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The clinical significance of insulin-like growth factor-1 and cystatin C in predicting the risk of developing complications of chemoresistant pulmonary tuberculosis in patients undergoing palliative treatment

O. M. Raznatovska*[A,E,F], H. V. Khudiakov[B,C,D]

Zaporizhzhia State Medical University, Ukraine

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Key words: drug-resistant tuberculosis, palliative care, insulin-like growth factor-1, cystatin C.

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***E-mail:** raxnatovskaya@gmail.com

In contemporary Ukraine, the urgency of pulmonary chemoresistant tuberculosis (CRTB) problem is evident as it is the cause of severe clinical condition, subjective and functional disorders causing disease-specific distress in patients. This disease is a common cause of palliative treatment (PT) for patients requiring professional medical care. The goal of PT for patients with pulmonary CRTB should be to improve the quality of life (QoL) by priority of stress reduction which occurred as a result of the underlying disease complications.

The purpose – to evaluate the clinical relevance of insulin-like growth factor-1 (IGF-1) and cystatin C for predicting the risk of pulmonary CRTB complications among patients in PT.

Materials and methods. The study enrolled 81 patients with pulmonary CRTB who were treated in a Communal Institution "Zaporizhzhia Regional Hospital" and a Specialized Tuberculosis Hospital at the State Institution "Sophia penal colony (№ 55)" of the Ministry of Justice of Ukraine in the Zaporizhzhia Region. All patients (100 %) were male. The main group consisted of 52 patients receiving PT, the average age was 35.0 (28.0; 51.7) years. The control group included 29 patients receiving antimycobacterial therapy (AMBT) by category 4 according to the drug resistance profile. Study groups were age- and gender-matched. Serum levels of cystatin C and IGF-1 were measured by an enzyme-linked immunosorbent assay (ELISA) with an immunoassay reader "Sirio S" using the kit "Human Cystatin C ELISA BioVendor Research and Diagnostic Products" (ng/ml; Czech Republic) and "Human IGF-1 ELISA" (ng/ml, Germany), respectively. The measurements were performed in the Immuno-enzymatic Laboratory of the Training Medical Laboratory Center of ZSMU.

Results. Among the patients with pulmonary CRTB who received the PT, high inflammatory process activity, pronounced decrease in the quality of life and underweight as well as decrease in serum concentrations of cystatin C and IGF-1 were determined 1 month after the beginning of inpatient treatment. It was found that palliative patients who died the following month after being treated in the hospital compared to those who continued the PT, showed 1,6 times increased serum level of TNF-α, a tendency to further decrease in both cystatin C and IGF-1 serum levels to 1572.8 (911.6; 2278.8) ng/ml and 5.0 (2.1; 6.4) ng/ml, respectively. The decrease in serum concentrations of these indicators was significantly correlated with all the studied parameters in palliative patients with pulmonary CRTB both, who continued the treatment and who died. At the same time, in palliative patients who died, a decrease in serum levels of cystatin C and IGF-1 was strongly correlated with a decrease in the quality of life: ($r = 0.927$; $P = 0.01$) and ($r = 0.820$; $P = 0.01$), respectively. The average body mass index (BMI) was 18.0 (15.8; 20.1) kg/m^2 in these patients indicating the prevalence of underweight among them, and the high direct correlation between BMI and low serum concentrations of IGF-1 ($r = 0.986$; $P = 0.01$) and cystatin C ($r = 0.728$; $P = 0.05$) was indicative of a close relationship between cachexia and a decrease in the levels of anabolic processes impairment biochemical marker (IGF-1) and early marker of heart failure (cystatin C). Autopsy-identified causes of these patients death were heart failure and cachexia on the background of a specific process. A direct correlation was also found between decreased serum concentrations of IGF-1 and cystatin C in palliative patients with pulmonary CRTB both, who continued the treatment and those who died: ($r = 0.901$; $P = 0.01$) and ($r = 0.732$; $P = 0.05$), respectively.

Conclusions. Determination of IGF-1 and cystatin C serum concentrations has a great clinical significance in predicting the risk of complications such as heart failure and cachexia in patients with pulmonary CRTB receiving palliative treatment.

Ключові слова: хіміорезистентний туберкульоз легень, паліативне лікування, інсуліноподібний фактор росту-1, цистатин С.

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Клінічне значення інсуліноподібного фактора росту-1 та цистатину С у прогнозуванні ризику розвитку ускладнень хіміорезистентного туберкульозу легень у хворих, які отримують паліативне лікування

О. М. Разнатовська, Г. В. Худяков

Нині в Україні не викликає сумніву актуальність проблеми хіміорезистентного туберкульозу (ХРТБ) легень, який є причиною розвитку тяжкого клінічного стану, розвитку суб'єктивних розладів і тяжких функціональних порушень, що призводить до страждань хворого. Це захворювання є частою причиною призначення пацієнту паліативного лікування (ПЛ), що потребує професійної паліативної допомоги. Метою паліативної допомоги хворим на ХРТБ легень має бути поліпшення якості життя (ЯЖ) передусім шляхом зменшення страждань, які виникли внаслідок розвитку ускладнень основного захворювання.

Мета роботи – оцінювання клінічного значення ІФР-1 і цистатину С у прогнозуванні ризику розвитку ускладнень ХРТБ легень у хворих, які отримують паліативне лікування.

Матеріали та методи. Обстежили 81 хворого на ХРТБ легень, які перебували на лікуванні в КУ «Запорізька обласна лікарня» та спеціалізованій туберкульозній лікарні при ДУ «Софіївська виправна колонія (№ 55)» Міністерства юстиції України в

Запорізькій області. Усі пацієнти (100 %) – чоловічої статі. Основна група – 52 особи, які отримували ПЛ, середній вік – 35,0 (28,0; 51,7) року. У групу порівняння ввійшли 29 пацієнтів, які отримували антимікобактеріальну терапію за категорією 4 відповідно до профілю медикаментозної резистентності. Дослідження рівнів цистатину С, ІФР-1 у сироватці крові виконали методом твердофазного імуноферментного аналізу на приладі імуноферментний ридер Sirio S, застосовуючи такі набори: для цистатину С – «Human Cystatin C ELISA BioVendor Research and Diagnostic Products» (Czech Republic), (нг/мл); для ІФР-1 – «Human IGF-1 ELISA» (Germany), (нг/мл). Дослідження виконали в лабораторії імуноферментних досліджень навчального медико-лабораторного центру ЗДМУ.

Результати. У хворих на ХРБТ легень, які отримували паліативне лікування, через 1 місяць від початку стаціонарного лікування визначили високу активність запального процесу, різке зниження якості життя, дефіцит маси тіла на тлі зниження концентрацій у сироватці крові цистатину С та ІФР-1. У паліативних хворих, які померли уже через 1 місяць від початку стаціонарного лікування, визначена тенденція до вищого в 1,6 раза рівня TNF-α у сироватці крові, тенденція до зниження в сироватці крові рівнів цистатину С до 1572,8 (911,6; 2278,8) нг/мл та ІФР-1 до 5,0 (2,1; 6,4) нг/мл. У паліативних хворих на ХРТБ легень (і тих, які продовжують ПЛ, і в осіб, які померли) встановлена вірогідна кореляційна залежність зниження концентрацій цих показників у сироватці крові від усіх досліджуваних показників. У паліативних хворих, які померли, була сильніша кореляційна залежність рівнів цистатину С та ІФР-1 у сироватці крові та зниження якості життя: r = 0,927, p = 0,01 і r = 0,820, p = 0,01 відповідно. Середній показник ІМТ = 18,0 (15,8; 20,1) кг/м^2 у цих пацієнтів вказує на переважання дефіциту маси тіла, а висока пряма кореляційна залежність ІМТ із низькими концентраціями в сироватці крові ІФР-1 (r = 0,986; p = 0,01) та цистатину С (r = 0,728; p = 0,05) свідчить про тісний зв'язок кахексії зі зниженням рівнів біохімічного маркера погіршення анаболічних процесів (ІФР-1) і раннього маркера серцевої недостатності (цистатину С). Результати розтину цих пацієнтів свідчать, що причинами смерті були серцева недостатність і кахексія на тлі специфічного процесу. Пряма кореляційна залежність у паліативних хворих на ХРТБ легень – тих, які продовжують ПЛ, та осіб, які померли – встановлена між зниженнями концентрацій у сироватці крові ІФР-1 і цистатину С: r = 0,901, p = 0,01 і r = 0,732, p = 0,05 відповідно.

Висновки. Визначення концентрацій ІФР-1 і цистатину С у сироватці крові має важливе клінічне значення у прогнозуванні ризику розвитку таких ускладнень, як кахексія та серцева недостатність у хворих на ХРТБ легень, які отримують паліативне лікування.

Клиническая значимость инсулиноподобного фактора роста-1 и цистатина С в прогнозировании риска развития осложнений химиорезистентного туберкулеза легких у больных, которые находятся на паллиативном лечении

Е. Н. Разнатовская, Г. В. Худяков

Ключевые слова: химиорезистентный туберкулез легких, паллиативное лечение, инсулиноподобный фактор роста-1, цистатин С.

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В Украине не вызывает сомнения актуальность проблемы химиорезистентного туберкулеза (ХРТБ) легких, который является причиной развития тяжелого клинического состояния, развития субъективных расстройств и тяжелых функциональных нарушений, что приводит к страданиям больного. Это заболевание – частая причина назначения пациенту паллиативного лечения (ПЛ), требует профессиональной паллиативной помощи. Целью паллиативной помощи больным ХРТБ легких должно быть улучшение качества жизни (КЖ) в первую очередь путем уменьшения страданий, которые возникли в результате развития осложнений основного заболевания.

Цель работы – оценка клинической значимости ИФР-1 и цистатина С в прогнозировании риска развития осложнений ХРТБ легких у больных, находящихся на паллиативном лечении.

Материалы и методы. Обследовали 81 больного ХРТБ легких, находившихся на лечении в КУ «Запорожская областная больница» и специализированной туберкулезной больницы при ГУ «Софиевская исправительная колония (№ 55)» Министерства юстиции Украины в Запорожской области. Все пациенты (100 %) были мужского пола. Основную группу составили 52 больных, находившихся на ПЛ, средний возраст – 35,0 (28,0; 51,7) года. В группу сравнения вошли 29 пациентов, получавших антимикобактериальную терапию по категории 4 в соответствии с профилем медикаментозной резистентности. Исследование уровней цистатина С, ИФР-1 в сыворотке крови проводили методом твердофазного иммуноферментного анализа на приборе иммуноферментный ридер Sirio S с применением наборов: для цистатина С – «Human Cystatin C ELISA BioVendor Research and Diagnostic Products» (Czech Republic), (нг/мл), для ИФР-1 – «Human IGF-1 ELISA» (Germany), (нг/мл). Исследования проводили в лаборатории иммуноферментных исследований учебного медико-лабораторного центра ЗГМУ.

Результаты. У больных ХРБТ легких, находившихся на паллиативном лечении, через 1 месяц после начала стационарного лечения определена высокая активность воспалительного процесса, резкое снижение качества жизни, дефицит массы тела на фоне снижения концентрации в сыворотке крови цистатина С и ИФР-1. У паллиативных больных, умерших уже через 1 месяц после начала стационарного лечения, установлена тенденция к повышению в 1,6 раза уровня TNF-α в сыворотке крови, тенденция к дальнейшему снижению в сыворотке крови уровней цистатина С до 1572,8 (911,6; 2278,8) нг/мл и ИФР-1 до 5,0 (2,1; 6,4) нг/мл. У паллиативных больных ХРТБ легких (и у тех, которые продолжают ПЛ, и у умерших) определена достоверная корреляционная зависимость снижения концентраций этих показателей в сыворотке крови от всех исследуемых показателей. У умерших паллиативных больных отмечена более сильная корреляционная связь снижения уровней цистатина С и ИФР-1 в сыворотке крови со снижением качества жизни: r = 0,927, p = 0,01 и r = 0,820, p = 0,01 соответственно. Средний показатель ИМТ = 18,0 (15,8; 20,1) кг/м^2 у этих пациентов указывает на преобладание дефицита массы тела, а высокая прямая корреляционная зависимость ИМТ с низкими концентрациями в сыворотке крови ИФР-1 (r = 0,986, p = 0,01) и цистатина С (r = 0,728; p = 0,05) указывает на тесную связь кахексии со снижением уровней биохимического маркера ухудшения анаболических процессов (ИФР-1) и раннего маркера сердечной недостаточности (цистатина С). Данные вскрытия этих пациентов свидетельствуют, что причинами смерти были сердечная недостаточность и кахексия на фоне специфического процесса. Установлена прямая корреляционная зависимость у паллиативных больных

ХРТБ легких – и продолжающих ПЛ, и умерших – между снижением концентраций в сыворотке крови ИФР-1 и цистатина С: r = 0,901, p = 0,01 и r = 0,732, p = 0,05 соответственно.

Выводы. Определение концентраций ИФР-1 и цистатина С в сыворотке крови имеет большое клиническое значение в прогнозировании риска развития таких осложнений, как кахексия и сердечная недостаточность у больных ХРТБ легких, которые находятся на паллиативном лечении.

In contemporary Ukraine, the urgency of pulmonary chemoresistant tuberculosis (CRTB) problem is evident as it is the cause of severe clinical condition, subjective and functional disorders causing disease-specific distress in patients. This disease is a common cause of palliative treatment (PT) for patients requiring professional medical care. The goal of PT for patients with pulmonary CRTB should be to improve the quality of life (QoL) by priority of stress reduction which occurred as a result of the underlying disease complications [1,2].

After cause-of-death analysis among patients with pulmonary CRTB, we have concluded [3] that one of the major causes of death is heart failure and cachexia. Therefore, for pulmonary CRTB patients receiving PT, the assessment of cardiovascular disease markers is useful to diagnose heart failure and cachexia and their progression so as to optimize pathogenetic therapy which should improve the quality of life, reduce distress and prolong life in these patients.

Insulin-like growth factor-1 (IGF-1) is produced mainly by the liver and has properties such as anabolic, antioxidant, anti-inflammatory, and cytoprotective effects on tissue repair [4,5]. At the same time, the low level of IGF-1 was directly correlated with the risk of developing heart failure, increasing cardiovascular morbidity and mortality according to J. E. Puche and E. Castilla-Cortazar (2012) [6] and decreased production of IGF-1 in metabolic syndrome promotes high levels of insulin, which in turn can contribute to myocardial hypertrophy via stimulation of IGF-1 receptors [4].

Dronova A. et al. (2010) [7] indicate that the decrease in the level of IGF-1 plays an important pathogenetic role in myocardial remodeling, exhaustion syndrome and progression of chronic heart failure (CHF). Since increased catabolic activity due to chronic inflammatory process, low level of IGF-1 is a biochemical marker of anabolic processes disturbance in CHF.

Tuberculosis is accompanied by endogenous intoxication, which is one of the reasons of cachexia development. Data about the role of IGF-1 in the pathogenesis of cachexia suggest that its low levels were determined in debilitated patients [8].

Literature information indicates [9,10] that cystatin C stimulates the synthesis or decomposition of intracellular structures in many pathologies of the human body, which include diseases such as heart failure and acute coronary syndrome. It was shown that elevated levels of cystatin C were directly correlated with an increase in body weight. In a prospective study using Cox regression analysis it was revealed that in patients with acute heart failure and normal or mildly impaired renal function, cystatin C was an early marker of heart failure and had a high accuracy in predicting cardiac mortality [11].

The purpose

To evaluate the clinical relevance of insulin-like growth factor-1 (IGF-1) and cystatin C for predicting the risk of pulmonary CRTB complications among patients in PT.

Materials and methods

The study enrolled 81 patients with pulmonary CRTB who were treated in a Communal Institution “Zaporizhzhia Regional Hospital” and a Specialized Tuberculosis Hospital at the State Institution “Sophia penal colony (№ 55)” of the Ministry of Justice of Ukraine in the Zaporizhzhia Region. All patients (100 %) were male. The main group consisted of 52 patients receiving PT, the average age was 35.0 (28.0; 51.7) years. The control group included 29 patients receiving antimycobacterial therapy (AMBT) by category 4 according to the drug resistance profile in compliance with the Unified Clinical Protocol of Medical Care “Tuberculosis” (the Order of the Ministry of Health of Ukraine № 620 of 04.09.2014) [12], the mean age was 41.3 ± 1.8 years.

Study groups were age- and gender-matched. Serum levels of cystatin C, IGF-1 and TNF-α were measured by an enzyme-linked immunosorbent assay (ELISA) with an immunoassay reader “Sirio S” using the kits “Human Cystatin C ELISA BioVendor Research and Diagnostic Products” (ng/ml; Czech Republic), “Human IGF-1 ELISA” (ng/ml, Germany) and “Bender MedSystems GmbH” (pkg/ml, Austria), respectively. The measurements were performed in the Immuno-enzymatic Laboratory of the Training Medical Laboratory Center of ZSMU.

To calculate the body mass index (BMI), a New Body Mass Index (New BMI) calculator (kg/m^2) was used. The quality of life (QoL) was assessed using the MOS SF-36 questionnaire (St. Petersburg, 1998) based on component summaries: a physical component summary (PCS) by scales from 1 to 4, mental component summary (MCS) by scales from 5 to 8 and health-related QoL (HRQoL) which included all the questionnaire scales (1–8) (conv. un.).

Renal function was normal in all patients enrolled in this study. The glomerular filtration rate (GFR) was within the normal range. All the patients signed an informed written consent to participate in the study.

The study results were processed on a personal computer using the statistical package of the licensed program Statistica, version 13 (Copyright 1984–2018 TIBCO Software Inc. All rights reserved. License No. JPZ8041382130ARCN10-J). The Shapiro–Wilk test was used for normal-distributed quantitative data. Descriptive statistics including median and interquartile range – Me [Q25; Q75] were calculated to express the variables, which were not normally distributed. Differences between values were compared using Mann–Whitney test. All statistical tests were two-sided. Statistical significance was defined at $P < 0.05$. Correlation analyses were performed using the Pearson correlation coefficient (r).

Results

The study was conducted 1 month after the beginning of patient’s treatment. The results of TNF-α, HRQoL, MCS, PCS and BMI parameters studied in these groups, we presented

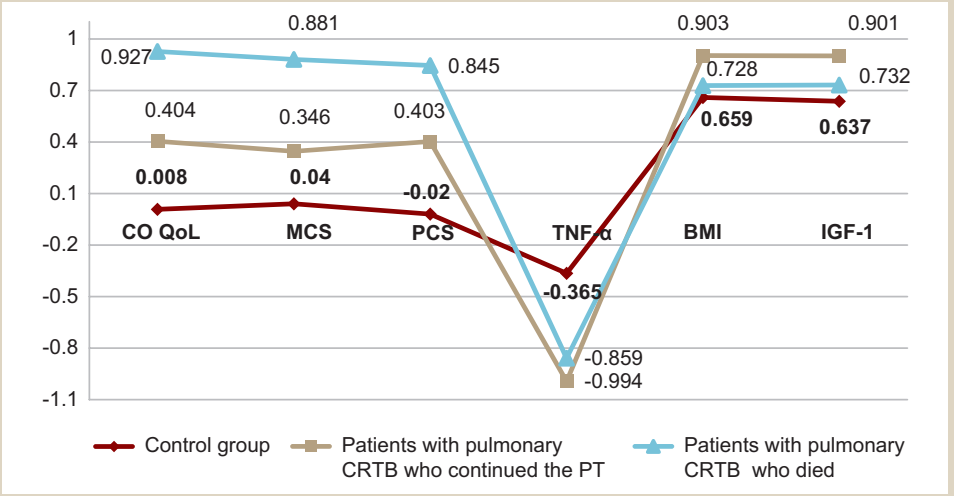

Fig. 1. Correlation indexes of serum cystatin C in patients with pulmonary CRTB.

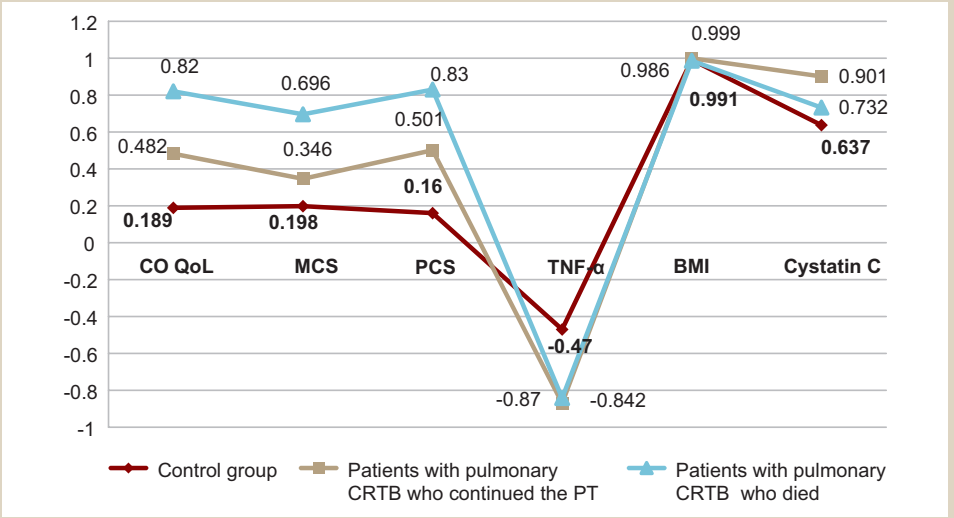

Fig. 2. Correlation indexes of serum IGF-1 in patients with pulmonary CRTB.

in the previous paper [13], pointing out that their levels were significantly worse in pulmonary CRBT patients in PT compared with pulmonary CRTB patients receiving AMBT.

The concentration of cystatin C was not significantly different between the groups, but it had a tendency to almost 1.2 times decrease in the main group of patients as compared to those of the comparison group: 1615.1 (1298.1; 2094.7) ng/ml versus 1880.4 (1658.8; 2364.3) ng/ml (>0.05), respectively. The concentration of IGF-1 was significantly 1.4 times lower in patients of the main group than in the control group: 5.1 (4.1; 7.8) ng/ml versus 7.1 (5.4; 8.7) ng/ml (<0.001), respectively.

During 9-month follow-up from the moment of admission to the hospitals, among PT patients with pulmonary CRTB, 8 people died (15.4 %). Autopsy-identified causes of all 8 patients (100 %) death were heart failure and cachexia on the background of a specific tuberculosis process. The study of HRQoL, MCS, PCS, BMI and TNF-α, cystatin C and IGF-1 levels determined 1 month after the beginning of inpatient treatment (*Table 1*), we found no significant differences in the main group between patients who continued the treatment and those who subsequently died. At the same time, palliative patients who died the following month after being treated in the hospital compared to those who continued PT, showed 1,6 times increased serum level of TNF-α, 290 (70; 810) pg/ml versus 180 (80; 620) pg/ml), a tendency to further decrease in serum levels of both cystatin C (1572.8 (911.6; 2278.8) ng/ml versus 1625.3 (1332.3; 2089.2) ng/ml) and IGF-1 5 (2.1; 6.4) ng/ml versus 5.3 (4.1; 7.8) ng/ml).

The assessment of cystatin C correlations (*Fig. 1*) revealed the following: in comparison group, the level of serum cystatin C was significantly negatively correlated with an increase in TNF-α serum level (r = -0.365; P = 0.05) and directly correlated with a reduction in BMI (r = 0.659; P = 0.01) and serum concentration of IGF-1 (r = 0.637; P = 0.01).

In patients with pulmonary CRTB who continued the PT, a decrease in cystatin C concentration was significantly directly correlated with a decrease in QoL (r = 0.404; P = 0.01), BMI (r = 0.903; P = 0.01), serum concentration of IGF-1 (r = 0.901; P = 0.01) and negatively correlated with an increase in serum TNF-α level (r = -0.994; P = 0.01). The QoL was reduced due to a decrease in both MCS (r = 0.346; P = 0.05) and PCS (r = 0.404; P = 0.01) component summaries. In palliative pulmonary CRTB patients who died, a decrease in cystatin C concentration was significantly directly correlated with a decrease in QoL (r = 0.927; P = 0.01), BMI (r = 0.728; P = 0.05) and serum

Table 1. Comparison between groups of indicators, Me [Q25; Q75]

Indicator	The control group (n = 29)	The main group (n = 52)	
		Pulmonary CRTB patients who continued PT (n = 44)	PT patients with pulmonary CRTB who died (n = 8)
TNF-α, pkg / ml	80 (60; 120)	180 (80; 620)*	290 (70; 810)*
HRQoL, conv. un.	66.9 (51.3; 72.1)	49.4 (38.9; 60.0)*	50.3 (36.5; 70.9)*
MCS, conv. un.	61.9 (53.5; 69.8)	52.1 (37.5; 57.7)*	47.1 (38.0; 64.7)*
PCS, conv. un.	68,5 (51.7; 77.2)	49.6 (39.0; 61.0)*	53.3 (37.6; 68.7)*
BMI, kg/m^2	20.8 (18.9; 23.0)	18.1 (16.8; 21.2)*	18.0 (15.8; 20.1)*
Cystatin C, ng/ml	1880.4 (1658.8; 2364.3)	1625.3 (1332.3; 2089.2)	1572.8 (911.6; 2278.8)
IGF-1, ng/ml	7.1 (5.4; 8.7)	5.3 (4.1; 7.8)*	5.0 (2.1; 6.4)

#: significant difference in the parameters between studied groups (P < 0.05); ***:** significant difference in the parameters compared with the control group (P < 0.05).

concentration of IGF-1 (r = 0.732; P = 0.05) and negatively correlated with an increase in serum TNF-α level (r = -0,859; P = 0.01). The QoL was also reduced due to a decrease in both MCS (r = 0,881; P = 0,01) and PCS (r = 0.845; P = 0.01) component summaries.

The assessment of IGF-1 correlations (*Fig. 2*) revealed the same trend of changes in the groups as for cystatin C correlations. Thus, in the comparison group, the level of serum IGF-1 was significantly negatively correlated with an increase in serum levels of TNF-α (r = -0.470; P = 0.01) and directly correlated with a decrease in BMI (r = 0.991; P = 0.01) and serum levels of cystatin C (r = 0.637; P = 0.01).

In patients who continued PT, the decreased concentration of IGF-1 was significantly directly correlated with the reduced QoL (r = 0.482; P = 0.01), BMI (r = 0.999; P = 0.01), serum cystatin C (r = 0,901; P = 0.01) and negatively correlated with increased serum levels of TNF-α (r = -0.870; P = 0.01). The QoL was reduced due to a decrease in both MCS (r = 0.346; P = 0.05) and PCS (r = 0.501; P = 0.01). In palliative patients with pulmonary CRTB who died, the decrease in IGF-1 concentration was significantly directly correlated with the decrease in QoL (r = 0.820; P = 0.01), BMI (r = 0.986; P = 0.01), serum cystatin C (r = 0.732; P = 0.05) and negatively correlated with the increased serum levels of TNF-α (r = -0.842; P = 0.01). The QoL was also reduced but only due to a decrease in PCS (r = 0.830; P = 0.01).

Discussion

Among the patients with pulmonary CRTB who received the PT, high inflammatory process activity, pronounced decrease in the quality of life (due to decrease in both physical and mental components of health) and underweight as well as decrease in serum concentrations of cystatin C and IGF-1 were determined 1 month after the beginning of inpatient treatment as compared to patients with pulmonary CRTB who received AMBT.

It was found that palliative patients who died the following month after being treated in the hospital compared to those who continued the PT, showed 1,6 times increased serum level of TNF-α, a tendency to further decrease in both cystatin C and IGF-1 serum levels to 1572.8 (911.6; 2278.8) ng/ml and 5.0 (2.1; 6.4) ng/ml, respectively.

The decrease in serum concentrations of cystatin C and IGF-1 was significantly correlated with all the studied parameters (TNF-α, HRQoL, MCS, PCS and BMI) in palliative patients with pulmonary CRTB both, who continued the treatment and who died.

At the same time, in palliative patients who died, a decrease in serum levels of cystatin C and IGF-1 was strongly correlated with a decrease in the quality of life: (r = 0.927; P = 0.01) and (r = 0.820; P = 0.01), respectively. The average BMI was 18.0 (15.8; 20.1) kg/m^2 in these patients indicating the prevalence of underweight among them, and the high direct correlation between BMI and low serum concentrations of IGF-1 (r = 0.986; P = 0.01) and cystatin C (r = 0.728; P = 0.05) was indicative of a close relationship between cachexia and a decrease in the levels of anabolic processes impairment biochemical marker (IGF-1) and early marker of heart failure (cystatin C). Autopsy-identified causes of these patients death were heart failure and cachexia on the background of a specific process.

A direct correlation was also found between decreased serum concentrations of IGF-1 and cystatin C in palliative patients with pulmonary CRTB both, who continued the treatment and those who died: (r = 0.901; P = 0.01) and (r = 0.732; P = 0.05), respectively.

As a result, we have confirmed the scientific data:

– Mangileva, T. A., Gafarova, N. Kh. (2015) [4] that the low level of IGF-1 directly correlates with the risk of developing heart failure;

– Dronova A. V. et al. (2010) [7] that the decrease in the level of IGF-1 plays an important pathogenetic role in exhaustion syndrome and progression of heart failure;

– Kravchun P. G. et al. (2015) [8] on the role of IGF-1 in the pathogenesis of cachexia (its is low level was determined in exhausted people);

– Velkov V. V. (2011) [9], Kurkina T. V., Shemetova G. N. (2013) [10] that a low level of cystatin C can be a marker of the secondary cardiovascular pathology development and heart failure progression.

Conclusions

Thus, determination of IGF-1 and cystatin C serum concentrations has a great clinical significance in predicting the risk of complications such as heart failure and cachexia in patients with pulmonary CRTB receiving palliative treatment.

Prospects for further research. Development of pathogenetic therapy for serum levels of IGF-1 and cystatin C correction in palliative care patients with pulmonary CRTB.

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Information about authors:
Raznatovska O. M., MD, PhD, DSc, Professor of Department of Phthisiology and Pulmonology, Zaporizhzhia State Medical University.
ORCID ID: 0000-0003-2252-9063
Khudiakov H. V., MD, Postgraduate student of the Department of Phthisiology and Pulmonology, Zaporizhzhia State Medical University.

Відомості про авторів:
Разнатовська О. М., д-р мед. наук, професор каф. фтизіатрії і пульмонології, Запорізький державний медичний університет, Україна.
Худяков Г. В., аспірант каф. фтизіатрії і пульмонології, Запорізький державний медичний університет, Україна.

Сведения об авторах:
Разнатовська Е. Н., д-р мед. наук, профессор каф. фтизиатрии и пульмонологии, Запорожский государственный медицинский университет, Украина.
Худяков Г. В., аспирант каф. фтизиатрии и пульмонологии, Запорожский государственный медицинский университет, Украина.

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