Prognostic Value of Jugular Venous Diameters and Compliance in Patients with Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) exacerbations constitute a significant proportion of patients presenting to the emergency department (ED). It has been suggested that measurement of jugular venous diameter and compliance may have prognostic value in patients with heart failure. We hypothesized that these measurements may also be valuable in patients with advanced COPD. **Methods:** This study was a single-center, prospective, and cross-sectional study conducted in a university hospital between November 2020 and November 2021. In the study, internal jugular vein (IJV) diameters (inspiration, forced expiration, and rest) and jugular venous compliance were measured with ultrasound in patients who presented to the ED with COPD exacerbation. One month later, data about mortality, intensive care unit (ICU) admission, and any hospitalization were obtained and evaluated together with a range of laboratory parameters. **Results:** Data from a total of 93 patients were analyzed. Of these, 17 (18.2%) died, 19 (20.4%) were admitted to the ICU, and 36 (38.7%) were hospitalized at the end of the 1-month period. Consequently, a total of 44 patients (47.3%) were in the good outcome group and 49 patients (52.7%) were in the poor outcome group. In terms of mortality, inspiratory IJV diameter was 5.6 ± 2.9 mm in the survived group (n = 76) and 7.6 ± 3.9 mm in the deceased group (n = 17) (P = 0.031). There was no difference between the venous compliance values and other diameter measurements of the patients. In the analysis performed with the subgroup with high N-terminal prohormone brain natriuretic peptide values, it was shown that both resting and inspiration diameter measurements were higher in the group with poor outcomes. **Conclusion:** There was no difference between the jugular vein compliance values in terms of mortality in patients admitted to the ED with COPD exacerbation. However, these measurements may have prognostic value in patients with COPD exacerbations complicated by heart failure.

Keywords: Chronic obstructive pulmonary disease, compliance, emergency department (MeSH database), jugular vein, prognosis

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation that is not fully reversible. As COPD progresses, patients may experience worsening dyspnea, fatigue, and reduced exercise tolerance, ultimately leading to right-sided heart failure.[1,2] The development of right-sided heart failure in COPD patients is associated with a poor prognosis, and identifying patients at risk for this complication is critical for effective management in the emergency department (ED).[3]

Recent studies have suggested that the measurement of jugular venous diameter and compliance may have prognostic value in patients with heart failure.[4-6] These noninvasive ultrasonographic measures of right heart function have shown promising results in predicting adverse cardiovascular events and mortality in heart failure patients. It is known that COPD will ultimately lead to pulmonary hypertension and cor pulmonale. Although there are some noninvasive methods to estimate pulmonary artery pressure using echocardiography, these methods may be difficult in COPD

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because of overinflated lungs.[7] Given the similarities between the pathophysiology of heart failure and COPD-related right heart failure, we hypothesize that jugular venous diameter and compliance may also be valuable in predicting outcomes in patients with advanced COPD.

This potential prognostic tool could aid in the early identification of COPD patients at risk for right heart failure, allowing for the implementation of appropriate management strategies to prevent or delay its development.[7] Therefore, the aim of this study was to investigate the prognostic value of jugular venous diameter and compliance in patients with COPD exacerbation.

Materials and Methods

Study design

This was a single-center, prospective, and cross-sectional observational study in the ED of a university hospital between November 2020 and November 2021. The ED deals with approximately 55,000 patient attendances annually. The study was conducted in accordance with the Declaration of Helsinki and was initiated following the approval of the ethical committee (IRB approval number: KÜ GOKAEK-2020/05.08). The written informed consent was obtained from all patients participating in the study.

Study population

This study was carried out with patients who were admitted to the ED with the complaint of shortness of breath and were diagnosed with COPD exacerbation. After the patient was taken to the ED from triage, the doctor who would examine the patient was informed. As a result of the patient's history and physical examination, patients who were diagnosed with COPD exacerbation were treated according to the current GOLD guidelines.[1] The diagnosis of COPD exacerbation was determined according to the GOLD guidelines available at the start of the study. Accordingly, COPD exacerbation was defined as "sudden worsening of symptoms resulting in additional therapy."

Patients over 18 years of age with a diagnosis of COPD who presented to the ED with exacerbation and agreed to participate in the study by signing the relevant informed consent form were included in the study. Patients who were given mechanical ventilation in the ED, who have anatomical obstructions that may cause inaccuracy of ultrasonographic measurements, such as a history of jugular vein vascular surgery, jugular catheter, neck mass, neck infection, and/or pericardial effusion, and patients who were incompatible with respiratory maneuvers, such as those with altered mental status or hearing loss, were excluded from the study.

Measurements

After exacerbation treatment, ultrasonography was performed for internal jugular vein (IJV) evaluation and jugular venous compliance measurement by the co-investigator in patients who agreed to participate in the study. Similar to the IJV evaluation in patients with heart failure performed by Pellicori *et al*. in 2015, this evaluation was performed by raising the patient's head 45°, moving to the right of the patient, turning the patient's neck to the right, and aiming at the left IJV.[4] A mobile ultrasonography device and 4–12 MHz linear probe were used for measurement (Philips Lumify L12-4 Linear Array transducer, Koninklijke Philips Electronics N. V., Holland). The IJV was found by scanning from the apex of the sternocleidomastoid muscle to the angle of Louis and measurements were started after centering the probe on the image area.

While the patient was at rest, the diameter of the IJV was measured in expiration and the jugular venous diameter (JVD) was recorded at the rest (expiratory) section (JVD-Rest). Then, the measurement was made after asking the patient to take a deep breath and the result was recorded as the JVD inspiration (JVD-Insp). Immediately after the deep inspiration, the patients were asked to expire the air and strain. At this time, the IJV diameter was measured again and this measurement was recorded as the maximum JVD (JVD-Max). The jugular vein compliance was calculated using the formula ([JVD-Max-JVD-Rest]/JVD-Max). After the measurements, the routine ED follow-up and treatment of the patients continued. Hospitalization and discharge of the patients were decided according to current guidelines.

Outcomes

The primary outcome measure was mortality within 1 month after the patient was discharged from the ED. Secondary outcome measures were intensive care unit (ICU) admission, need for hospitalization, and overall poor outcome within 1 month. If any of the primary and secondary outcomes were met, the patient was included in the poor outcome group. If none occurred, the patient was classified in the good outcome group. A subgroup analysis was also performed in patients with suspected heart failure, using a cutoff value of 500 pg/mL for N-terminal prohormone brain natriuretic peptide (NT-proBNP). The aim of this subgrouping was to investigate the potential difference that may occur in JVD measurements between patients with and without potential underlying cardiac disease.

Statistical analysis

Study data were analyzed using SPSS, version 16.0 (IBM Corp., Armonk, NY, USA). The conformity of the data to the normal distribution was evaluated with the Kolmogorov–Smirnov test. Student-t test was used for the analysis of continuous variables with normal distribution and data were expressed as mean and standard deviation. The Mann–Whitney U test was used for the analysis of continuous variables that did not fit the normal distribution, and the data were expressed as the median and interquartile range (IQR). Chi-square and Fisher's exact tests were used in the analysis of categorical variables, and data were expressed as numbers and percentages. Mean differences are presented with 95% confidence intervals (CIs). An alpha value of 0.05 was considered the nominal level of statistical significance.

Results

A total of 97 patients were assessed for eligibility and data from 93 patients were analyzed after exclusion criteria were implemented [Figure 1]. At the end of the 1-month period, 17 (18.2%) of these patients had died, 19 (20.4%) had been admitted to the ICU, and 36 (38.7%) had been hospitalized. Thus, we categorized 44 (47.3%) in the good outcome group and 49 (52.7%) in the poor outcome group.

Assessment of demographic and baseline clinical data showed that males were prevalent in the poor outcome group and patients in this group were more tachycardic [Table 1]. The median modified Medical Research Council (mMRC) scores of the included patients were 3 (IQR: 2-4). More than half of them had infiltrates on chest X-ray (52.7%) and were tachypneic. Sixty-seven (72.0%) of the patients were admitted to the ED with exacerbation within the last year. Thirty-six (73.5%) patients with poor outcomes and 31 (70.5%) patients with good outcomes had recurrent admissions ($P = 0.746$). There was no significant difference in terms of the laboratory results of the patients with the exception of the poor outcome group being significantly more desaturated ($P < 0.001$) and they also had higher lactate levels ($P = 0.017$) [Table 2].

Regarding mortality, which was the primary outcome of the study, no difference was found between the jugular vein compliance of patients who died and those who survived (mean difference: 0.1, 95% CI: −0.1–0.1). While there was no significant difference between JVD-Rest and JVD-Max measurements, the mean JVD-Insp was 7.6 ± 3.9 mm in deceased patients and 5.7 ± 3.0 mm in surviving patients. The difference between these two measurements was significant (mean difference: 1.9 mm, 95% CI: 0.2–3.5, $P = 0.031$) [Table 3].

A difference was found between JVD-Rest measurements when comparing ICU and non-ICU patients (mean difference: 1.6, 95% CI: −3.2 to-0.1, $P = 0.049$). A similar difference was also found for JVD-Insp measurements between ICU and non-ICU patients (mean difference: 2.1, 95% CI: 0.5–3.7, $P = 0.013$). There was no significant difference in terms of any JVD measurement for composite good versus poor outcome and hospitalization versus non-hospitalized patients.

A subgroup analysis was performed for patients with NT pro-BNP >500 pg/mL ($n = 52$) and the effect of jugular vein diameters on the primary outcome measure of mortality was investigated [Table 4]. Accordingly, in patients with a potential for heart failure, the mean difference between patients who died and those who survived was 3.0 mm (95% CI: 1.0–5.0, $P = 0.004$) for JVD-Rest and 3.6 mm (95% CI: 1.5–5.8, $P = 0.001$) for JVD-Insp.

Discussion

In this study, the relationship between IJV diameters measured after respiratory maneuvers and different poor outcomes in

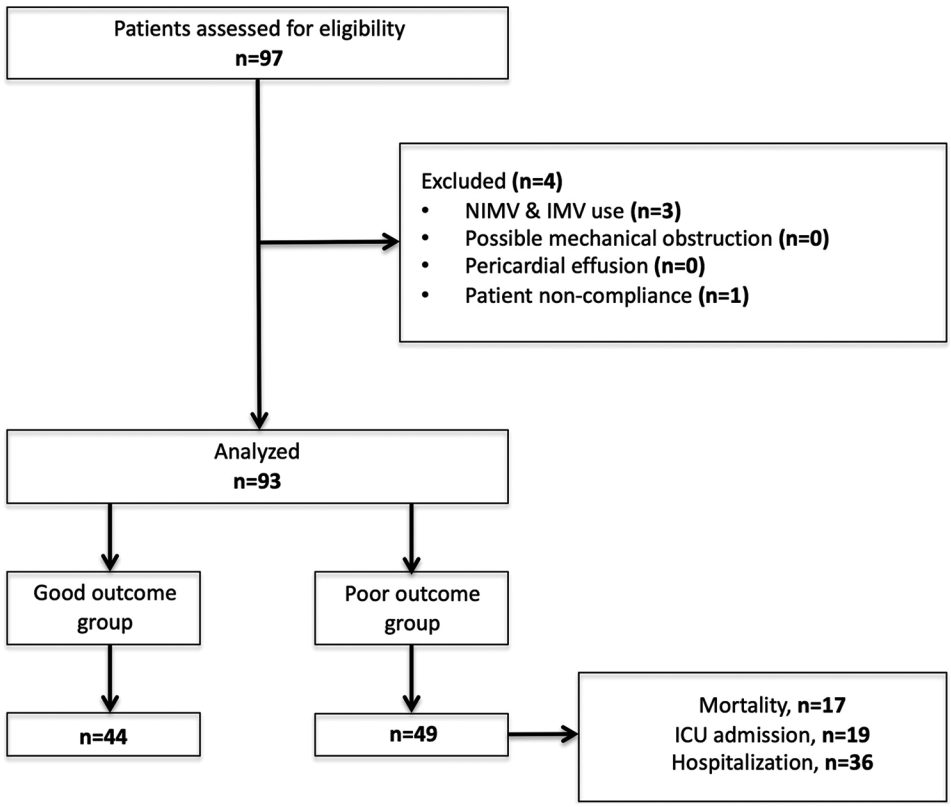

Figure 1: Patient flowchart

Table 1: Baseline characteristics of the study population

	All patients (*n*=93)	Good outcome (*n*=44)	Poor outcome (*n*=49)	*P*
Age, mean±SD	71±12	71±12	71±12	0.970
Male (sex), *n* (%)	62 (66.7)	24 (54.5)	38 (77.6)	0.019
Diabetes mellitus, *n* (%)	30 (32.3)	14 (31.8)	16 (32.7)	0.931
Hypertension, *n* (%)	59 (63.4)	27 (61.4)	32 (65.3)	0.693
Chronic renal disease, *n* (%)	14 (15.1)	9 (20.5)	5 (10.2)	0.168
History of stroke, *n* (%)	5 (5.4)	2 (4.5)	3 (6.1)	1.000
Congestive heart failure, *n* (%)	34 (36.6)	15 (34.1)	19 (38.8)	0.640
IMV (last 1 year), *n* (%)	5 (5.4)	1 (2.3)	4 (8.2)	0.365
NIMV (last 1 year), *n* (%)	13 (14.0)	4 (9.1)	9 (18.4)	0.198
mMRC score, median (IQR)	3 (2–4)	2 (2–3)	3 (3–4)	0.318
Exacerbation characteristics, *n* (%)				
Increase in sputum	20 (21.5)	8 (18.2)	12 (24.5)	0.460
Increase in sputum purulence	15 (16.1)	6 (13.6)	9 (18.4)	0.536
Cough	54 (58.1)	24 (54.5)	30 (61.2)	0.515
Chest pain	14 (15.1)	7 (15.9)	7 (14.3)	0.827
Pleural effusion	29 (31.2)	12 (27.3)	17 (34.7)	0.441
Infiltration on chest X-ray	49 (52.7)	21 (47.7)	28 (57.1)	0.364
Vital signs				
Temperature (°C), mean±SD	36.7±0.7	36.7±0.6	36.8±0.8	0.306
Pulse (beat/min), mean±SD	100±21	96±20	104±22	0.036
SBP (mmHg), mean±SD	144±24	148±25	141±22	0.114
Respiratory rate (breath/min), median (IQR)	28 (26–34)	28 (24–32)	30 (28–36)	0.749

IMV: Invasive mechanical ventilation, NIMV: Non-IMV, IQR: Interquartile range, SD: Standard deviation, SBP: Systolic blood pressure, mMRC: modified Medical Research Council

Table 2: Laboratory evaluation of chronic obstructive pulmonary disease exacerbations according to composite outcome

	Good outcome (*n*=44)	Poor outcome (*n*=49)	*P*
Hemoglobin (g/dL), mean±SD	11.9±2.6	12.3±2.5	0.416
Leukocyte count (cells ×10^3/μL), median (IQR)	9000 (6725–12,950)	9300 (7640–13,050)	0.772
Platelet count (cells ×10^6/μL), median (IQR)	248±91	249±90	0.957
Glucose (g/dL), median (IQR)	119 (105–153)	129 (111–153)	0.069
BUN (mg/dL), median (IQR)	18 (13–26)	20 (13–27)	0.719
Creatinine (mg/dL), median (IQR)	0.8 (0.7–1.2)	0.9 (0.7–1.2)	0.976
NT-proBNP (pg/mL), median (IQR)	555 (186–2017)	1225 (179–3913)	0.823
pH, median (IQR)	7.37 (7.34–7.41)	7.35 (7.31–7.41)	0.703
pCO_2, median (IQR)	45 (40–51)	50 (41–58)	0.101
HCO_3 (mmoL/L), mean (SD)	25.8±3.6	26.3±3.9	0.481
Lactate (mg/dL), median (IQR)	13 (11–18)	20 (11–26)	0.017
O_2 saturation (%), median (IQR)	94 (89–96)	87 (77–94)	<0.001

IQR: Interquartile range, SD: Standard deviation, NT-proBNP: N-terminal pro-B-type natriuretic peptide, BUN: Blood urea nitrogen

patients presenting to the ED with COPD exacerbation was investigated. There was a difference between JVD-Ins*P* values only in terms of mortality and ICU admission outcomes, but no difference was observed regarding other outcomes and jugular vein compliance. The same effect, although more pronounced, was observed in patients with COPD exacerbations potentially accompanied by heart failure. JVD diameters reflect right atrial pressure, however, many factors including neck anatomy, obesity, and operator skills may involve to accurate measurements.[4] The fact that the male gender was more common in the poor outcome group in our patient cohort may also have affected the results as a confounding factor.

In recent years, studies using IJV measurements to estimate right heart functions have become more common.[4-6,8-10] In 2010, Simon *et al*. conducted a study investigating the role of the IJV diameter area measured ultrasonographically in the noninvasive detection of increased right atrial pressure.[8] A total of 67 patients who underwent right heart catheterization were included in the study and the IJV diameters of these patients were measured by ultrasonography at rest and during Valsalva. A >17% increase in the IJV diameter area measured during Valsalva relative to the resting IJV diameter. This was found to predict high right atrial pressure with 90% sensitivity, 74% specificity, and 94% negative predictive value. Since this publication, the IJV diameter

Table 3: Jugular venous diameters and compliance values according to different outcomes

	JVD-rest (mm)	JVD-inspiration (mm)	JVD-maximum (mm)	Compliance
Composite poor outcome				
Poor outcome	8.6±3.7	6.4±3.7	13.1±3.9	0.4±0.2
Good outcome	8.4±2.4	5.6±2.5	12.9±3.5	0.3±0.2
Mean difference (95% CI)	0.2 (−1.5–1.2)	0.8 (−2.2–0.5)	0.2 (−1.8–1.4)	0.1 (−0.1–0.1)
	P=0.785	*P*=0.217	*P*=0.792	*P*=0.587
Mortality				
Deceased	9.5±3.8	7.6±3.9	14.1±4.1	0.3±0.2
Alive	8.2±3.0	5.7±3.0	12.8±3.6	0.3±0.2
Mean difference (95% CI)	1.3 (−3.0–0.4)	1.9 (0.2–3.5)	1.3 (−3.3–0.7)	0.1 (−0.1–0.1)
	P=0.133	*P*=0.031	*P*=0.187	*P*=0.529
ICU admission				
Admitted	9.8±4.0	7.7±4.0	13.8±4.0	0.3±0.2
Not admitted	8.2±2.9	5.6±2.9	12.8±3.7	0.4±0.2
Mean difference (95% CI)	1.6 (−3.2–−0.1)	2.1 (0.5–3.7)	1.0 (−3.0–0.9)	0.1 (−0.1–0.1)
	P=0.049	*P*=0.013	*P*=0.281	*P*=0.344
Hospitalization				
Hospitalized	7.9±3.6	5.8±3.4	12.6±3.7	0.4±0.2
Discharged from ED	8.9±2.8	6.2±3.1	13.3±3.7	0.3±0.2
Mean difference (95% CI)	1.0 (−0.4–2.3)	0.4 (−1.0–1.7)	0.7 (−0.9–2.3)	0.1 (−0.1–0.1)
	P=0.155	*P*=0.602	*P*=0.371	*P*=0.139

ICU: Intensive care unit, CI: Confidence interval, ED: Emergency department, JVD: Jugular venous diameter

Table 4: Jugular venous diameters and compliance values according to mortality in patients with heart failure

	Survived (*n*=42)	Deceased (*n*=10)	Mean difference	*P*
JVD-rest (mm)	8.5±2.7	11.5±3.5	3.0 (1.0–5.0)	0.004
JVD-inspiration (mm)	6.0±2.8	9.6±3.6	3.6 (1.5–5.8)	0.001
JVD-maximum (mm)	12.4±3.4	14.9±4.2	2.4 (−4.9–0.2)	0.073
Compliance ([maximum−rest]/maximum)	0.3±0.2	0.2±0.2	0.1 (−0.1–0.2)	0.181

JVD: Jugular venous diameter

measurement has gained importance in the evaluation of right atrial pressure.

After a study by Pellicori *et al*., in which IJV ultrasonography was used as a determinant of the volume status of patients,[9] the same group performed another study predicting hospitalization and mortality due to decompensation in patients with heart failure.[4] The results of this subsequent study showed that patients with lower jugular venous compliance had an approximately 10-fold increase in adverse effects. When 3.95 was taken as the cutoff for the value of jugular venous compliance, it was found to be 77% specific and 60% sensitive in predicting mortality and hospitalization. Thus, an increase in both inspiratory and resting diameters of the jugular vein was associated with increased adverse effects.

It can be expected that the width and distensibility of the vena cava and associated veins will be affected by many conditions and diseases related to the circulatory system. Previously, it has even been shown that the width of the inferior vena cava is associated with adverse outcomes, independent of left ventricular ejection fraction in patients with chronic heart failure.[11] One of the most important conditions affecting the caval system is COPD-related pulmonary hypertension. Many reports claimed that the prevalence of pulmonary hypertension increased with COPD severity. While mild pulmonary hypertension is observed in the majority of COPD patients (30.2%), a minority (7.2%) of patients have severe disease symptoms.[12] Since most patients admitted to the ED with a COPD exacerbation do not undergo right heart catheterization or echocardiography, early recognition of those who may be worsening may be valuable. In a study by Doepp *et al*., patients with COPD and pulmonary hypertension were found to have significantly increased IJV valve incompetence compared to healthy controls.[13] The rationale of our study was whether this effect would be seen in all COPD exacerbations. However, we found negligible differences in jugular venous measurements in an undifferentiated population of COPD exacerbations when compared by good and poor prognosis. The exception was in mean JVD-Insp, which was found to be 7.6 ± 3.9 mm in deceased patients and 5.7 ± 3.0 mm in surviving patients and this was significant ($P = 0.031$). This effect was particularly evident in the population complicated with heart failure ($P = 0.001$) and a significant difference was also found for the parameter JVD-Rest ($P = 0.004$) in this population.

In the study performed by Pellicori *et al*., two logistic regression models including many clinical and echocardiographic variables were designed.[4] According to their results, they determined that the JVD-Rest and JVD-Ins*P* values might be predictive of mortality and poor outcome in patients with heart failure. There are also confounding factors that directly point to heart failure, such as NT-proBNP, in the models they established. In the present study, JVD-Rest and JVD-Ins*P* values were found to be different in terms of mortality and ICU need, and this difference was more pronounced in the heart failure subgroup.

Limitations

Our study has several limitations that might have influenced our results. First, the sample size was relatively small, and a larger sample might have provided more statistical power to detect significant relationships. Because our study coincided with the end of the COVID-19 pandemic, fewer patients were recruited than expected. Despite this, we believe that the statistically significant difference that will be achieved with a larger sample size is less likely to be reflected in the clinical difference. Second, we only measured jugular venous diameters at one time, and trends in these parameters over time might have a more significant impact on clinical outcomes. Finally, our study only included patients with COPD exacerbation in a single center, and the findings might not be generalizable to other populations.

Conclusion

The results of this study demonstrated that JVD-Ins*P* values are higher in patients with mortality and ICU admission. Although the results for JVD-Ins*P* values are statistically significant, they may not be useful in terms of clinical significance. However, in COPD exacerbations with heart failure, JVD values may also differ and the difference may become evident clinically. Further studies with larger sample sizes are needed to confirm these findings and explore other ultrasonographic determinants of clinical outcomes in this population.

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Conflicts of interest

There are no conflicts of interest.

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