (p<0.001) συγκριτικά με τον γενικό πληθυσμό. 25.8% των εκπαιδευτικών ανέφεραν απόλυτη συμμόρφωση με την πολιτική του σχολείου τους ως προς τον έλεγχο του καπνίσματος. Οι καπνιστές εκπαιδευτικοί ήταν λιγότερο πιθανό να αναφέρουν ότι μιλούν για την πρόληψη του καπνίσματος στην τάξη τους (p<0.001), σε σχέση με τους μη καπνιστές. Η πλειοψηφία των καθηγητών συμφώνησε και θα προσφέρουσαν να εργασθούν εθελοντικά σε εκπαιδευτικά προγράμματα που στοχεύουν στη μείωση του καπνίσματος μεταξύ των μαθητών τους.

Συμπέρασμα:
Οι εκπαιδευτικοί της Αττικής εμφάνισαν σημαντικά χαμηλότερο επιπολασμό καπνίσματος σε σχέση με τον γενικό πληθυσμό και επιπλέον είχαν θετική και προληπτική στάση απέναντι στην εφαρμογή του νόμου για την απαγόρευση του καπνίσματος στους σχολικούς χώρους.


Λέξεις - Κλειδιά: Κάπνισμα, Επιπολασμός, Στάσεις, Εκπαιδευτικοί, Νόμος για τον έλεγχο του καπνίσματος, Σχολικά προγράμματα

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The role of psychological factors in the management of severe asthma in adult patients

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SUMMARY
Asthma is a long-lasting and life threatening condition. Patients with asthma often have unpleasant subjective complaints regarding their respiratory symptoms. Many studies highlight the association between psychosocial factors and asthma. Asthmatic patients have higher prevalence of anxiety and depressive disorders. Focusing on physiological and psychological elements is important for treatment. Management strategies combining pharmacologic with non-pharmacologic treatment are more effective in controlling asthma. Psychotherapeutic interventions aim to reduce patients’ complaints, improve quality of life and disease self-management. Various psychotherapeutic approaches/techniques have been studied; Cognitive Behavioral and Analytic Therapy, Psychodynamic psychotherapies, Counseling, psycho-educational interventions, self-management education, relaxation, music therapies, hypnosis, biofeedback. Meta-analytic studies show that psychotherapy works. Following this, many studies tried to specify if psychotherapy is effective specifically for patients with moderate to severe asthma. Results show that psychological interventions have a positive supplementary impact on patients’ traditional medical treatment. Variables examined are health-care services utilization, asthma symptoms, lung function, medication use, absence from work, quality of life, coping skills, self efficacy, locus of control, anxiety, depression. Future research should focus on high-quality, well-conducted and reported randomized trials. Research on psychological interventions in asthmatic patients provide the health care professionals with accurate information about the appropriate psychotherapeutic technique and the frequency of intervention needed for each patient. Asthma morbidity and mortality are still increasing and severe asthma accounts for half of the health service costs related to asthma. Therefore, it is urgent for patients, health-care services and professionals to manage and reduce asthmatic patients’ symptoms and, by extension, hospital visits and admissions.

INTRODUCTION

Asthma is a long-lasting, life-threatening and disabling condition. According to Global Initiative for Asthma (GINA) “Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation.” Patients with asthma often have unpleasant subjective complaints regarding their respiratory symptoms, which include wheeze, shortness of breath, chest tightness and cough.

There is a considerable psychological literature devoted to asthma. A number of studies highlight the association between psychosocial factors and asthma. There is empirical evidence that apart from physiological functions, various psychological factors are related to bronchial asthma. Patients with asthma encounter many psychosocial implications following the diagnosis, such as negative illness perceptions, feeling different than other people, feeling left out of group activities or sports.

Thus, focusing on both physiological and psychological elements is very important for the treatment of asthma. Patient-oriented management strategies which combine pharmacologic with non-pharmacologic treatment are more effective in controlling asthma than disease-oriented strategies.

Psychological factors related to asthma may also trigger attacks. Psychotherapeutic interventions in adult patients with asthma aim to reduce patients’ complaints and improve quality of life as well as self-management of the disease. Specifically, patients learn strategies which help them to reduce emotions, e.g. fear or panic, improve their breathing and respiratory function and, by extension, to ameliorate their general health.

Early theories on psychosocial parameters associated with asthma, indicated it as a psychosomatic illness and focused on mother-child attachment. However, nowadays asthma is considered a multi-factorial illness.

PSYCHOLOGICAL CO-MORBIDITY IN PATIENTS WITH ASTHMA

Many studies show that patients with asthma seem to have greater psychological burden than other patients. However, it is not clarified whether psychological factors trigger asthma symptoms or asthma deteriorates patients psychologically.

There is evidence that asthmatic patients have a higher prevalence of anxiety and depressive disorders than general population, which results to poorer asthma control, medication adherence and increased hospitalization.

A review by Lehrer et al shows that asthmatic patients tend to report a high level of negative emotion, while the periods with higher levels of emotionality are linked temporally to asthma exacerbations, with bidirectional causality. However, in a previous study conducted in 1988 by Corec1ny et al, anxiety does not appear to have a direct role in asthma exacerbation.

Almost half (49%) of the patients with difficult-to-control asthma, studied by Heaney et al, had a psychiatric co-morbidity, while the most common diagnosis was depressive illness (29%). However, authors concluded that psychiatric disturbances are often not detected or diagnosed in difficult-to-control asthmatic patients.

Apart from other psychosocial factors, the association between asthma and psychological co-morbidities may occur as patients with asthma and patients with psychological disorders (e.g. depression or anxiety) have similar dysregulation in key biologic systems, such as neuroendocrine stress response or cytokine system. These aspects predispose people to both asthma and psychiatric illness.

PSYCHOLOGICAL INTERVENTIONS FOR ASTHMATIC PATIENTS

Psychological factors seem to have a major role in asthma; thus, including psychological therapies in patients’ treatment is quite reasonable. Many different psychological interventions, individually or in combination, have been suggested to improve symptoms for adult patients with asthma, complementary to their drug therapies.

Psychotherapeutic approaches that have been studied are Cognitive, Behavioral, Cognitive Behavioral, Cognitive Analytic Therapies, Psychodynamic Psychotherapies and Counseling. Psychotherapeutic interventions usually teach asthmatic patients how to cope with their condition by recognizing and addressing their feelings, thoughts and behaviors related to asthma.

Particularly, as described by Smith and Jones, cognitive therapy recognizes unhelpful thoughts that the patients may have and aims to enable constructive management of these dysfunctional thoughts. Behavioural therapy tries to identify through which processes the patients have learned specific behaviours. Then a variety of interventions (e.g. reward or punishment, bio-feedback) is used in order to help patients modify their behaviours. The combination of these two approaches, Cognitive Behavioural Therapy, helps the patients to develop and practice...
coping strategies in order to resolve their problems.

Psychodynamic psychotherapies attempt to locate the emotional issues and response styles that result in maladaptive behaviours. Nevertheless, there is little evidence that psychodynamic interventions can be useful in a significant number of patients with asthma. Counseling explores the immediate concerns a patient may have. These concerns may be different from session to session.

Additionally, several scientific fields related to psychological interventions in adult patients with asthma have been under study. For example, there are reviews on psycho-educational interventions and self-management education for adults, relaxation and music therapies, hypnosis and biofeedback.

Psycho-educational interventions involve education, training in self-management and targeting psychosocial issues. Self-management programmes range from teaching patients behavioural skills (e.g. using inhalers appropriately) to self-management skills (e.g. control and reduction of their anger and anxiety). Relaxation methods aim to reduce patients’ fear and panic and consciously produce body’s relaxation, such as slower breathing, lower blood pressure and a sense of calmness. In bio-feedback patients are taught how to monitor biological indicators and how to control them with relaxation techniques.

Another technique used in the management of asthma is therapeutic writing, which is a form of a patient’s written emotional disclosure.

**PSYCHOLOGICAL INTERVENTIONS’ EFFECTIVENESS**

In general, meta-analytic studies show that psychotherapy works. Following this, a number of studies have been conducted in order to specify if psychotherapy is effective specifically for patients who suffer from moderate to severe asthma.

When we examine psychological interventions’ effectiveness for patients with asthma we should bear in mind a very important issue; whether these interventions are more effective alone or when combined with each other, and if patients should receive therapeutic help individually or in a group.

A study, conducted by Sommaruga et al in 1995, examined an educational programme and a cognitive-behavioural intervention in patients with asthma. They found that psychological interventions are effective on the cognitive skills involved in the way asthmatic patients perceive and manage their illness after 1 year. In addition, according to their findings Put et al indicated that psycho-education, cognitive and behavioural techniques helped asthmatic patients in many different ways mentioned below. Recently, a British prospective randomized trial showed that patients who received a brief cognitive behavioural intervention had lower levels of asthma-specific panic fear immediately after treatment and at 6 months follow-up.

Another psychological intervention that has been thoroughly studied is the self-management of asthma. This technique seems to be quite effective for patients with asthma, particularly when including a written care plan. According to Creer, asthmatic patients utilize self-management skills to manage their illness with greater consistency, imagination and confidence than expected and there is often remission of asthma symptoms.

Another randomized prospective trial demonstrated that progressive muscle relaxation is effective in improving blood pressure, heart rate and lung function, as well as reducing anger levels in pregnant women with bronchial asthma. Hence, pregnant women have a better health-related quality of life.

**OUTCOMES MEASURED**

Most of the studies regarding the efficacy of psychological interventions for adults with asthma examined variables such as health-care services utilization, symptoms related to asthma, lung function measurements, medication use, absence from work and psychological health issues, e.g. quality of life, coping skills, self efficacy and locus of control, self-esteem, anxiety, depression.

**HOW DO PSYCHOLOGICAL INTERVENTIONS AFFECT OUTCOMES?**

**Health-care services utilization**

The length of hospitalization and the number of emergency visits appear to be decreased for both the Asthma Rehabilitation Group and the control group in a trial conducted in 1995. There is some evidence that psycho-educational interventions have positive effects on hospital admissions in adults with asthma. Self-management seems also to reduce the proportion of patients who were hospitalized or had unscheduled visits to their physicians. On the other hand, Parry et al in 2012 found that service use costs were not reduced
for patients who received a brief cognitive behavioural treatment.25

Symptoms related to asthma

The symptoms related to asthma were measured in various studies. Psychological techniques led to substantial but non-sustained improvement in morning peak-flow expiratory rate.13 Compared to the control group, the programme group, which received an individualized asthma programme aiming at behavioural change, reported significant less obstruction, fatigue and irritation but not dyspnoea and hyperventilation12. Number of patients suffering from nocturnal asthma was also reduced for adults receiving self-management education.26

Lung function measurements

Many studies examined intervention effects on patients’ lung function. Compared to the placebo group, the treatment group improved significantly in measures of lung function (FEV1/FVC) in a randomized controlled study.29 Another study showed that forced oscillation pneumography measurements were improved in patients receiving Heart Rate Variability (HRV) biofeedback as a complementary treatment for asthma.21

Medication use

Relaxation treatment reduced drug consumption in adults with asthma.2,30,31 Another study showed that patients who received a psychotherapeutic intervention alongside their medical therapy had significant improvement in reducing their bronchodilator medication in comparison to the patients who received only medical treatment.6

Absence from work

Sommaruga et al24 concluded that both the Asthma Rehabilitation Group and the control group have significantly less absences from work. Furthermore, Gibson et al26 revealed that the self-management education in asthmatic patients reduced the number of patients who had days off work.

Psychological health issues

Quality of life: Cognitive Behavioural Therapy seems to improve quality of life and asthma control for adult patients with severe asthma.7 Ross et al13 found an improvement in asthma-related quality of life for adults suffering from asthma and co-existing panic disorder. There is also a significant improvement in the total score of the Asthma Quality of Life Questionnaire (AQLQ) for patients receiving Cognitive Behavioural Treatment and Asthma Psycho-Education.12

Coping skills: According to Aalto et al patients’ coping style can predict asthma morbidity.

Self efficacy: Self-efficacy seems to be improved in patients receiving psychological interventions.12,31

Health locus of control: It includes internal beliefs, external control through powerful others and chance. When examined this parameter, Sommaruga et al24 found no significant differences.

Anxiety: When compared with usual care, anxiety levels seem to improve with Cognitive Behavioural Therapy.7 When patients with asthma and co-existing panic disorder received a Cognitive Behavioural Treatment combined with Asthma Education there were substantial and durable anti-panic and anti-anxiety treatment effects.9 On the other hand, Epstein et al30 found no significant differences between the groups.

Depression: It seems there is no statistical improvement in the Beck Depression Inventory scores between groups.13 Kew et al7 also did not find clearly improved depression scale scores for patients receiving Cognitive Behavioural Therapy.

GUIDELINES AND RECOMMENDATIONS ON PSYCHOLOGICAL ISSUES RELATED TO ASTHMA

It is worth mentioning that the Global Initiative for Asthma (GINA), the European Respiratory Society (ERS) and the British Thoracic Society (BTS) refer to psychological issues related to asthma. Recent GINA guidelines urge health-care professionals to provide to asthmatic patients guided self-management education. GINA guidelines also acknowledge that psychological support may be necessary for effective medication delivery and that psychological interventions may be helpful for some patients with severe asthma. The ERS33 and the BTS34 guidelines acknowledge psychological co-morbidity in patients with difficult-to-control and severe asthma. In addition, the BTS guidelines34 include behavioural techniques, counseling and psychological therapies as means of promoting adherence to regular treatment.

SUGGESTIONS FOR FUTURE RESEARCH

When discussing about moderate and severe asthma
in adult patients, medical treatment has been thoroughly studied. On the other hand, there is not enough research regarding the psychological parameters. In order to determine whether psychological techniques improve asthmatic patients’ treatment and draw reliable conclusions regarding their effectiveness, future research should focus on high-quality, well-conducted and reported randomized trials.

Undoubtedly, many different variables are associated with asthma and multiple psychological approaches are proposed for asthma complementary treatment. Khateeb’s meta-analyses\(^3\) show that the efficiency of different psychotherapeutic interventions in asthma is largely dependent on the variables examined. It is, therefore, very important to design and conduct trials carefully paying great attention to such parameters. In addition, Yorke et al\(^4\) propose that future studies should include larger sample sizes, use specific randomization and blinding techniques and monitor participants for sufficient time. Smith and Jones\(^1\) also propose a 12-month post-intervention patient assessment in order to eliminate the possibility of bias related to symptom changes due to seasonality. Schmal-Sing et al\(^3\) suggest that an interesting issue that should be addressed in future studies is patients’ motivation to adhere with their medication.

Another very important issue that must be taken into consideration by future investigators is the purpose that the patients need psychological treatment. As there is often psychological co-morbidity in asthmatic patients, it must be clear whether patients need to get psychotherapeutic treatment for asthma or for their psychological disease. Last but not least, there is little evidence on how Cognitive Analytic Therapy helps asthmatic patients to cope with their illness. This therapeutic intervention has become popular and quite promising for several mental health problems\(^2\) and its framework can be usefully applied to a non-clinical population to good effect.\(^2\)

CONCLUSIONS: TAKE HOME MESSAGES

Undoubtedly, emotional stress deteriorates asthma. A number of studies show that psychological interventions in patients with moderate or severe asthma have a positive supplementary impact on their traditional medical treatment. Large randomized trials, reported with accurate, valid and reliable details should be conducted in order to determine the effectiveness of various psychotherapeutic techniques used to treat severe asthma in adults. Nevertheless, as all trials conducted have a number of methodological weaknesses, interpretation of the research results should be made with caution.

Research on psychological interventions helping adult patients to cope with asthma is a very important area for clinical staff. Studies’ results provide health practitioners with accurate information about the appropriate psychotherapeutic technique and the frequency of intervention needed for each patient individually. Thus, clinicians are trained to identify which psychological strategies are more effective for each patient enhancing an informed decision making. Accordingly, all international guidelines for asthma management should mention the importance of psychological interventions for patients with severe and difficult-to-control asthma.

Asthma morbidity and mortality are still increasing worldwide. At the same time, severe asthma accounts for about half of the health service costs related to asthma. Under these circumstances, it is urgent for all, patients, health-care professionals and health-care services to manage and reduce asthmatic patients’ symptoms and, by extension, hospital visits and admissions.

ΠΕΡΙΛΗΨΗ

Ο ρόλος των ψυχολογικών παραγόντων στην διαχείριση του σοβαρού άσθματος σε ενήλικες ασθενείς

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Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης, Θεσσαλονίκη

Το άσθμα είναι μία μεγάλης διάρκειας κατάσταση υγείας, που τις περισσότερες φορές είναι απειλητική για την ανθρώπινη ζωή. Οι ασθενείς με άσθμα συχνά έχουν δυσάρεστα δυσάρεστα υποκειμενικά παράπονα όσον αφο-
ρά στα αναπνευστικά τους συμπτώματα. Πολλές μελέτες υπογραμμίζουν την σχέση που υπάρχει ανάμεσα στους ψυχολογικούς παράγοντες και στο άσθμα. Στους ασθματικούς ασθενείς συναντούμε υψηλότερο επιπόλασμο ως προς τις αγκώδεις και καταθλιπτικές διαταραχές. Είναι σημαντικό για τη θεραπεία του άσθματος να επικεντρωνόμαστε σε φυσιολογικά και ψυχολογικά στοιχεία. Οι στρατηγικές διαχείρισης που συνδυάζουν τη φαρμακευτική με ψυχο-φαρμακευτικές θεραπείες είναι πιο αποτελεσματικές στον έλεγχο του άσθματος. Οι ψυχοθεραπευτικές παρεμβάσεις αποσκοπούν στο να μειώσουν τα παράπονα των ασθενών, να βελτιώσουν την ποιότητα ζωής και την αυτό-διαχείριση της ασθένειας. Έτσι, πολλές μελέτες επιχείρησαν να προσδιορίσουν αν η ψυχοθεραπεία είναι αποτελεσματική ειδικά για ασθενείς με μέτριο προς σοβαρό άσθμα. Τα αποτελέσματα δείχνουν ότι οι ψυχολογικές παρεμβάσεις λειτουργούν με θετικό τρόπο, συμπληρωματικά στην παραδοσιακή ιατρική περίθαλψη των ασθενών. Μεταβλητές που έχουν εξεταστεί είναι οι εξής: χρήση υπηρεσιών υγείας, συμπτώματα του άσθματος, πνευμονική λειτουργία, χρήση των φαρμάκων, απουσία από την εργασία, ποιότητα ζωής, ικανότητες διαχείρισης, αυτό-αποτελεσματικότητα, σημείο ελέγχου, άγχος, κατάθλιψη. Οι μελλοντικές έρευνες θα πρέπει να επικεντρωθούν σε υψηλής ποιότητας τυχαιοποιημένες μελέτες. Η έρευνα όσον αφορά στις ψυχολογικές παρεμβάσεις σε ασθματικούς ασθενείς παρέχει στους επαγγελματίες υγείας ακριβείς πληροφορίες σχετικά με την κατάλληλη ψυχοθεραπευτική τεχνική και την συχνότητα της παρέμβασης που χρειάζεται ο κάθε ασθενής. Η νοσηρότητα και η θνησιμότητα λόγω του άσθματος συνεχίζουν να αυξάνονται και το σοβαρό άσθμα ευθύνεται για το 50% των υπηρεσιών υγείας που σχετίζονται με το άσθμα. Επομένως, επειδή τόσο για τους ασθενείς όσο και για τις υπηρεσίες και τους επαγγελματίες υγείας να ελέγξουν και να μειώσουν τα συμπτώματα των ασθματικών ασθενών, και κατ’ επέκταση των επισκέψεων και εισαγωγών τους στα νοσοκομεία.


Λέξεις - Κλειδιά: Άσθμα, ψυχολογικές παρεμβάσεις, ψυχοθεραπεία, ΓΑΨ

REFERENCES


The effects of obstructive sleep apnea syndrome (OSAS) on the executive functions of the brain before and after treatment

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Key words:
- Obstructive Sleep Apnea Syndrome,
- Executive Functions,
- Neurocognitive Battery,
- Neurocognitive Functions

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INTRODUCTION

The obstructive sleep apnea syndrome (OSAS) is a disorder of breathing during sleep characterized by prolonged periods of full or partial obstruction of the upper airway¹, thus reducing oxygen saturation and causing brief awakenings². Evidence from studies indicates that it affects at least 9 to 15% of middle aged people³. Compared to women the prevalence of OSAS among males is 1.5 to 3 times greater⁴. International literature indicates that patients with OSAS show deficits in most cognitive and executive brain functions⁵.
regions and that the severity of the syndrome correlates strongly with the scores of various neuropsychological tests.

The literature review of Andreou et al (2014) concludes that further research is needed to clarify which are the precise executive functions that have suffered damage in patients with OSAS.

The treatment of OSAS is performed by tonsillectomy, by mandibular treatment and by the most prevalent therapy of granting a positive air pressure device (CPAP). CPAP therapy is based on restoration of the air flow on the upper airway during sleep, so that the air passes to the lungs freely. Recent studies indicate that treatment using a CPAP device is associated with cognitive and executive improvements. The use of a CPAP device is effective in reducing the symptoms of drowsiness and in improving cognitive and executive function regions. Patients with OSAS exhibit a poorer performance in certain cognitive functions and a reduced volume of gray matter in the hippocampus, in the parietal cortex and in the frontal regions of the brain. After CPAP treatment there have been improvements in memory, attention, executive functions and an increase of gray matter in the above areas.

Crawford-Achour et al (2015) observed that out of 126 patients aged 65 years and above, only 26% had proper treatment of more than 6 hours per night. Finally Zimmermann et al (2006) found that memory decline was eight times more likely to be smoothed out with an average use of 6 hours of CPAP per night.

The purpose of this literature review is to study the effects of the obstructive sleep apnea syndrome (OSAS) in the executive functions of the brain in adult patients, before and after any treatment and whether the treatment may improve the decline that brain regions may have suffered.

METHOD

A literature search was conducted on the interval from 20/01/2017 to 20/04/2017 on the Pub Med database. The selection of the literature was done aiming at a comprehensive coverage of the topic. The keywords used were: obstructive sleep apnea syndrome, executive functions, neurocognitive battery, neurocognitive functions. The primary studies which have been used in this paper regard scientific research, qualitative and quantitative, which has been published in international journals.

Selected studies involve adult patients. Articles that involved patients with comorbidities, review articles and meta-analysis articles were excluded. Using the above keywords 126 articles were found in the PUBMED database.

From these 126 articles we excluded: 24 articles about children, 3 which were off topic, 16 articles that involved comorbidities and finally 36 reviews and meta-analysis articles. In conclusion, 49 articles were selected about OSAS relation to the executive functions, and 45 of them were used in this literature review because the remaining 4 were not written in English. Out of the 44 articles used, 30 articles concerned OSAS and the executive functions without offering treatment while the remaining 14 articles included treatment (Figure I).

On the basis of the above keywords we tried to retrace the chronological appearance of the articles. The first article mentioning OSAS and executive functions was from Bédard et al 1991 in the journal J clin Exp Neuropsych17 while the first article that included some treatment was from Montplaisir et al 1992 in the journal Sleep18. Finally, the journals with the most published articles on the relation of OSAS to the executive functions were the Sleep, the J Sleep Res and the Sleep Breath.

RESULTS

The severity of OSAS is significantly associated with neurological damage and blood cortisol levels, which account for 16% of the variance in the areas of learning, memory and working memory. Also the reduction of the executive functions is directly linked to the severity of the syndrome and not to daytime drowsiness.

The study of Bédard et al (1991) found that, compared to the control group, moderate and severe OSAS presented differences in many cognitive functions and that both frequent awakenings and the nocturnal hypoxemia can contribute to cognitive and executive dysfunction. The severity of OSAS is associated with the damage of brain tissues in the various cognitive areas; also the syndrome may increase the susceptibility of the brain resulting in an ageing population.

Severe OSAS promotes the loss of neuro-axles and causes impairment of myelin, the white substance and the frontal lobe resulting in irreversible damage to the cognitive and executive fields. The study of Hrubos-Strom et al (2012) noted that the problem of verbal memory and executive function was mild in adults at high risk of OSAS. The average oxygen saturation was the index of
obstructive apnea and found to be significantly associated with cognitive function\textsuperscript{23}.

Patients with moderate and severe OSAS exhibit deficits in working memory and memory capacity\textsuperscript{24} as well as reduced information processing rate, reduced working memory capacity and lack of attention\textsuperscript{25}. Also the mild and moderate OSAS has an impact in the areas of attention, executive function, processing rate\textsuperscript{26}, decision making\textsuperscript{27}, visual-spatial and executive functions\textsuperscript{28,29}, attention\textsuperscript{30}, working memory\textsuperscript{31,32}, learning and also disorders in executive and neurocognitive functions as a whole\textsuperscript{33}.

Park et al (2016) in a recent study of 151 people noted that the OSAS group presented abnormalities in the parietal, frontal lobe and left hemisphere, regions responsible for proper cognitive function\textsuperscript{34}. Patients with OSAS also exhibit reduced frontal activation\textsuperscript{35}.

Using electroencephalography (EEG) on OSAS patients, changes were observed during the REM stage not only in the frontal region of the brain but also across the entire range of neuropsychological functions\textsuperscript{36}, while using magnetic resonance imaging (MRI) it was found that grey matter density and the reduction of metabolic activity were changed even in patients without cognitive disorders, suggesting that the brain changes precede the onset of neurocognitive deficits\textsuperscript{37}.

According to Goya et al (2016) a group of patients with OSAS exhibited latency and procrastination during ongoing work\textsuperscript{38}. Nemeth et al (2012) found that the memory performance was reduced in the OSAS group compared to the control group, but the learning process was similar in both groups\textsuperscript{39}.

Sharma et al (2010) reported in their survey that pa-
Patients with OSAS had significantly reduced performance in tests of alertness, working memory, inhibition of responsiveness, problem-solving, executive function and reduced information processing rate resulting in reduced short-term memory.40

Despite the fact that IQ testing is an important predictor of reduced attention and reduced executive function, no correlation with the above was found in the Olathe et al (2015) study.41

Shpirer et al (2012) noted a correlation of cognitive function in patients with OSAS to nightly hypoxemia.29 Edwards et al (2014) after research concluded that cortisol levels are considered prognostic markers of cognitive functions.19 Sales et al (2013) also demonstrated that Oxidative Stress is increased in patients with OSAS.42 Borges et al (2013) note that OSAS without comorbidities does not lead to cognitive impairment.43 Finally, another study of Chen et al (2011) of 394 people demonstrated that the MoCA method is a more sensitive tool for detecting cognitive impairment of patients with OSAS than the MMSE method.44

In contrast to the above studies, the literature mentions items where no correlation between OSAS and the executive functions was found. In a study of 20 patients with OSAS, no deficits were found in executive functions.45 While the literature states that hypoxemia is an important cognitive deficit factor, Hoth et al (2013) found that the group with high hypoxemia displayed better levels of verbal memory in relation than the low hypoxemia group.46

In a study of Rouleau et al (2002), there were no deficits in learning skills in patients with OSAS.47 Finally, as noted by Shpirer et al (2012) the executive functions in certain patients, are not related to polysomnographic parameters (Table I).

### Treatment using a CPAP device

The study by Crawford - Achour et al (2015), after a 10-year study, demonstrated that CPAP treatment protects cognitive and executive performance, particularly in memory and normalizes the mental state of patients with OSAS.48 Following a 3-month treatment with a CPAP device, Canessa et al (2011) observed significant improvement in memory, attention and executive functions. There was also an increase in the volume in the hippocampus and frontal regions.49

Kushida et al (2012), after analysing the results, concluded that CPAP treatment leads to a transient enhancement of executive and frontal lobe function.50 Also in the study of Lau et al (2010), where they tried to compare the state of 37 patients before and 3 months after treatment, there was an improvement in the quality of sleep and a reduction in daytime drowsiness in patients with OSAS.51

According to Dalmases et al (2015) there was an improvement in brain function after 3 months of treatment, increasing the connectivity of the default mode network (DMN) and diluting the cerebral cortex.52 It was also found that since the first month of treatment with CPAP, there was a complete reversal of white matter abnormalities, fractional imbalance, average diffusion and improved memory, attention and executive functions.53

Finally, the study by Ferini-Ssrambi et al (2003) observed at the onset of treatment with CPAP, deficits in attention, learning, visual-spatial learning and executive functions. After 15 days of CPAP treatment improvement was observed and after 4 months CPAP treatment no further improvement was observed in the above areas, the results confirm the hypothesis of partial reversibility of cognitive dysfunction in patients with OSAS following treatment with CPAP.54

In contrast to the above results, there are studies in which no improvement has been observed after treatment with a CPAP device in brain regions associated with cognitive functions. In a study by Berlowitz et al (2013), after treatment using a CPAP device for 6 months, there was no improvement in neurocognitive functions compared to virtual CPAP treatment.55 The same conclusion is reached by Saunamaki et al (2010) in which no improvement in the performance of patients with OSAS was observed after 6 months of treatment.56

Also in a study conducted before CPAP treatment there was a slightly disturbed mental state, deficits in executive functions and learning while after 6 months of treatment no improvement was found in the above categories.57 Naegele et al (1998) found that of short-term memory impairment was evident in patients with OSAS despite CPAP treatment of 4 and 6 months.58

### Damage resoration by surgical intervention

In a study conducted in 51 patients with OSAS improvement in learning and memory was seen after tonsillectomy (UPPP) as well as improvement in executive functions due to better oxygenation.12

Teqelberg et al (2012) concluded that after 6 months of mandibular treatment an improvement was observed concerning the awakenings, attention and executive function in patients with severe OSAS. The findings suggest that mandibular treatment can be an important treatment for OSAS.12 (Table II).
<table>
<thead>
<tr>
<th>Study</th>
<th>Study Group</th>
<th>Age (years)</th>
<th>Methods</th>
<th>Neuropsychological Tests</th>
</tr>
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<tbody>
<tr>
<td>Yilmaz et al</td>
<td>Total n=43</td>
<td>18 – 60 years</td>
<td>PSG, ESS, MRI</td>
<td>WCST, SCWT</td>
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<tr>
<td>(2016)</td>
<td>Patient n=28</td>
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<td></td>
<td>Control n=15</td>
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<tr>
<td>Park et al</td>
<td>Total n=151</td>
<td>Patient = 48.3±9.2 years</td>
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<td>BDI-II, BAI, PSQI</td>
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<tr>
<td>(2016)</td>
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<td>Control = 47.6±9.1 years</td>
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<tr>
<td>Goya et al</td>
<td>Total n=35</td>
<td>40-65 years</td>
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<td>MMSE, WASI, BCI-II, SCWT</td>
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<td></td>
<td>Control n=15</td>
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<tr>
<td>Delazer et al</td>
<td>Total n= 50</td>
<td>Mean age = 51.0</td>
<td>PSG, IED, SSS</td>
<td>HADS, VFT, TMT, WMS, VLMT, IGT</td>
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<tr>
<td>Olaithe et al</td>
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<td>18 years and above</td>
<td>PSG, ESS</td>
<td>COWA, TMT, NART</td>
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<td>(2015)</td>
<td>Patient n=134</td>
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<td></td>
<td>Control n= 16</td>
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<tr>
<td>Chen et al</td>
<td>Total n= 241</td>
<td>1 = 32.53±10.20</td>
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<td>(2015)</td>
<td>Patient n=201</td>
<td>2 = 33.33±7.97</td>
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<td>3 = 35.40±10.43</td>
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<td>4 = 32.80±9.94</td>
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<td>5 = 34.53±9.95</td>
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<tr>
<td>Gelir et al</td>
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<td>PSG, ESS</td>
<td>TMT, N-Back task, MDT</td>
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<tr>
<td>Edwards et al</td>
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<td>PSG</td>
<td>WAIS, DSST, BVMT, HVLT, TMT, DVT, SCWT, TWFT</td>
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<td>Tulek et al</td>
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<td>PSG, ESS</td>
<td>TPT, BDI, DSST, WCST, RL</td>
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<td>(2013)</td>
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<td>Control n= 13</td>
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<tr>
<td>Sales et al</td>
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<td>BDI-II, SCWT, TAI, MMTE</td>
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<td>Patient Moderate-Severe OSAS n= 24</td>
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<td></td>
<td>Control n= 14</td>
<td>Control = 49.6</td>
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<tr>
<td>Hoth et al</td>
<td>Total n= 40</td>
<td>Patient = 55.6</td>
<td>PSG, ESS</td>
<td>BDI, AMNART, PASAT, TMT, COWAT, LNST, HVLT-R, GP</td>
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<tr>
<td>(2013)</td>
<td>Patient High Hypoxemia n= 20</td>
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<td>Control Low Hypoxemia=20</td>
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<tr>
<td>Borges et al</td>
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<td>BAI, BDI, SCWT, RPM, VAMS, VFT, TMT, DS, CORSI, CPT</td>
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<tr>
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<tr>
<td>Hrubos-Strom</td>
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<td>Mean age = 48.2</td>
<td>PSG, ESS</td>
<td>BQ, SCWT, RAVLT</td>
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<tr>
<td>et al (2012)</td>
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<tr>
<td>Shpirer et al</td>
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<td>Mean age 53.3</td>
<td>PSG, EDS</td>
<td>CPT, TMT, BDI, STAI, ADHD, SRS, SRS, ASRS, MMSE, WAIS, TOL, WCST, VFT, DS</td>
</tr>
<tr>
<td>(2012)</td>
<td>patients</td>
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<tr>
<td></td>
<td>Mild OSAS n=11</td>
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<td>Severe OSAS n=14</td>
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### TABLE I. (continued) Study data without treatment

<table>
<thead>
<tr>
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<th>Methods</th>
<th>Neuropsychological Tests</th>
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<tr>
<td>Torelli et al (2011)</td>
<td>Total n = 30 Patient Moderate-Severe n=16 Control n= 14</td>
<td>Patient = 55.8±6.7 Control = 57.0±5.2</td>
<td>ESS, MRI</td>
<td>MMSE, RAVL, DS, VMT, ROCF, SVFT, SCWT</td>
</tr>
<tr>
<td>Greneche et al (2011)</td>
<td>Total n = 22 Patient n=12 Control n= 10</td>
<td>Patient = 51.8 Control= 49.6</td>
<td>PSG, ESS</td>
<td>MMSE, WMS, WCST, VAS, DS, PF, ST</td>
</tr>
<tr>
<td>Zhang et al (2011)</td>
<td>Total n = 18 Patient n=9 Control n = 9</td>
<td>Patient =38.4 Control =37.9</td>
<td>PSG, ESS, MRI</td>
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<tr>
<td>Chen et al (2011)</td>
<td>Total n= 394 Primary snoring n = 46 Mild OSAS n = 92 Moderate OSAS n = 70 Severe OSAS = 186</td>
<td>Primary snoring = 44.5±10.2 Mild OSAS = 46.2 ± 12.1 Moderate OSAS = 47.2±10.9 Severe OSAS = 46.0±11.0</td>
<td>PSG, ESS, EDS MoCA, MMSE</td>
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<tr>
<td>Sharma et al (2010)</td>
<td>Total n = 75 Patient Severe osa n=50 Control n= 25</td>
<td>Patient = 43±7.5 Control = 45.6±6.2</td>
<td>PSG, ESS</td>
<td>WAIS, DSST, WCST, DS, SCWT</td>
</tr>
<tr>
<td>Yaouhi et al (2009)</td>
<td>Total n= 30 Patient n=16 Control n= 14</td>
<td>Patient = 54.75±5.71 Control = 52.71±7.01</td>
<td>PSG, ESS, MRI</td>
<td>SAQLI, MMSE, BDI-II, WMS</td>
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<tr>
<td>Lis et al (2008)</td>
<td>Total n= 30 Patient n=20 Control n= 10</td>
<td>Patient =57.9 Control =53.6</td>
<td>PSG</td>
<td>SRT, SDT, CRT, CRT-vig, N-back tasks</td>
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<tr>
<td>Sagaspe et al (2007)</td>
<td>Total n = 35 Patient OSAS n=20 Control INSOMNIA n = 10</td>
<td>Patient OSAS =45.7±9.5 Control INSOMNIA = 47.4±12.4</td>
<td>PSG, ESS</td>
<td>RT, SSRT</td>
</tr>
<tr>
<td>Quan et al (2006)</td>
<td>Total n = 141 Patient n=67 Control n= 74</td>
<td>Patient mean age = 54.4 Control mean age = 57.4</td>
<td>PSG, ESS</td>
<td>GP, DSST, WAIS, SCWT, TMT, LNS, DS</td>
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<tr>
<td>Alchanatis et al (2004)</td>
<td>Total n = 46 Patient OSAS n= 22 OSAS Subgroup n=14 Control n= 10</td>
<td>OSAS = 49±9.7 OSAS Subgroup = 48±10.1 Control = 42.9±10.5</td>
<td>MRS, PROBE, T1, FRAIR</td>
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<tr>
<td>Vestaeretn et al (2004)</td>
<td>Total n= 65 Patient n=33 Control n= 32</td>
<td>Mean age = 48.3</td>
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<td>TMT, SDMT, SCWT, WAIS, FPT, RT, DS, VVS</td>
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<td>Rouleau et al (2002)</td>
<td>Total n = 46 Patient n=28 Control n= 18</td>
<td>Patient = 47.4 Control n = 47.2</td>
<td>PSG, MSLT, FCRTT, D2T, TMT, WCST, VFT, WMS, RAVL, WAIS, MTI, DS, RVT</td>
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<tr>
<td>Salorio et al (2002)</td>
<td>Total n= 52 Patient n=28 Mild OSAS n = 10 Moderate OSAS n = 6 Severe OSAS= 14 Control n= 24</td>
<td>28-60 years</td>
<td>PSG</td>
<td>WCST, VFT, CVLT,</td>
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<tr>
<td>Morisson et al (1998)</td>
<td>Total n= 31 Patient n=21 Control n= 10</td>
<td>Mean age = 44</td>
<td>EEG, MSLT, EDS</td>
<td></td>
</tr>
<tr>
<td>Bédard et al (1991)</td>
<td>Total n = 30 Control n=10 Moderate n=10 Severe n=10</td>
<td>Control =50.0 Moderate =53.2 Severe = 51.5</td>
<td>PSG, EDS, MSLT, WAIS, RAVL, WMS, VFT, TMT, VMT, FCRTT, WISC</td>
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</table>

**Notes:**
- **ESS:** Epworth Sleepiness Scale
- **MRI:** Magnetic Resonance Imaging
- **MMSE:** Mini-Mental State Examination
- **RAVL:** Rey Auditory Verbal Learning Test
- **DS:** Digit Span
- **VMT:** Visual Memory Test
- **ROCF:** Rey-Osterrieth Complex Figure Test
- **SVFT:** Symbolic Vocabulary Free Test
- **SCWT:** Symbolic Comparison With Times
- **PSG:** Polysomnography
- **WMS:** Wechsler Memory Scale
- **WCST:** Wisconsin Card Sorting Test
- **VAS:** Visual Analogue Scale
- **DSST:** Digit Symbol Substitution Test
- **WAIS:** Wechsler Adult Intelligence Scale
- **RT:** Reaction Time
- **MRS:** Proton Magnetic Resonance Spectroscopy
- **FRAIR:** Functional Resonance Analysis of InfraRed
- **TMT:** Trail Making Test
- **VFT:** Verbal Fluency Test
- **CVLT:** California Verbal Learning Test
- **TMT:** Trail Making Test
- **VVS:** Visual Vigilance
- **EEG:** Electroencephalography
- **MSLT:** Multiple Sleep Latency Test
- **FPT:** Five-Point Test
- **DCST:** Digit Symbol Coding Test
- **DS:** Digit Span
- **Rpt:** Reaction Time
### TABLE II. Study data with treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>Study group</th>
<th>Age (years)</th>
<th>Therapy</th>
<th>Follow ups</th>
<th>Methods</th>
<th>Neuropsychological Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crawford-Achour et al (2015)</td>
<td>Total n=126 Patient n=93 (χωρίς CPAP) Control n=33 (με CPAP)</td>
<td>Patient = 74.7±1.1</td>
<td>CPAP</td>
<td>10 Years</td>
<td>PSG, ESS</td>
<td>MMSE, WAIS, VAS, PDS, GB, BT, SCWT, VFT</td>
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<tr>
<td>Dalmases et al (2015)</td>
<td>Total n=66 Patient n=33 Cpp n= 17 CC n = 16</td>
<td>Patient = 71.30 ± 5.51</td>
<td>CPAP</td>
<td>3 Months</td>
<td>PSG, ESS, MRI, QSO</td>
<td>HANDS, RAVLT, MMSE, TMT, VFT, DIGIT SPAN</td>
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<tr>
<td>Castronovo et al (2014)</td>
<td>Total n=32 Patient n=17 Control n=15</td>
<td>Patient = 43.23</td>
<td>CPAP</td>
<td>3-12 Months</td>
<td>PSG, MRI</td>
<td>MMSE, DS, CORSI, RL, TMS, SCWT, PASAT, RPM</td>
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<tr>
<td>Berlowitz et al (2013)</td>
<td>Total n=1098 Patient active n=556 Control sham n=542</td>
<td>Mean age= 52</td>
<td>CPAP</td>
<td>6 Months</td>
<td>PSG, ESS</td>
<td>PNTTT, BSRT-SR, SWMT-OMD</td>
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<tr>
<td>Kushida et al (2012)</td>
<td>Total n=1098 Patient n=556 Control n=542</td>
<td>Patient = 52.2</td>
<td>CPAP</td>
<td>2-6 Months</td>
<td>PSG, ESS</td>
<td>PFN-TOTL, BSRT-SR, SWMT-OMD</td>
</tr>
<tr>
<td>Tegelberg et al (2012)</td>
<td>Total n=45 Patient - Severe n= 30 Control - Moderate n=15</td>
<td>Mean age = 20-65</td>
<td>Θεραπεία κάτω γνάθου</td>
<td>6 Months</td>
<td>PSG, ESS</td>
<td>WMT, CPT-IP, TMT</td>
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<tr>
<td>Canessa et al (2011)</td>
<td>Total n=32 Patient n=17 Control n=15</td>
<td>Patient mean age = 44 Control mean age = 42.15</td>
<td>CPAP</td>
<td>3 Months</td>
<td>PSG, ESS, MRI</td>
<td>SF-36, BDI, DS, SCWT, RL, MMSE, PASAT, WSRT, CORSI, TMT</td>
</tr>
<tr>
<td>Saunamaki et al (2010)</td>
<td>Total n=37 Patient n=20 Control n=17</td>
<td>Mean age = 20-65</td>
<td>CPAP</td>
<td>6 Months</td>
<td>PSG, ESS</td>
<td>ROCFT, TMT, WAIS, DS, DSS, BDS, TWFT, IEDSS, CANTAB</td>
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<tr>
<td>Lan et al (2010)</td>
<td>Total n=64 Patient n=37 Control n=27</td>
<td>Patient = 57.9</td>
<td>CPAP</td>
<td>3 Months</td>
<td>PSG, ESS</td>
<td>PSQI, DS, VMST, WMS, N-back task, WAIS, WCST, WISC, TMT, WMS, SCWT</td>
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<tr>
<td>Saunamaki et al (2009)</td>
<td>Total n=60 Patient n=40 Control n=20</td>
<td>Patient = 47.2±7.8 Control = 42.9±10.3</td>
<td>CPAP</td>
<td>6 Months</td>
<td>PSG, ESS</td>
<td>IEDSS, WAIS, CANTAB, ROCFT, WCST, DSST, BDS, TMT, TWFT</td>
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<tr>
<td>Ferini-Ssrambi et al (2003)</td>
<td>Total n=46 Patient severe OSAS n=23 Control n=23</td>
<td>Mean age = 56.5 ± 6.13</td>
<td>CPAP</td>
<td>15 Days</td>
<td>PSG, ESS</td>
<td>BDI, DS, CORSI, TMT, SCWT TR2, PPT, ROCF, VFT, RPM</td>
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<tr>
<td>Dahlöf et al (2002)</td>
<td>Total n=104 Patient n=51 Control n=53</td>
<td>Mean age= 50</td>
<td>Αμυγδα-λεκτομή</td>
<td>6 Month</td>
<td>PSG</td>
<td>WCST, BVRT, SRB, CDT, WAIS</td>
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<tr>
<td>Naegele et al (1998)</td>
<td>Total n=34 Patient n=17 Control n=17</td>
<td>Patient = 44,80</td>
<td>CPAP</td>
<td>4-6 Months</td>
<td>PSG</td>
<td>TMT, DBL-CANC, SCWT, CORSI, DS, DC, WISC, VER-L, VIS-L, VFT</td>
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<tr>
<td>Montplaisir et al (1992)</td>
<td>Total n=30 Patient n=20 Control n=10</td>
<td>Mean age = 35-65</td>
<td>CPAP</td>
<td>6 Months</td>
<td>EDS, MSLT</td>
<td>WMS, TWFT, FCRTT, WAIS, ROCF, TMT, BDS</td>
</tr>
</tbody>
</table>
**ABBREVIATIONS**

**A**
- ADHD = Attention-Deficit Hyperactivity Disorder
- AMNART = American National Adult Reading Test
- Apfg = Anterior Prefrontal Guri
- ASRT = Alternating Serial Reaction Time

**B**
- BAI = The Beck Anxiety Inventory
- BDI = The Beck Depression Inventory
- BD = Block Design
- BQ = Berlin Questionnaire
- BSRT-SR = Buschke Selective Reminding Test-Sum Recall
- BT = Buschke Test
- BVMT = Brief Visuospatial Memory Test-Revised
- BVRT = Benton visual retention test

**C**
- CASI = Cognitive Ability Screening Instrument
- CANTAB = Cambridge Neuropsychological Test Automated Battery
- CBF = Cerebral Blood Flow
- CD = The Claeson–Dahl test
- CORSI = Visuo-spatial short-term memory
- COWAT = Controlled Oral Word Association task
- CRT = Choice Reaction Task
- CPT = Continuous Performance Test
- CPT-IP = Continuous, Performance Test, Identical Pairs Version
- CRT-vig = Vigilance Version of the CRT
- CVLT = California Verbal Learning Test

**D**
- DBL-CANC = Digit-Cancellation Task
- DC-SPAN = Double-Encoding Task
- D2T = Test of Attention
- DS = Digit-span Forward and Backward
- DSST = Digit Symbol Substitution Test
- DVT = Digit Vigilance Test

**E**
- EDS = Excessive Daytime Sleepiness
- ESS = Epworth Sleepiness Scale

**F**
- FC = Regional Functional Connectivity
- FCRTT = Four-Choice Reaction Time Test
- FPT = Flexibility Point Test

**G**
- GP = Grooved Pegboard

**H**
- HVLT = Hopkins Verbal Learning Test-Revised

**I**
- IEDSS = Intra-Extra Dimensional Set Shifting test

**L**
- LNST = Letter-Number Sequencing Test

**M**
- MMSE = Mini-Mental State Examination
- MoCA = Montreal Cognitive Assessment
- MRI = Magnetic Resonance Imaging
- MSLT = Multiple Sleep Latency Test
- MSNA = Muscle Sympathetic Nerne Activity
- MTT = Mirror Tracing Task

**N**
- NART = The National Adult Reading Test
- N-Back Tasks = were used with two versions of WM load

**P**
- PASAT = Paced Auditory Serial Addition
- PDS = Pichot Depression Scale
- PF = Pichot scale of fatigue
- PPN-TOTL = Pathfinder Number Test-Total Time
- PNTT = Pathfinder Number Test-Total Time
- PPT = Purdue Pegboard test
- PSG = Polysomnography
- PSQI = Pittsburg Sleep Quality Inventory

**Q**
- QAQ = Quebec Sleep Questionnaire

**R**
- RAVLT = Rey Auditory Verbal Listening Test
- RL = Rey list learning, recall, and recognition verbal long-term memory
- ROCF = Rey-Osterreith Complex Figure
- RPM = Raven Progressive Matrices
- RPT = Rotary Pursuit Task
- RST = Reading Span Task
- RT = Reaction Time

**S**
- SAS = Supervisory Attentional System
- SAQLI = Calgary Sleep Apnea Quality of Life Index
- SCWT = Stroop Color Word Test
- SDMT = Symbol Digit Modalities Test
- SDT = Stimulus Discrimination Task
- SF-36 = The Short Form (36) Health Survey
- SOC = Stockings of Cambridge
- SPECT = Single Photon Emission Computed
- SRB = Synonyms Reasoning and Block design test
- SRS = Self-Report Scale
- SRT = Simple Reaction Task
- SSRT = Stop Signal Reaction Time
- SSS = Stanford Drowsiness Scale
- STAI = State-Trait Anxiety Inventory
- ST = Stenberg Tasks
- SVFT = Semantic Verbal Fluency Task
- SWMT = Sustained Working Memory Test-Overall Mid-Day Index
- SWMT-OMD = Sustained Working Memory Test-Overall Mid-Day Index

**T**
- TAI = Trait Anxiety Inventory
- TOL = Tower of London test
- TMS = Trail Making Test
- TMF = Trail Making Test
- TR2 = Reaction Time Test
- TPT = Toulouse Pieron Test
- TWFT = Thurstone Word Fluency Test

**V**
- VAMS = Visual Analogue Mood Scales
- VAS = Visual Analogue Scale
- VER-L = Verbal Learning Tests for Long-Term Memory
- VFT = Verbal Fluency Test
- VIS-L = Visual learning tests for long-term memory
- VLMT = Verbal Learning Memory Test
- VMST = Verbal memory scanning task
- VMT = Visual memory test
- VVS = Visual Vigilance Test

**W**
- WAIS = Wechsler Adult Intelligence Scale
- WCST = Wisconsin Card Sorting Test
- WMT = Working memory test
- WMS = Wechsler Memory Scale
- WMS-R = Wechsler Memory Scale-Revised
- WSRT = Wilcoxon Signed Rank Test
DISCUSSION

OSAS inarguably causes neurocognitive deficiency and that the severity of the syndrome is responsible for the extent of neurocognitive dysfunction. Patients with OSAS exhibit depression, anxiety, drowsiness, reduced daily functionality and decreased quality of life. The treatment in adult patients with OSAS is: 1) treatment with continuous positive air pressure (CPAP) which is considered to be the most prevalent form of treatment, 2) mandible treatment and 3) tonsillectomy. The above methods act protectively against the maintenance and improvement of neurocognitive deficits.

The literature review of Gagnon et al (2014) is in agreement with the above data. The authors indicate that OSAS is directly linked to the cognitive and executive dysfunction and the possibility of permanent brain damage as well as the presence of dementia in elderly patients.

Vaessen et al (2015) observed that cognitive deficiency appears to be partly related to daytime somnolence and that the impact of CPAP treatment on cognitive functions requires further study and investigation, conclusions which agree with our review.

The study by Decary et al (2000) also agrees that cognitive performance test batteries vary even if they evaluate the same cognitive or executive function.

The same conclusion is reached by Gurubhagavatula (2010) that OSAS causes a multitude of medical consequences caused by the fall of hemoglobin saturation and the repeated awakening during sleep. It also provides new data about OSAS being responsible for the risk of increased motor and occupational accidents and that treatment, besides the improvement offered in the above deficits and the quality of life, also helps to reduce the enormous financial burden on the state in patients diagnosed with OSAS.

Grigg-Damberger et al (2012) observed that snoring increases the risk of neurocognitive damage and that middle-aged people with severe OSAS are at a greater risk for cognitive impairment than young adults with apnea of equal severity.

Also, Weaver et al (2007) report data consistent with this review that most articles in the international literature support the use of a CPAP device. Following treatment, elderly patients with OSAS have improved alertness, memory and executive function and the disruption of sleep from nocturia was also reduced. Finally, a positive effect of the treatment was observed in the factors that affect heart function.

Regarding the limitations of this literature review the search took place only on the Pub Med databases. The articles that were used included the keywords: Sleep Apnea Syndrome, Executive Functions, Neurocognitive Battery, Neurocognitive Functions. The search was age-targeted to adult patients. Articles that included comorbidities, literature review articles as well as articles of meta-analysis were excluded. Finally, only articles in English were used.

In conclusion, OSAS arguably causes neurocognitive deficiency and reduced activation of brain regions responsible for cognitive function. The severity of the syndrome is significantly related to the scores of various neuropsychological batteries – tests. The most prevalent form of treatment is the use of a CPAP device which acts as a protective factor in neurocognitive function, nevertheless further research is required because few studies have evaluated the effect of treatments with a CPAP device while the time period and the population that needs to be studied remain uncertain.

ΠΕΡΙΛΗΨΗ

Η επίδραση του Συνδρόμου της Αποφρακτικής Άπνοιας Ύπνου (ΣΑΑΥ) πριν και μετά τη θεραπεία στις εκτελεστικές λειτουργίες του εγκεφάλου

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1Πνευμονολογική Κλινική Πανεπιστημίου Θεσσαλίας, Εργαστήριο Διαταραχών της Αναπνοής στον Ύπνο, Ιατρική Σχολή Πανεπιστημίου Θεσσαλίας, Λάρισα, 2Μονάδα Μελέτης Ύπνου, Αιγινήτειο Νοσοκομείο, Ιατρική Σχολή Αθηνών, Αθήνα

Σκοπός: Να συνοψίσει τις πληροφορίες των δημοσιευμένων μελετών σχετικά με την επίδραση του ΣΑΑΥ στις εκτελεστικές λειτουργίες του εγκεφάλου σε ενήλικες ασθενείς πριν και μετά την οποιαδήποτε θεραπεία. Μέθοδος: Πραγματοποιήθηκε εκτεταμένη αναζήτηση βιβλιογραφίας στις βάσεις δεδομένων Pub
Med. Αποτελέσματα: Το ΣΑΑΥ αναμφισβήτητα προκαλεί νευρογνωστική ελλειπματικότητα και μειωμένη ενεργοποίηση περιοχών του εγκεφάλου που είναι υπεύθυνες για τη γνωστική λειτουργία. Οι τρόποι θεραπείας είναι με συσκευή θετικής πίεσης αέρα (CPAP), θεραπεία κάτω γνάθου και αμυγδαλεκτομή, οι παραπάνω τρόποι θεραπείας προσφέρουν κάποιοι είδους προστασία στις γνωστικές περιοχές του εγκεφάλου. Η σοβαρότητα του συνδρομού σχετίζεται έντονα με τις βαθμολογίες των διαφόρων νευροψυχολογικών μεταρρυθμίσεων, οι μεταρρυθμίσεις αυτές ποικίλλουν ακόμη και εάν αξιολογούν την ίδια λειτουργία. Συμπεράσματα: Η σοβαρότητα του Συνδρομού είναι υπεύθυνη για τον βαθμό νευρογνωστικής δυσλειτουργίας. Η ποιοτική διαδομένη θεραπευτική αντιμετώπιση είναι η χρήση συσκευής με θετική πίεση αέρα CPAP η οποία δρα και ως προστατευτικός παράγοντας στη νευρογνωστική λειτουργία. Απαιτείται περαιτέρω έρευνα διότι λίγες μελέτες έχουν αξιολογήσει την επίδραση της θεραπείας με συσκευή CPAP και είναι ακόμη ασαφή το χρονικό διάστημα και ο πληθυσμός που πρέπει να απευθύνεται.


Λέξεις - Κλειδιά: Συνδρόμο Αποφρακτικής Άπνοιας Ύπνου, Εκτελεστικές λειτουργίες, Νευρογνωστικές συ- στοιχίες, Νευρογνωστικές λειτουργίες

REFERENCES


Coexistence of pulmonary arteriovenous malformation and inferior vena cava agenesis in a patient presenting with hemoptysis

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Key words:
- Hemoptysis
- Pulmonary arteriovenous malformation
- Inferior vena cava agenesis

INTRODUCTION

Pulmonary arteriovenous malformations (PAVMs) are abnormal vascular structures that connect a pulmonary artery to a pulmonary vein, thus bypassing the normal pulmonary capillary bed¹. Population-wide screening programs using thoracic computed tomography scans suggest a prevalence of 1 in 2630 individuals². The majority of PAVMs are congenital and associated with hereditary hemorrhagic telangiectasia (HHT) also known as Osler-Weber-Rendu syndrome. HHT affects on average one in two to 10,000 people, although the incidence is reported to be higher in certain geographic areas³. HHT may lead to abnormal development of arteriovenous...
communications in virtually every organ. Arteriovenous malformations and smaller telangiectatic vessels develop at multiple sites, including nasal, mucocutaneous, pulmonary, hepatic, gastrointestinal, and cerebrovascular beds. PAVMs can also occur as isolated entities, but this diagnosis should not be considered until HHT has been formally sought in the proband and family members. Non-HHT-related PAVMs are idiopathic or associated with acquired causes such as chest surgery, schistosomiasis, cirrhosis, metastatic carcinoma and mitral stenosis. PAVMs can also occur secondary to hepatopulmonary syndrome.

Congenital anomaly of the inferior vena cava (IVC) is an uncommon vascular malformation. This entity was first recognized by Abernethy in 1793, who described a congenital mesocaval shunt and azygos continuation of the IVC in a 10-month-old infant with dextrocardia. IVC agenesis has an estimated prevalence of less than 1% in the general population and is often discovered incidentally during imaging studies performed for other purposes. IVC agenesis cases have been published mainly as case reports or case series, mostly associated with idiopathic deep venous thrombosis (DVT) and pulmonary embolism in young patients.

Even if IVC agenesis has been recognized as predisposing factor of DVT, the combination of pulmonary arteriovenous malformation and IVC agenesis has been mentioned only once in published literature. Herein, we describe the interesting case of an adult patient with pulmonary arteriovenous malformation, whose evaluation revealed an underlying IVC agenesis.

**CASE PRESENTATION**

A 24-year-old, Greek, non-smoker, obese (BMI >30), otherwise healthy male was admitted to hospital for investigation of recurrent episodes of hemoptysis. He denied any associated symptoms of chest pain, fever or breathlessness. On admission, he had a pulse rate of 90 beats per minute, blood pressure of 120/75 mm Hg, temperature of 37.2°C, and pulse oximetric saturation of 92% on breathing ambient air. A widening of the superficial vascular network in the abdominal area was observed. The rest of the physical examination was normal. Apart from a total leukocyte count of 15,000/mL, with a predominance of neutrophils, no remarkable findings resulted from the rest of laboratory tests. Immunological tests (ANA, ANCA, RF, C3, C4, immunoglobulins) did not provide any abnormal findings. Chest radiograph was normal. High resolution chest CT scan was performed, revealing a lesion in the posterior basal segment of the right lower lobe along with an extensively dilated azygos vein (Figures 1, 2). CT pulmonary angiography excluded pulmonary embolism. Flexible bronchoscopy was performed with normal findings. Sputum smears were persistently negative for acid-fast bacilli by Ziehl-Neelsen technique. Sputum culture grew out of normal oropharyngeal flora.

In order to investigate the azygos vein dilation, an abdominal ultrasonography was performed illustrating a liver of normal size, no evidence of portal hypertension.
and absence of IVC depiction under the mesogastrium. An abdominal CT scan revealed IVC agenesis and widening of the azygos and lower epigastric veins, signs of adjacent vein system development. The findings of IVC absence in combination with the widening of azygos system and the presence of the pulmonary lesion raised the suspicion that a certain vascular malformation could be the cause of hemoptysis. A selective right pulmonary angiography was subsequently performed and depicted a lesion in contact with a bronchopulmonary bundle, supplying from one of the branches of pulmonary artery (Figure 3). Transthoracic contrast echocardiography with agitated saline also revealed a right to left shunt.

The patient’s skin, oral and nasal cavities were carefully examined, but there were not identified telangiectatic lesions. There were no family members who had been diagnosed with visceral arteriovenous malformations before. Gastroscopy and colonoscopy ruled out gastrointestinal telangiectasia, while brain MRI did not show any enhancing lesions. As there were no evidences suggesting the diagnosis of HHT, the patient was regarded as having non-HHT-related pulmonary arteriovenous malformation.

The patient was managed with intravenous fluids, tranexamic acid, cough suppressants and antibiotics. Due to the current unavailability of embolization method in our hospital, the patient was initially referred to an expert center. However, further episode of massive hemoptysis was observed and the patient eventually underwent a right lower lobectomy. Histopathology of the excised specimen was consistent with a pulmonary arteriovenous malformation. Postoperative period was uneventful and the patient remains asymptomatic at follow-up.

**DISCUSSION**

PAVMs may be single or multiple, unilateral or bilateral, simple or complex and are usually located at the lower lobes. Asymptomatic hypoxemia due to right-to-left shunting is the most common manifestation. Platypnea is frequent, attributed to basal predominance of PAVMs and occasionally masked by obesity. Hemoptysis or hemothorax are rarely presented, though these episodes tend to be more common and fatal during the period of pregnancy. Neurological events due to paradoxical emboli are common and include ischemic strokes, brain abscesses and/or migraine headaches. Interestingly, these manifestations may precede the official PAVM diagnosis for years.
The majority of PAVMs (80-90%), as previously mentioned, is hereditary and associated with HHT, an autosomal dominant vascular disorder. HHT diagnosis can be difficult and rely mostly on clinical criteria, known as Curacao criteria which consist of the following four components14: (1) epistaxis (spontaneous, recurrent); (2) telangiectases (multiple at lips, oral cavity, fingers or nose); (3) visceral lesions, including gastrointestinal telangiectasia (with or without bleeding), pulmonary, hepatic, cerebral, and spinal arteriovenous malformations; and (4) family history of a first-degree relative with HHT according to these criteria. Three of these four criteria confirm the diagnosis14. Our patient did not have any evidence suggesting the diagnosis of HHT.

The pathogenesis of PAVMs is highly interesting and includes several mechanisms. The vascular system is remarkably well regulated and malformations are fortunately rare; however disruption in pathways involved in vascular stability can occur. Biological data from endothelial cells derived from arteriovenous malformations, show a high proliferation rate and absence of sensitivity to inhibitory cytokines, such as interleukin (IL)-1b, tumour necrosis factor-a (TNF-a), transforming growth factor-b (TGF-b) and interferon-g (IFN-g). Therefore, genes that regulate angiogenic processes, and more specifically proliferation and/or apoptosis, may be involved in the etiopathogenesis of AVMs. Other probable candidates are genes encoding proteins that are essential for vessel identity, such as ephrin B2, expressed in arteries, and its specific receptor, Eph-B4, present in veins15. The genes mutated in HHT encode proteins which are involved in the TGF-b superfamily signaling pathway1.

The diagnosis of PAVMs on the basis of radiological findings is generally straightforward; however, several pulmonary parenchymal diseases and congenital anomalies that closely resemble pulmonary arteriovenous malformations may cause diagnostic confusion16. Radiographic appearances on a plain chest radiograph range from normality to a mass with visible feeding or draining vessels while the gold standard method for diagnosis has been pulmonary angiography and CT scan6 to 12 months after embolization and then every 3 to 5 years15. Since PAVMs occur after 15% of embolizations and results from recanalization of occluded PAVMs, collateralization from adjacent arteries, or missed accessory pathways5. As for the follow-up period, it is recommended to perform CT scan 6 to 12 months after embolization and then every 3 to 5 years15.

Interestingly, anomalies of the IVC are extremely rare and present only in 0.3-0.5% of healthy individuals17. About 90% of congenital IVC malformations involve the hepatic and suprarenal segments, whereas only about 6% involve the renal or infrarenal segments18. IVC agenesis has an incidence of less than 1% and may occur as isolated entity or coexist with anomalies of other anatomic structures, mainly the heart (situs inversus, dextrocardia) or the spleen (polysplenia, asplenia)17. In our case, the patient did not have any associated congenital heart or splenic defects. IVC agenesis is divided into 3 segments (retrohepatic, renal and postrenal segments) and is often associated with azygos and/or hemiazygos continuation which allow drainage into the caudal segment up to the right atrium through the connection with the superior vena cava17.

Several mechanisms are involved in the pathogenesis of IVC agenesis. The IVC and adjacent urogenital drainage system undergo complex embryogenesis between weeks 6 and 8 of embryonic life. Two hypotheses have been described to explain the origin of the malformation: changes during the process of embryogenesis or intrauterine/
perinatal thrombosis that consecutively influences the postnatal development of the venous system\textsuperscript{19}.

The clinical importance of these congenital anomalies lies in the fact that they have been particularly associated with unprovoked DVT in young patients, although they are usually not considered because of their rarity. Indeed, it has been reported an incidence of IVC agenesis of about 5\% in young patients affected by DVT\textsuperscript{9}. Accordingly, Ruggeri et al suggest a thorough investigation with a CT scan or venous angiography in all young patients with idiopathic DVT affecting the inguinal and iliac region, for exclusion of this abnormality\textsuperscript{9}. However, apart from a few cases of pulmonary embolism\textsuperscript{8,10}, no connection with pulmonary disorders has ever been described.

In conclusion, to the best of our knowledge, there is only one description of the combination of PAVM with IVC agenesis in published literature\textsuperscript{12}. Indeed, given the very limited epidemiologic evidence of IVC agenesis, we could not theorize that this entity presents a true association rather than an interesting coincidence. Nevertheless, physicians should be mindful of the possibility of an undiagnosed pulmonary arteriovenous malformation in adults presenting with hemoptysis; the possibility of associated anatomic abnormalities and multiorgan anomalies should also be considered. Furthermore, as unanswered questions remain regarding the pathogenetic correlation of these vascular malformations, further investigation is needed on PAVMs and their pathogenesis.

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.
REFERENCES

Symptomatic Bochdalek hernia with kidney in an elderly patient
A case report

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SUMMARY
Bochdalek hernia (BH), resulting from the failure of posterolateral diaphragmatic foramina to fuse, is the most common congenital diaphragmatic hernia and usually manifests in pediatric age with life-threatening complications. We present the case of an elderly man with chronic pulmonary obstructive disease, who presented with chronic atypical chest pain. Computed tomography scans of the chest demonstrated left-sided BH containing kidney and spleen. Thus, it is essential to be aware of the coexistence of BH appearing in adult life.

INTRODUCTION
Congenital diaphragmatic hernias (CDH) are a result of failure of fusion of the developmental components of the diaphragm. CDH occur in 1 in approximately 2,000 to 10,000 births¹, they are more frequent in males and have been correlated with chromosomal abnormalities². They can be classified into three subtypes: i. Bochdalek hernia (BH), ii. Morgagni hernia and other anterior hernias, iii. Central hernia. BH, was first described by Alexander Bochdalek in 1848³. Table 1 shows the main differences between Bochdalek and Morgagni hernia.

In this paper, we report the case of a symptomatic left-sided BH in an

TABLE 1. Main differences between Bochdalek and Morgagni hernia.

<table>
<thead>
<tr>
<th>Bochdalek hernia</th>
<th>Morgagni hernia</th>
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<tbody>
<tr>
<td>Most common CDH (90%)</td>
<td>Less common CDH (2%)</td>
</tr>
<tr>
<td>Posterior</td>
<td>Anterior</td>
</tr>
<tr>
<td>Occurs earlier</td>
<td>Occurs later</td>
</tr>
<tr>
<td>More often left-sided</td>
<td>More often right-sided</td>
</tr>
</tbody>
</table>

CDH: Congenital diaphragmatic hernia
81-year-old man, who was admitted to our emergency department with chronic atypical chest pain.

CASE PRESENTATION

An 81-year-old man, arrived in the emergency department with breathlessness, dry cough and chronic atypical left sided chest pain for more than 5 years. He had a history of chronic obstructive pulmonary disease (COPD) and received the appropriate medication. The pain had been attributed to musculoskeletal problems and COPD. Upon examination, he was hemodynamically stable and non febrile. The electrocardiograph was normal and his oxygen saturation was at 88%. Routine hematology and biochemistry blood tests were unremarkable. The chest x-ray gave the impression elevation of the left hemidiaphragm (Figure 1). Computed tomography (CT) scan of the chest showed a left-sided BH containing kidney and spleen and emphysema (Figure 2). Owing to his advanced age, poor lung function and the lack of severe direct complications from the hernia or ectopic kidney, surgical repair was not indicated.

DISCUSSION

BH forms in the posterolateral region of the diaphragm and rarely contains hernia sac. It occurs more commonly on the left side of diaphragm (85%) because the right pleuroperitoneal fold fuses earlier than the left and the liver acts as a barrier. About 10% of BH occurs on the left side and only 5% is bilateral. In a large series of CT, the incidence of BH in adults was 0.17%. The content of BH varies and depends on the position of the hernias. Therefore, the content of left-sided BH may include colon, stomach, spleen, omentum, pancreas, adrenal gland and kidney; while the right-sided BH may include liver, gallbladder, kidney and omentum.

The majority of BH manifests in infancy and the clinical presentation includes respiratory distress, absent breath sounds on one side of the chest and scaphoid abdomen. Due to herniation of the abdominal organs, there is pulmonary hypoplasia on the side of the hernia and pulmonary hypertension is common. In adult life, the symptoms are nonspecific and chronic and they range from asymptomatic to emergency. The diagnosis of BH in adults is not easy and many times, it is misdiagnosed due to low rarity of BH and a variety of symptoms. At the diagnosis, 86% of patients have hernia related symptoms and only in 14% of patients was BH detected incidentally. Thus, BH may occur as an asymptomatic chest mass, atypical chest, upper abdominal pain or discomfort, breathlessness, cough, dysphagia and gastrointestinal obstructive symptoms such as vomiting and constipation due to herniation of the stomach or bowel. Moreover, BH may occur as an emergency due to strangulation and gastric volvulus. Our patient suffered from chronic pulmonary obstructive disease and was admitted into the emergency department with breathlessness, dry cough and chronic atypical left-sided chest pain.

The manifestations of BH mainly depend on the content of hernia and may include life threatening complications depending on the content of hernia (Table 2).
Concerning this particular case, BH includes the left kidney and spleen. The intrathoracic location of an ectopic kidney is very rare and represents 5% of all the ectopic kidneys. Additionally, the incidence of intrathoracic kidney with BH is very rare and specifically less than 0.25%. The intrathoracic kidney with BH differs from other intrathoracic renal ectopias, because they tend to be mobile and are reduced due to pressure from other organs.

More often than not, BH is diagnosed with plain film frontal and lateral chest radiography. A normal previous chest x-ray may not exclude BH, because the herniation of content may be intermittent. In this specific case, chest x-ray gave the impression elevation of the left hemidiaphragm. However, due to the low sensitivity of plain film chest radiography, the differential diagnosis includes other thoracic disorders, such as, phrenic nerve palsy, mediastinal and pulmonary cyst or tumor, and pleural effusion. Consequently, in most cases, BH is confirmed by CT or MRI. CT has a sensitivity of 78% for left-sided diaphragmatic hernia and 50% for the right-sided diaphragmatic hernia. Furthermore, ultrasound may help in the diagnosis of suspected cases of BH. The treatment of hernia is surgical and BH repair can be performed via a transabdominal or transthoracic approach, depending on the content and complications.

CONCLUSION

BH is the most common congenital diaphragmatic hernia and is usually symptomatic. It is essential to be aware of the coexistence of BH occurring in adult life, since many times it is responsible for mild to severe manifestations and complications. Frontal and lateral chest radiography is a useful imaging tool, however, CT is more sensitive for these lesions.
REFERENCES


Superior vena cava occlusion related collateral pathway

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A 70-year-old patient, diagnosed a year ago with adenocarcinoma of the right upper lobe, presented unilateral, left sided plethora of the head and oedema of the neck, during hospitalization due to recurrent haemoptysis. The patient had not received any treatment since diagnosis. Symptoms were suggestive of superior vena cava (SVC) obstruction, so a Multi Detector Computed Tomography (MDCT) of the chest was performed. As far as thoracic venous system is concerned, imaging revealed complete occlusion of the SVC, right brachiocephalic, right internal jugular and right azygos veins (Fig. 1) as well as thrombosis of the right subclavian, right axillary and left brachiocephalic veins (Fig. 2). Interestingly, an excessive collateral venous pathway formed by the right sided internal mammary (Fig. 1), intercostal (Fig. 3), chest wall (Fig. 1), epigastric, epiphrenic and perinephric (Fig. 3) space veins was revealed (type Stanford IV). Gradual obstruction of SVC along with the development of a sufficient collateral pathway determines the paradox, mild, unilateral and left sided clinical findings of the patient, despite complete obstruction of the right venous system. Moreover, imaging of collateral pathways by MDCT and 3D imaging (Fig. 4), is advantageous in the evaluation of SVC obstruction, especially in cases of nontypical clinical appearance².

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REFERENCES

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