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Original article

Epidemiology and Outcomes of Acute Respiratory Syndrome in Aged Patients with Overlap Syndrome

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Abstract

Objectives: The aim of this study was to determine the complication and prognostic criteria in patients with overlap syndrome developing respiratory failure due to chronic obstructive pulmonary disease. ***Materials and Methods:*** The files of 418 patients 358 (85.6%) male and 60 (14.4%) female aged 65 years and over who were treated in İzmir Eşrefpaşa Hospital and İstanbul Okmeydanı Training Hospital intensive care units between January 2016 and January 2019 were included in the study. In this study, we retrospectively evaluated treatment modalities, complications and prognosis in aged patients with overlap syndrome. ***Results:*** It was determined that 192 (78.04 %) of the cases with complications were exitus and that 62 (36.04 %) of the 172 cases without complications were exitus. There was a statistically significant difference between the two groups with regard to mortality ($p< 0.05$). ***Conclusion:*** In conclusion, it was considered that the complication rate is high in aged OSAS patients with respiratory syndrome due to COPD requiring intensive care treatment and that complication development increases mortality.

Keywords: ***Acute respiratory syndrome, Overlap syndrome, intensive care unit, complication, aged patients***

Introduction

Chronic obstructive pulmonary disorder (COPD) is a disease group that generally develops due to smoking, comprised of emphysema and chronic bronchitis components which is characterized by expiratory air flow. Even though it is fundamentally a benign disease, its prognosis is bad and it is among the most frequently encountered causes of death in the world[1]. Obstructive Sleep Apnea Syndrome (OSAS) is characterized by the repeated collapse of the upper respiratory tract during sleep, nocturnal hypoxemia and interrupted sleep[1,2]. It is the most frequent among sleep disorders. Many different results are presented on the mortality rates of patients hospitalized with acute attack. The prognosis of patients that require treatment at intensive care units is especially worse compared to patients with stable prognosis[3]. Hypoxia, hypercapnia and acidosis that develop due to respiratory failure that develops in COPD cases have adverse impacts on many different systems. Many complications may develop in these patients due to the disease itself as well as the applied treatment, advanced age and the interventions made which in turn increase morbidity and mortality[4,5].

On the other hand, Oxygenation is impaired in both OSAS and COPD. In cases where both diseases occur together, the deterioration in oxygenation becomes very serious. Night hypoxemia not only disrupts the structure of sleep but also causes the hypoxemia-related complications which are expected to be seen in later stages in both diseases. OSAS prevalence has been determined as 3-7% for males and 2-5% for females as a result of many studies carried out all over the world[6].

The aim of this study was to determine the treatment modalities, interventions and complications in aged patients with overlap syndrome in intensive care unit (ICU) because of COPD-induced acute respiratory syndrome and to determine the relationship between complications and mortality.

Materials and Method

A total of 254 cases aged 65 and above who have been treated at the Izmir Eşrefpaşa Hospital and Istanbul Okmeydanı Education Hospital Intensive Care Units during the dates of 01.01.2016-01.01.2019 and who have been exitus during the monitoring period along with 164 cases aged 65 and above who have been discharged with the same diagnosis have been included in the study. The files of all cases were examined retrospectively and the applied treatment methods, invasive methods, complications that developed during monitoring, durations of hospitalization and prognosis recorded for cases. Complications and complication ratios were compared between the two groups. Chi-square test was used for

statistical analysis in the study. Values of $p < 0.05$ were accepted as statistically significant.

Results

Of the patients with an age average of 72.06 ± 9.66, 60 (14.4 %) were female and 358 (85.6 %) were male. The age average of female patients was 68.03 ± 5.32; while the age average of male patients was 76.03 ± 4.71.

All patients in the exitus group (99.21 %) excluding 2 cases who have underwent conservative medical treatment (MT) were subject to invasive mechanical ventilation (IMV), while 20 cases (12.20 %) in the discharged group were subject to MT and 82 cases were subject to non-invasive mechanical ventilation (NIMV). Of the patients subject to NIMV, 44 were also subject to IMV as well. The number of cases subject to IMV in the discharged group was 106 (64.63 %).

Central venous catheterization was applied on 36 cases, bronchoscopy on 28 cases, tracheotomy on 8, thoracentesis on 4 and chest drain on 4 as a result of which no complications developed.

Complications that developed ICU monitoring were recorded from the case files which were then grouped as metabolic, renal, neuropsychic, cardiovascular system, gastrointestinal system and respiratory system complications.

Cardiovascular system complications developed in 184 (72.44 %) cases in the exitus group and 38 cases (23.17 %) in the discharged group. The difference was statistically significant (p: 0.00000).

It was observed that metabolic complication developed in 132 (51.97 %) of the exitus patients and 32 (19.51 %) of the discharged patients. There was a statistically significant difference between the two groups (p: 0.00000).

It was determined upon examining the renal complications that; a renal system complication developed in 112 (44.09 %) cases in the exitus group and 28 (17.07 %) cases in the discharged group. The difference was again statistically significant (p: 0.00005).

Whereas a gastrointestinal system complication was observed in 72 (28.35 %) of the exitus group patients, this number was 64 (39.02 %) for the discharged group. There was no statistically significant difference between the two groups ($p > 0.05$).

A respiratory system complication developed in 76 (29.92 %) of the exitus cases and 32 (19.51 %) of the discharged cases during their ICU monitoring period. However, the difference was not statistically significant ($p > 0.05$).

While neuropsychic complications were observed in 20 (7.87 %) of the exitus cases and 10 (6.09 %) of the discharged cases. There was no statistically significant difference between the groups ($p > 0.05$). Table 1 presents the distribution of the developed complications according to the systems.

Cardiovascular system complications were determined as arrhythmia, hypertension, hypotension and acute myocardial infarction (AMİ). Hypotension was the most frequently observed cardiovascular system complication in the Exitus group with 124 (48.82 %) cases. This was followed by arrhythmia with 90 cases (35.43 %). Atrial fibrillation and atrial chaotic rhythm were the most frequently detected arrhythmias. Whereas hypertension was the most frequently observed cardiovascular system complication in the discharged group with 20 cases (12.19 %). Cardiovascular system complications in the cases are presented in Table 2.

Table 1: Complications That Developed in the Cases during Monitoring

	Case n %	Exitus n %	Discharged n %	p
CVS*	222 53.11	184 72.44	38 23.17	**0.001**
Metabolic	164 39.23	132 51.97	32 19.51	**0.002**
Renal	140 33.49	112 44.09	14 17.07	**0.001**
GIS**	136 32.54	72 28.35	64 39.02	**0.062**
Respiratory	108 25.84	76 29.92	32 19.51	**0.071**
Neuropsychic	30 7.18	20 7.87	10 6.09	**0.083**

CVS: Cardio Vascular System, GIS**: Gastro Intestinal System*

Electrolyte imbalance (hypernatremia, hyponatremia, hypokalemia, hyperkalemia, hypocalcemia, hypercalcemia etc.), hyperglycemia and hypoglycemia were included in the study from among the metabolic complications. Electrolyte imbalances were observed in 102 (40.16 %) of the exitus cases. Whereas hyperglycemia was ranked number one which developed in 22 (13.41 %) of the discharged cases. Metabolic complications that developed in the cases during follow-up are given in Table 2.

Renal complications were evaluated in two sub-groups in the present study as acute renal failure (ARF) and prerenal azotemia. Both complications were observed more in exitus patients, while prerenal azotemia was the most frequently observed renal complication in all patients. Acute renal failure developed in 34 (13.38 %) cases in the exitus group and 6 (3.65 %) cases in the discharged group. Renal complications can be seen in Table 2.

The gastrointestinal system complications that developed in the patients during their follow-up and treatment at the ICU were; gastrointestinal system bleeding, treatment requiring constipation and diarrhea. Even though no statistically significant difference was observed between the two groups when the GIS complications were evaluated in general, there was a statistically significant difference (p: 0.0006) between the groups with regard to GIS bleeding observed in 52 cases (20.47 %) in the exitus group and 6 cases (3.66 %) in the discharged group. Table 2 shows the GIS complications.

Table 2: Different system complications in aged cases

CARDIOVASCULAR COMPLICATIONS	**Arrhythmia (n) %**	**Hypertension (n) %**	**Hypotension (n) %**	**AMI (n) %**
Exitus	90 (21,5)	20 (04,7)	124 (29,6)	18 (04,3)
Discharged	12 (02,8)	20 (04,7)	10 (02,3)	2 (0,47)
Total	102 (24,4)	40 (09,5)	134 (32,0)	20 (04,7)
METABOLIC COMPLICATIONS	Electrolyte imbalance (n) %	Hypoglycemia (n) %	Hyperglycemia (n) %	
Exitus	102 (24,4)	12 (02,8)	50 (11,9)	
Discharged	1 (0,23)	2 (0,47)	22 (5,26)	
Total	20 (04,7)	14 (03,3)	72 (17,2)	

RENAL COMPLICATIONS	Prerenal Azotemia (n) %	Acute Renal Failure (n) %
Exitus	78 (18,61)	34 (8,13)
Discharged	22 (5,26)	6 (1,43)
Total	100 (23,91)	40 (9,51)

GIS COMPLICATIONS	Bleeding (n) %	Constipation (n) %	Diarrhea (n) %
Exitus	52 (12,44)	36 (8,61)	48 (11,48)
Discharged	6 (1,43)	52 (12,44)	30 (7,17)
Total	58 (13,87)	88 (21,05)	78 (18,66)

RESPIRATORY COMPLICATIONS	Pulmonary Emboli (n) %	Pneumonia (n) %	Pnx. (n) %	Larynx Edema (n) %	Tracheal Stenosis (n) %
Exitus	6 (1,43)	72 (17,11)	4 (0,95)	6 (1,43)	-
Discharged	-	22 (5,26)	-	24 (5,74)	2 (0,47)
Total	6 (1,43)	94 (22,48)	4 (0,95)	30 (7,17)	2 (0,47)

NEUROPSYCHIC COMPLICATIONS	Cerebrovascular Disease (n) %	Psychosis (n) %
Exitus	20 (4,78)	-
Discharged	2 (0,47)	8 (1,91)
Total	22 (5,26)	8 (1,91)

Respiratory system complications observed in the cases were pulmonary emboli, nosocomial pneumonia, pneumothorax, larynx oedema and tracheal stenosis. The respiratory system complications that developed and the number of cases are presented in Table 2.

A statistically significant difference was not observed between the exitus and discharged groups when all respiratory system complications were evaluated as a whole. However, there was a statistically significant difference (p: 0.01158) between the two groups when nosocomial pneumonia was evaluated separately which developed in 72 exitus group cases (28.3 %) and 44 discharged group cases (13.4 %).

Nosocomial pneumonia evaluation was carried out according to increase in the amount and phlegm purulence, fever, increase in leukocyte level and new infiltration development in lung graphy. The bacteriological evaluation results for the phlegm of patients with nosocomial pneumonia development were examined. Phlegm bacteriological examination could not be carried out in 26 (27.66 %) out of 94 cases with nosocomial pneumonia as a respiratory system complication. Growth was not observed in 8 (11.76 %) of the cases subject to bacteriological examination. The most frequently observed growing active agent was gram (-) non-fermentative bacilli with 64.70 % (44 cases). Microorganisms that most frequently grew in the phlegm of cases with nosocomial pneumonia are given in Table 3.

Table 3: Microorganisms Growing in Cases with Nosocomial Pneumonia

Active microorganism	Cases n %	Active microorganism	Cases n %
Gr(-)nonferm. b.	44 64.70	**M. catarrhalis**	2 2.94
S. aureus	6 8.82	**S. pneumoniae**	2 2.94
Enterobactericea	4 5.88	**C. difteriae**	2 2.94

Treatment requiring psychosis and cerebrovascular disease were among the neuropsychic complications observed in cases. Psychosis diagnosis was placed as a result of psychiatric consultation, while cerebrovascular disease diagnosis was placed after neurological consultation. Minor depression, intensive care related temporary agitations were not included in the evaluation. Table 2 presents the neuropsychic complications that developed in the cases.

The cases were included in the study after evaluating their durations of stay in the hospital, ICU and invasive mechanical ventilator.

The average duration of stay in the hospital was 11.92 ± 10.76 days for the exitus group and 21.13 ± 11.54 days for the discharged group. The difference was statistically significant (p: 0.000).

The average duration of stay in the ICU was 7.76 ± 7.38 days for the exitus group while it was 10.76 ± 6.49 days for the discharged group. The difference was statistically significant (p: 0.003).

The average duration of stay in the mechanical ventilator was 5.52 ± 5.50 days for the cases in the exitus group who received mechanical ventilator support, while the average duration of stay in the mechanical ventilator was 2.79 ± 3.37 days for the cases in the discharged group. There was a statistically significant difference between the groups (p: 0.000).

Table 4 presents the durations of stay in the hospital, ICU and mechanical ventilator for the cases.

Table 4: Durations of Stay in the Hospital, ICU and MV for the Cases

Duration (days)	All cases	Exitus	Discharged	p
Hospital stay	15.54 ± 11.93 (1-75)	11.92 ± 10.76 (1-52)	21.13 ± 11.54 (5-75)	**0.000**
ICU* stay	8.93 ± 7.18 (1-40)	7.76 ± 7.38 (1-38)	10.76 ± 6.49 (1-40)	**0.003**
MV stay**	4.45 ± 4.96 (1-38)	5.52 ± 5.50 (1-38)	2.79 ± 3.37 (1-14)	**0.000**

**ICU:İntensive Care Unit, ** MV:Mechanical Ventilation*

Discussion

Many complications develop during ARF in COPD characterized by increased respiratory workload and respiratory pump failure especially in aged OSAS patients, moreover proneness to mechanical ventilator complications increases. It is reported that these complications trigger early period prognosis[3,4,5].

Various cardiovascular system (CVS) complications (arrhythmia, hypotension, hypertension, cardiac arrest etc.) during Acute Respiratory Failure (ARF). Factors such as hypoxemia, cor pulmonale, metabolic disorders, coronary artery disease and medication toxicity are effective in the development of these complications[7]. Even though arrhythmias are observed frequently as complications, majority of them is not serious[8]. Sometimes dysrhythmias that develop secondary to severe hypoxemia and myocardial infarction may be the cause of death[9]. It has been emphasized in many different studies that the development of coronary failure during the intensive care treatment of the cases is indicative for bad prognosis[10]. In a study examining the factors affecting short / long term prognosis in patients with overlap syndrome and hospitalized with acute exacerbation of COPD, 30% cardiac arrhythmia was observed[11]. We also determined CVS complications most frequently in our cases (in 53 % of the cases) and determined that these complications are higher at a statistically significant level in the exitus group in comparison with the discharged group. Arrhythmia and hypotension was distinctively higher in especially the exitus patients. We attributed the fact that hypotension is observed more frequently in patients subject to invasive mechanical ventilation to increased intrathoracic pressure and decrease in blood returning to the heart. Of the 20 cases with acute myocardial infarction development, 18 were also in the exitus group. We were of the opinion that the cardiovascular system complications which developed increased the rate of mortality by making the hemodynamics worse which were already disturbed due to respiratory failure.

Fluid-electrolyte balance and metabolic disorders are observed frequently in ARF cases with overlap syndrome that requires treatment at the ICU. Changes in nutritional state (enteral and/or parenteral nutrition) as well as many oscillating factors (activation of the renin-anjiotensin-aldosteron system, increase in katekolamins, increase in atrial natriuretic factor etc.) and the medications used (corticosteroids, diuretics, antibiotics etc.) play a role in this[12]. We determined 39 % metabolic complications (hyponatremia, hyperkalemia, hypokalemia, hypoglycemia, and hyperglycemia) in our study which were determined to be high at a statistically significant level in exitus patients.

Acute renal failure at a rate of 10-20 % was observed in ARF patients with overlap syndrome at the ICU which was determined to have an impact on mortality[13]. High levels of BUN is put forth as an indication of bad prognosis in many publications and studies on aged patients with overlap syndrome emphasize the relation between mortality and the onset of renal failure in patients at the ICU during follow up and treatment[14]. Renal complications in our study had a ratio of 33 % and 34 out of the 40 cases with acute renal failure were in the exitus group. Similarly, we observed that renal complications were higher at a statistically significant level in aged exitus patients in comparison with aged discharged patients.

Gastrointestinal system (GIS) complications such as gastrointestinal stress ulcer and bleeding, distension, ileus, diarrhea are observed frequently in aged ARF cases[15]. Kumar et al. published a review on GIS complications that develop in intensive care patients undergoing mechanical ventilation treatment as a result of which the complications were reported as erosive esophagitis with 48 %, stress related mucosal damage with 74-100 %, diarrhea with 15-51 %, constipation with 15 %, ileus with 4-10 % and acute cholecystitis with 0.2-3 %. As a result, it was put forth that the development of these complications increases morbidity as well as the period of stay at the intensive care resulting in probable contributions to mortality as well. It was observed in the same study that GIS bleeding that develops in aged cases with overlap syndrome is related with mortality[16]. Even though there was no difference between the two groups with regard to GIS complications that were determined in 32 % of our cases, GIS bleeding was higher at a statistically significant level in our study in the exitus group.

Nosocomial pneumonia, pulmonary emboli, barotrauma, fibrosis and various respiratory complications related with the use of mechanical tools are reported in ARF cases with overlap syndrome followed up at the intensive care[17]. It is especially emphasized that the development of nosocomial pneumonia is a major source of morbidity and mortality in critically ill patients with invasive interventions indicated as the cause. It has been concluded in a previous study that the use of non-invasive mechanical ventilation instead of invasive mechanical ventilation treatment results in a lower risk of nosocomial infection, less antibiotics use, shorter intensive care periods and lower rates of mortality[18]. The respiratory complications detected at a ratio of 25 % in our study were not observed to be different among the two groups. However, nosocomial pneumonia was higher at a statistically significant level with a percentage of 22 % in the exitus group in accordance literature. This was thought to be related with IMV treatment and endotracheal intubation which is applied more on patients in the exitus group. Gram (-) non-fermentative bacilli were observed to reproduce most frequently during the bacteriological examinations of our cases.

Even though it is reported that pulmonary emboli develops in about 25 % of the ARF cases treated at the ICU, it is mostly difficult to place an accurate diagnosis due to many reasons that may imitate pulmonary emboli such as underlying lung diseases and abnormal gas exchange. In some studies, pulmonary embolism has been identified as the most common cause of death in patients with COPD in ICU, and prophylactic anticoagulant therapy can reduce this rate[19]. It was considered that the relatively low ratio of pulmonary emboli in our study with 1.44 % is due to the fact that all cases were subject to prophylactic anticoagulant treatment if there are no contraindications.

Many factors play a role in the development of cerebrovascular pathologies in intensive care units such as hypertension, hypotension, cardiac and metabolic diseases. Obstructive lung disease is one of the most important reasons of cerebral ischemia. Failure to provide sufficient oxygen to the brain causes a severe life threatening complication such as hypoxic encephalopathy. In addition, severe anxiety, agitation and delirium cases which require psychoactive treatment can also be observed in cases followed up at the ICU[20].

We also determined that cerebrovascular diseases developed in 44 (5.26 %) of our cases and that severe psychosis developed in 8 (1.91 %). Twenty of the 44 cases with cerebrovascular disease were in the exitus group. We are of the opinion that this may be the result of the severity of cardiac and metabolic complications as well as respiratory failure observed more frequently in patients in the exitus group.

The requirement for intubation and invasive mechanical ventilation in COPD cases increases the period of stay at the ICU and the hospital thereby increasing the rates of morbidity and mortality. Even though the periods of stay at the hospital and the

ICU were longer in the discharged group in our study, the duration of stay in mechanic ventilator was longer in the exitus group and the mechanical ventilation requirement was related with mortality. The fact that the periods of stay at the ICU and the hospital were longer in the discharged group was attributed to the long periods of follow up after mechanical ventilator support.

It was thus concluded that the rates of complications are high in aged OSAS patients with acute respiratory failure due to COPD which is in turn related with mortality.

Conflict of Interest

No conflict of interest was declared by the authors.

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