Evaluation of pulmonary hypertension in COPD patients with diabetes

Makarevich AE, Valevich VE, Pochtavtsev AU*

Department of Internal Diseases N1
The Belarusian State Medical University, Minsk, Belarus

Abstract

Purpose: to assess pulmonary hypertension (PH) in patients with chronic obstructive pulmonary disease (COPD) plus diabetes mellitus (DM) using transcutaneous Doppler right jugular venous echo (tDErjv).

Material and methods: We examined 5 groups of patients and control group (30 healthy subjects). The 1st group consisted of 55 COPD in-patients in exacerbation with type II DM (DM2). The 2nd group was formed of 40 in-patients with sole COPD in exacerbation. 30 patients with sole DM2 were included in the 3rd group. The 4th group consisted of 15 COPD in-patients with type I DM (DM1). The 5th group was formed of 18 patients with DM1. The following parameters, using tDErjv, were determined: direction of flow (antegrade or retrograde), velocities of systolic (Sf) and diastolic flows (Df), which are in the strong correlation with the mean pulmonary artery pressure (mPAP). If the flow was biphasic, the ratio of velocities (Df/Sf) and mPAP were calculated.

Results: Antegrade biphasic flow was revealed in all patients. Sf>Df and Df/Sf<1 were detected in the 3rd and control groups. While, in the 1st and 2rd groups Sf<Df (1.14±0.12 and 0.90±0.07 in the 1st and 2rd groups respectively; $p<0.05$ vs control). In the 2nd group patients with Df=Sf the value of the mPAP ~25 mmHg was detected, whereas in the 1st group with Df/Sf>1, this value was >35 mmHg.

Conclusions: PH was more severe in COPD plus DM2 as compared with COPD only. tDErjv allowed determining mPAP in all COPD patients, even with the severe emphysema.

* CORRESPONDING AUTHOR:
Kirova str. 33-15A
Minsk 270030, Belarus
Tel: 37 5172278088 (home), Fax: 37 5172405842 (office)
e-mail: makae@bsmu.by (A. E. Makarevich)

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Introduction

Hypoxic PH is a common and serious complication of COPD as well as an independent factor of the bad prognosis (shorter survival rates) [1-5]. In COPD, PH tends to be of moderate severity and progresses slowly [6]. Right ventricle (RV) function is only mildly impaired with preservation of the cardiac output (CO) [7,8]. Indirect evaluation of mean pulmonary artery pressure (mPAP) in COPD patients by using standard echocardiography (SE) is often difficult due to concomitant severe lung emphysema.

The main morphologic substrate leading to lung pathology in DM is diabetic microangiopathy [9-11]. It is the part of the pathologic process in pulmonary tissue. The lung changes are the same as in diabetic microangiopathy in other organs (kidney, eyes), but it expressiveness is less and these changes develop later than in other organs [12,13].

DM favors hypoxic PH due to negative effects on pulmonary vessels [9,14]. Thus, the abundance of pulmonary microcirculation and connective tissue in lungs makes them often the organ-target in DM [15-18]. Chronic hyperglycemia is the trigger for the development of DM complications. Non-enzyme glycolysis (with the formation of glycated proteins) causes the tissues disorders, including pulmonary vessels (particularly the endothelium of capillaries). The disorders of microcirculation as well as nervous regulation present in DM favor to the changes for the worsening of pulmonary circulation [19-22]. Lungs disorders in COPD proceed across with development of diabetic microangiopathy, which strike first of all the morphological structures, having gas exchange function. This give the base to supposes diabetic pneumopathy progress

Table 1. **Baseline data of patient's groups**

Parameter	Control	COPD+DM2 (1st)	COPD (2nd)	DM2 (3rd)	COPD+DM1 (4th)	DM1 (5th)
Number of patients	30	55	40	30	15	18
males (%) mean age (years) smokers (%)	50 49±5 40	47 55±4 40	58 52±5 75	48 52±3 17	53 50±3 -	56 48±3 22
Mean duration (years) of: COPD DM	-	24±3 7±2	26±3 -	- 7±2	16±3** 13±4***	- 12±3
COPD severity (%) mild moderate severe	-	 36 36 27	 30 40 30	-	 100**	-
Body mass index (kg/m^2	24.0±1.6	31.3±2.0*	32.0±1.8*	32.7±2.0*	27.1±1.3*,***	28.3±1.9*
Glicated hemoglobin (HbA1c) %	4.5±0.4	9.6±1.8*	4.9±0.5	9.3±1.4*	10.6±2.8*	9.4±1.3*
Blood glucose (mmol/L)	5.0±1.7	13.8±3.5*	4.6±2.3	10.6±2.7*,**	15.4±5.2*,***	14.8±4.4*
Subcompensate carbohydrate metabolism (%)	-	36	-	60**		72**
decompensate carbohydrate metabolism (%)	-	64	-	40**	100**,***	38**
Retinopathy I grade, nephropaty I-II grade (%)	-	71	-	57	27**	44
Retinopathy II grade, nephropathy III grade (%)	-	18	-	13	73**, ***	56**
Autonomic neuropathy (%)		18		13	20	22
Neuropathic form of syndrome of diabetic foot (%)	-	51	-	47	80**, ***	44

* p<0.05 vs control; ** p<0.05 vs 1st group; *** p<0.05 vs 3rd group

by analogy with diabetic nephropathy as well as retinopathy [11,19].

A long period of time in COPD evolution with episodes of acute exacerbations leads to the profound disorders of microcirculation [23-25] which play the important role in the development of hypoxic PH in COPD. These disorders in DM become the additional and unfavorable factor in the case of such combined pathology (COPD plus DM). The aggravating disorders of microcirculation become the additional and burden factor which makes worse the present structural and functional disorders of bronchi and lungs in the case of combination of COPD and DM. The combination of COPD with DM2 has been detected in 5-20% of cases [26,27] and proceeds with small symptomatology and recurring course [18,28].

Abnormalities in the cardiac function can occur in the diabetic patients independently of other factors (such as hypertension, coronary atheromatosis) [29]. Metabolic changes within the heart in diabetics associated with hyperglycemia, hyperlipidemia or disinsulinemia appear to contribute to the contractile disorders of myocardium. It is now apparent that the alterations in fatty acids and glucose metabolism in the heart is an important contributing factor to the heart abnormalities in diabetics.

The peculiarities of pulmonary hemodynamics were evaluated earlier only in single COPD patients, but not in the combination of COPD plus DM.

The aim of this study was to assess of PH expressiveness by using tDErjv in COPD patients with acute exacerbation and concomitant DM as compared with sole COPD patients as well as to decide, if it is the evidence linking of PH severity with the same of concomitant DM.

Material and methods

This study was approved by the Human Studies Committee of the Belarusian State Medical University and informed consent has been obtained from the patients. The inclusion criteria for the study were established before the trial and strictly followed. These inclusion criteria were: different severity COPD with FEV1 increasing <15% during bronchodilatating test; duration of DM more than 1 year as well as presence of diabetic complications.

Patients

The 1st group consisted of 55 COPD inpatients (aged 36-60 years) (*Tab. 1*) with an acute exacerbation plus DM2. Mean duration of COPD, DM2 and age were 24.7 and 55 years respectively. Mild, moderate to severe COPD according to consensus "GOLD" [30] had 36%, 36% and 27% of these patients respectively. Current smokers were 40%. Body mass index (BMI) as well as glicated hemoglobin (HbA1c) – the marker of DM compensation for the period of the last 3 months made up 31.3 kg/m^2 and 9.6% respectively. Sixty-four percents of these patients had decompensate stage of carbohydrate metabolism

(mean glucose level was 13.8±3.5 mmol/L) and 36% – subcompensate stage (mean glucose level – 6.4±2.7 mmol/L). We observed the following diabetic complications in these patients: retinopathy I (non-proliferative) and nephropathy I-II (before to the clinical manifestation) grades (71%); retinopathy II (preproliferative) and nephropathy III grades (18%); neuropathic form of syndrome of diabetic foot (51%) and autonomic neuropathy (18%).

The 2nd group was comprised of 40 in-patients comparable according to COPD severity (mean age and COPD duration were 52 and 26 years; BMI – 32.0 kg/m^2) without DM. Current smokers were 75%. The mean levels of HbA1c and glucose made up 4.9±0.5% and 4.6±2.3 mmol/L respectively.

The 3rd group was formed by 30 patients with alone DM2 (mean age and disease duration were 52 and 7 years; BMI – 32.7 kg/m^2). Seventeen percents of these patients were current smokers. Forty percent of these patients had decompensated stage of carbohydrate metabolism (the levels of HbA1c and glucose achieved 9.3% and 10.6 mmol/L respectively). Sixty percents of these patients had subcompensate stage of carbohydrate metabolism (the levels of HbA1c and glucose achieved to 7.0% and 6.3 mmol/L respectively). Diabetic complications were revealed: retinopathy I and nephropathy I-II grades in 57% of these patients; retinopathy II and nephropathy III grades – in 13%; diabetic distal polyneuropathy – in 47%; neurophatic form of diabetic foot syndrome – in 47% and autonomic neuropathy – in 13% of these patients.

The 4th group consisted of 15 COPD in-patients (mean age and disease duration were 50 and 16 years respectively) with DM1 (mean duration – 13 years; BMI – 27.1 kg/m^2) in all patients with decompensated stage of carbohydrate metabolism (mean levels of HbA1c – 10.6±2.8% and glucose – 15.4±5.2 mmol/L; $p<0.05$ vs the 1st group). The small number of these patients was due to the infrequent combination of these two diseases. Diabetic retinopathy of I and nephropathy I-II grades were detected in 27% of these patients.

The 5th group was formed of 18 patients with sole DM1 (mean age and disease duration were 48 and 12 years respectively). Current smokers were 22%. Seventy-two percents of the patients had decompensated stage of carbohydrate metabolism (HbA1c=9.4±1.3%). Diabetic retinopathy and nephropathy I-II stages (preclinical stages) as well as obvious clinical stages of these complications were revealed in 44% and 56% of the patients respectively. Syndrome of diabetic foot and autonomic polyneuropathy were detected in 44% and 22% of these patients. Thus, in COPD patients with DM1 we observed more severe diabetic microangiopathy than in 1st and 3rd groups. We did not include the insulin resistance patients into this study.

Clinical symptoms and signs of mild COPD patients plus DM1 were comparable with the same of mild COPD with concomitant DM2 as well as in patients with sole mild COPD.

Control group was formed of 30 healthy subjects (male – 22, female – 8, mean age – 49 years, BMI – 24.0 kg/m^2; smokers – 40%).

Methods

We performed SE and tDErjv for the examination of pulmonary hemodynamics. SE was made up on apparatus "Siemens Sonoline G 605" (Germany). We detected by SE: maximal and mean blood flow in pulmonary artery (PA), gradient of blood flow and its integral in PA as well as mPAP value (according to the temporal parameters of systolic flow in outlet of right ventricle and formula of Kitabatake et al. [31]; Lg of mPAP= -2.8 AT/ET+2.4; where AT – time of acceleration of blood flow (msec) and ET – ejection time of pulmonary artery; diameter of pulmonary trunk artery (DPTA), stroke volume of right ventricle (SVRV=integral of blood flow in PA$\cdot 2\pi r^2$; where r=1/2 of DPTA) and cardiac output (CO=HR·SVRV).

Direction of flow (antegrade or retrograde), velocities of systolic (Sf) and diastolic flows (Df) (which strongly correlated with the mPAP) were determined by tDErjv. We calculated the ratio of velocities (Df/Sf) (if the flow was biphasic), diameter (mm) of right jugular vein at the moment of maximum inspiration as well as at the end of nonforced expiration and then mPAP according to the diagram of Matsuyama et al. [32].

The collapsing degree of right jugular vein (mm) was detected as difference of this vein diameter at the end of nonforced expiration and at period of maximum inspiration which was divided by the diameter of this vein at the end nonforced expiration and multiplied by 100%. The measurement of interior jugular vein diameter was made at the standard point – isthmus of the thyroid gland. The measurement of the vein diameter was performed in the transverse view from upper inner lager to lower inner lager of the vessel. We made the revision of Doppler angle in all cases, which was predisposed by our ultrasound device. All the patients had sinus rhythm.

The evaluation of diabetic retinopathy grade was made according to classification of Korner and Porta [33] and diabetic nephropaty grade according to Mogensen et al. [34] with determination of glomerular filtration and daily protein loss with urine. The diagnosis of autonomic neuropathy was made on the base of functional tests according to Williams and Pickup [35]. CRP was determined by an immunometric assay ("Diasys" kit).

Statistical analysis

The data are shown as mean ± SD unless otherwise indicated. The paired and unpaired t-test was used to test the significance of baseline characteristics of the 1st-4th groups as well as the treatment effects within the groups and between them. All p values were two tailed. The group comparison used the Student's t-test for quantitative variables and χ^2 method Fisher's exact test for qualitative variables. The χ^2 or Fisher exact test was used to compare categoric variables. The significance level was set at $p\leq 0.05$.

Results

HbA1c>8% and complain of dryness in mouth were detected in 40% of patients with sole DM2 as compared with 64% of patients COPD plus DM2 ($p<0.05$). Polyuria and thirst were revealed in 30% patients with DM2 only vs 56% of patients COPD with DM2 ($p<0.05$). Thus, these symptoms were observed more often in combination of COPD plus DM2 than in sole DM2.

***Table 2*. Acute phase biochemical tests in COPD patients plus diabetes and sole COPD patients**

Patients	N	+CRP (%)	α2-globulins (%)	γ-globulins (%)
COPD+DM2				
mild	20	20	10.6±0.3	15.4±0.6
moderate	20	30*	12.2±0.2*	17.1±0.8*
severe	15	60*, **	14.0±0.4*, **	19.5±0.9*, **
Mild COPD+DM1	15	13●●	9.7±1.4●, ●●	15.2±3.3●, ●●
COPD				
mild	12	25	10.2±0.3	15.0±0.7
moderate	16	25	11.9±0.2▼	16.7±0.6▼
severe	12	50▼, ▼▼	13.7±0.3▼, ▼▼	19.2±0.7▼, ▼▼

* p<0.05 vs mild COPD plus DM2; ** p<0.05 vs moderate COPD plus DM2; ● p<0.05 vs moderate COPD plus DM2; ●● p<0.05 vs severe COPD plus DM2; ▼ p<0.05 vs mild COPD; ▼▼ p<0.05 vs moderate COPD; + CRP – positive C-reactive protein

***Table 3*. Pulmonary hemodynamic parameters according to standard echocardiography**

Group	AT/ET	mPAP (mmHg)
Control (n=30)	0.43±0.02	16.0±2.0
COPD+DM2 (n=45)	0.32±0.04	32.0±3.4*,**,***
COPD (n=34)	0.34±0.03	29.0±3.0*, **
DM2 (n=30)	0.42±0.02	17.0±2.0
COPD+DM1 (n=15)	0.41±0.01	18.0±1.0
DM1 (n=18)	0.42±0.01	17.0±1.0

* p<0.05 vs control; ** p<0.05 vs DM2; *** p<0.05 vs sole COPD

***Table 4*. Pulmonary hemodynamics parameters in different groups according to standard echocardiography**

Parameter	Control	Mild COPD +DM2	Moderate to severe COPD+DM2	Mild COPD	Moderate to severe COPD	Mild COPD +DM1	DM1
DPTA, mm	17.0±1.3	17.5±1.5	20.0±1.4*,**	17.6±1.8	18.6±1.7▼▼	17.6±2.0▼▼	17.5±1.5▼▼
SVRV, mL	72.8±1.5	71.6±1.3	68.5±2.6*,**	71.8±1.6	70.7±1.8▼▼	71.5±1.0▼▼	72.6±1.3▼▼
CO, L/min	5.5±0.1	5.5±0.1	5.5±0.2	5.5±0.2	5.5±0.2	5.5±0.1	5.4±0.1
mPAP, mmHg	16.0±2.0	17.0±1.0	38.0±5.0*,**	17.6±1.1	35.6±2.8▼,▼▼	18.0±1.0▼▼	17.0±1.0▼▼

* p<0.05 vs control; ** p<0.05 vs mild COPD+DM2; ▼ p<0.05 vs mild COPD; ▼▼ p<0.05 vs moderate to severe COPD+DM2

Sixty-four COPD patients with concomitant DM2 were admitted >2 times per year to clinic by ambulance (four times – 25%; three times – 38%) as compared with 48% (p<0.05) patients with sole COPD. Forty-seven of mild COPD patients plus DM1 were admitted to clinic >2 times per year (four times – 13%; three times – 33%) as compared with 17% (p<0.05) of patients with sole mild COPD.

The biochemical acute phase tests of COPD inpatients on admission are presented in *Tab. 2*. As seen from this table, the activity of COPD exacerbation was more expressive in severe COPD patients with concomitant DM2.

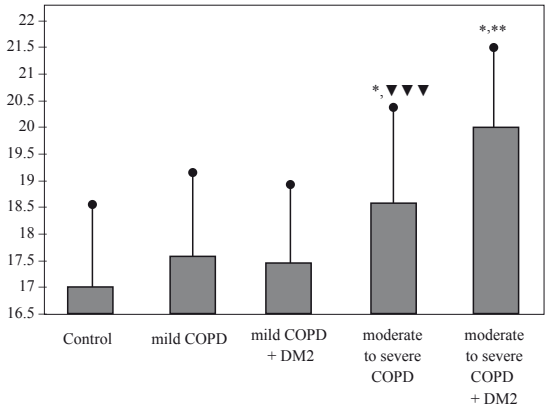
We can not detect mPAP by SE in 10 and 6 patients of the 1st and 2nd groups due to concomitant severe lung emphysema. The level of mPAP was the highest in patients of the 1st group (*Tab. 3*) vs the 2nd group, despite the fact that these groups did not differ according to COPD severity. mPAP was particularly high in moderate to severe COPD patients plus DM2 (*Tab. 4*) as compared with mild COPD plus DM2. The hemodynamic parameters of patients with sole DM1 or DM2 did not differ from the control. The mPAP, DPTA, CO and SVRV in mild COPD patients (with or without DM1-2) were comparable with the control too.

A significant increase of mPAP (by 2.4 and 2.2 times vs the control), DPTA (by 18% and 10% vs the control) and decrease of SVRV (by 6% and 3% vs the control) were noted only in moderate to severe COPD patients with DM2 and without it respectively.

DPTA in moderate to severe COPD patients with concomitant DM2 was larger (p<0.05) than in mild COPD plus DM2 (*Fig. 1*), sole moderate to severe COPD as well as in the control group (20.0±1.4 mm vs 17.5±1.5; 18.6±1.7 and 17.0±1.3 mm respectively). Meanwhile, SVRV in moderate to severe COPD patients with concomitant DM2 was smaller (by 3%; p<0.05) in contrast to sole moderate to severe COPD patients. Thus, SVRV in the moderate to severe COPD patients with DM2 made up 68.5±2.6 mL as compared with the control and mild COPD patients plus DM2 (72.8±1.5 mL and 71.6±1.3 mL respectively; p<0.05). CO in COPD patients of various degree of severity with or without DM did not significantly differ from the control.

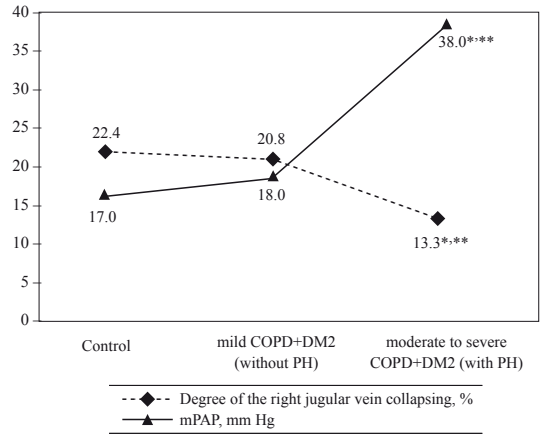
The antegrade biphasic flow by tDErjv was revealed in all patients. The ratio of Df/Sf did not differ among the control, DM1 and mild COPD plus DM1 groups (0.63±0.02; 0.64±0.01 and 0.67±0.01 respectively). Thus, mPAP values were made up 17.0±2.0; 17.0±1.0 and 18.0±1.0 mmHg respectively in these

***Figure 1*. Diameter of pulmonary trunk (mm)**



* p<0.05 vs control; ** p<0.05 vs mild COPD + DM2; ▼ p<0.05 vs mild COPD; ▼▼ p<0.05 vs moderate to severe COPD + DM2

***Figure 2*. Degree of the right jugular vein collapsing during inspiration in COPD plus DM2**



* p<0.05 vs control; ** p<0.05 vs mild COPD plus DM2

***Table 5*. The data of transcutaneous Doppler sonography of the right jugular vein in COPD and DM2 patients**

Parameter	Control (n=30)	COPD+DM2 (n=55)	COPD (n=40)	DM2 (n=30)
Systolic flow (Sf), m/s	0.19±0.02	0.07±0.03	0.10±0.02	0.17±0.02
Diastolic flow (Df), m/s	0.12±0.01	0.08±0.01	0.09±0.01	0.11±0.01
Ratio of Df/Sf	0.63±0.02	1.14±0.12	0.90±0.07	0.65±0.02
mPAP, mm Hg	17.0±2.0	34.2±4.0*, **,***	30.3±3.0*	17.0±2.0

* p<0.05 vs control; ** p<0.05 vs DM2; *** p<0.05 vs sole COPD

***Table 6*. The data of transcutaneous Doppler sonography of the right jugular vein according to COPD severity**

Parameter	Mild COPD +DM2	Moderate to severe COPD +DM2	Mild COPD	Moderate to severe COPD
	(n=20)	(n=35)	(n=12)	(n=28)
Sf, m/s	0.18±0.01	0.06±0.01	0.18±0.01	0.07±0.02
Df, m/s	0.12±0.01	0.08±0.01	0.12±0.01	0.09±0.01
Ratio of Df/Sf	0.67±0.02	1.33±0.08	0.67±0.02	1.28±0.04
mPAP, mm Hg	18.0±1.0	38.5±5.0*,**,***	18.0±1.0	34.0±4.0

* p<0.05 vs mild COPD+DM2; ** p<0.05 vs mild COPD; *** p<0.05 vs moderate to severe sole COPD

groups (p>0.05). In sole COPD patients as well as in COPD plus DM2 was detected the level of mPAP ~25 mm Hg at the ratio of Df=Sf, meanwhile at the ratio of Df:Sf>1.0, mPAP was >35 mm Hg. Sf was greater than Df in the control and DM2 groups (*Tab. 5*).

There was an increase of the ratio Df/Sf in the 1st and 2nd groups in a contrast to the control (by 2.0 times and 1.8 times respectively; p<0.05 vs the control). That is, while of Df/Sf ratio increased, mPAP increased too. The level of mPAP in the moderate to severe COPD patients was about the same that was obtained by SE according to tDErjv (*Tab. 6*).

The comparative analysis showed the high informing value of the collapsing degree of the right jugular vein at inspiration for PH diagnosis in COPD patients. Thus, decrease of degree collapsing of this vein at inspiration (at the standard point – isthmus of the thyroid) was the objective qualitative marker of PH. The collapsing degree of right jugular vein at inspiration was equal to 22.4±0.5%; 22.4±0.3% and 20.8±0.2% in the control, DM1 and mild COPD patients plus DM1 respectively (p>0.05). There were no significant differences of the collapsing degree of right jugular vein in mild COPD patients plus DM2 as compared with the control.

The collapsing level of this vein was higher (p<0.05) in the mild COPD plus DM2 patients without PH as compared with 13.3±0.2% in the moderate-severe COPD patients plus DM2 with PH (mPAP=38.0±5.0 mm Hg by SE). Thus, mPAP was increased in the process decreasing of the collapsing degree of the right jugular vein at inspiration (*Fig. 2*).

We have found the high and significant correlations among a collapsing degree of the right jugular vein at inspiration and mPAP level (r= -0.76; p<0.05 in COPD patients plus DM2 and r=-0.92; p<0.05 in the moderate to severe COPD plus DM2 patients burdened by PH). We revealed that tDErjv was more sensitive method for verification PH in COPD patients than SE (χ^2=13.5; p<0.05). Thus, tDErjv allowed determining the mPAP in all COPD patients, even with the severe lung emphysema.

Discussion

Hypoxic PH in COPD progresses over the time and its severity usually correlates with the degree of airflow obstruction and impairment of pulmonary gas exchange [4,6]. The rate of PH progression is slow (at an average rate 0.6 mm Hg per year) [4] and usually mPAP is only moderately elevated, even in the patients with advanced COPD [6]. The development of PH was more closely linked to the evolution of arterial gases than to initial PH value [4].

In COPD, changes in pulmonary circulation may start several years before PH is apparent at rest. Hypoxic pulmonary vasoconstriction and remodeling of pulmonary vessels are the most significant factors, which contribute to the development and maintenance of PH in COPD [36]. Hypoxic stimulus exerts opposite actions on systemic and pulmonary circulation – dilates systemic arteries and constricts pulmonary arteries. Probably, the impairment of endothelial function is associated with an altered response to hypoxic stimulus that further worsens of the gas exchange.

Pulmonary vascular abnormalities in COPD patients with middle-to-moderate severity mainly consist of thickening of the intima of pulmonary muscular arteries which reduces the lumen size and an increased proportion of muscularised arterioles [37-40]. The results of morphometric studies showed conspicuous changes in the structure of pulmonary muscular arteries in patients with mild COPD [37,38].

An endothelial dysfunction in pulmonary arteries has been shown at both ends of COPD spectrum – end-stage disease and early mild disease [38,41]. The impairment of endothelial function results from changes in the expression and release of vasoactive mediators (NO, prostacyclin, ET-1).

In COPD patients with a hypoxic PH, mPAP is not markedly elevated and the rate of progression PH is slow [36]. Therefore, RV has some time to adapt to such a modest increase in the pressure load. When mPAP is chronically elevated, RV dilates, with the increases in both end-systolic and end-diastolic volumes. In COPD, the SVRV is usually maintained, whereas the RV ejection fraction (RVEF) is reduced [36]. Systolic ventricular dysfunction is defined by a decrease of RVEF. In COPD, RVEF can be reduced and its value is inversely related to mPAP [42].

Disorders of RV function could be a cause by the action of hypoxemia on myocardium. It leads to the systolic dysfunction of RV. A verification of this fact is the significant decrease of SVRV in the moderate to severe COPD patients (against a background of the marked bronchial obstruction) with concomitant DM2 as compared with mild COPD patients.

We detected the strong significant correlation between SVRV and CO, which increased during COPD development (from r=0.65 in mild COPD plus DM2 up to r=0.82 in the moderate to severe COPD plus DM2). These data could be an evidence of the remodeling process in RV as well as development hypertrophic stage of heart adaptation to appearance of PH.

It has been shown [43,44] that in clinically stable COPD patients the contractility of RV lies within normal limits, irrespective of mPAP value. But, during acute exacerbation of COPD, when mPAP increases markedly, the contractility of RV is reduced in patients with clinical signs of right-heart failure [8,45]. In COPD the CO is usually preserved and it might even rise during exacerbation episodes [46,47], even when there are apparent signs of RV failure.

A combination of COPD plus DM1 had negative interdependence. Thus, an acute exacerbation of COPD caused decompensation of DM1 in all these patients and (we detected I grade of ketoacidosis in 87% of cases) it required an increasing of the usual insulin dose. COPD acute exacerbation with concomitant DM2 caused additionally: the increase of insulin dose in 18% of these patients; combined therapy in 15% and switch on base bolus regimen of insulin treatment in 31% of the patients. In part, decompensation of current DM2 or DM1 had negative consequences on the evolution of COPD, favored to a long persistence inflammation in pulmonary tissue and reduced the term of COPD remission. Meanwhile, in mild COPD patients with DM1 the parameters of pulmonary hemodynamics were comparable with the control. This fact could testify the compensation of systolic function of RV in these patients.

More evident expressiveness of PH in COPD plus DM2 patients was caused by an increase of the hypoxia against a background of DM2 decompensation as well as by more pronounced disorders of microcirculation and gases balance of venous blood in these patients as compared with sole COPD patients ($pvO2=28.9\pm3.2$ vs 32.0 ± 2.2 mm Hg respectively; $p<0.05$). In view of that hypoxia is the condition, which can be corrected in the process of therapy, probably; steady and irreversible character of microvascular disorders caused larger increase of mPAP in patients with such combined pathology.

We also performed the parallel comparison of diagnostic value of PH assessment by the collapsing degree of right jugular vein at inspiration as well as by SE (with quantitative evaluation of PH). This analysis showed the high informative value of qualitative detection of PH by the collapsing degree of right jugular vein in these patients (criterion of McNamara $\chi^2=6.21$; $p<0.05$) even in severe lung emphysema and obesity.

It has been recognized for many years that DM has a significantly greater incidence of angina pectoris, acute myocardial infarctions, congestive heart failure and other manifestation of atherosclerosis as compared to non-diabetic population [48,49]. More recently it has been shown that ventricle performance can be impaired (diabetic cardiomyopathy), even in absence of ischemic heart disease [50-59]. Both left ventricle systolic [55,60] and diastolic functional abnormalities [56-58] occur in DM2 patients. Diastolic dysfunction can even be seen in young diabetics [59]. It has been shown recently that early abnormalities in cardiac function can occur in DM2 patients with only minor abnormalities in glucose metabolism [61].

Conclusions

Decreasing of the collapsing degree of the right jugular vein during inspiration was the objective qualitative marker of hypoxic PH in COPD patients. Transcutaneous Doppler sonography of the right jugular vein revealed about the same mPAP as by SE, but allowed to determine mPAP in all COPD patients, even with the severe lung emphysema. DM2 had a negative influence on pulmonary hemodynamics. Thus, PH was more

severe in COPD plus DM2 patients as compared with COPD only.

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