Оригінальні дослідження UDC: 616.12-089.82-64]-036.3-071

RIGHT HEART CATHETERIZATION FOR HEMODYNAMIC EVALUATION OF PULMONARY HYPERTENSION

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Key words: *pulmonary hypertension, right heart catheterization, 6-minute walk test.*

Bukovinian Medical Herald. V.21, № 4 (84). P. 114-119.

DOI:
10.24061/2413-0737. XXI.4.84.2017.131

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Objective *description of clinical characteristics of patients, their physiological and hemodynamic parameters during right heart catheterization in the center of pulmonary hypertension in Ukraine.*
Material and methods. *The procedure fof the right heart catheterization according to national and international protocols was performed in 108 patients with intermediate or high probability of pulmonary hypertension according to expert echocardiography. Physiological evaluation at the time of diagnosis includes a 6-minute walk test, a NTpro-BNP level, and an expert echocardiography with expanded protocol and an assessment of the right ventricular function.*
Results. *We confirmed the presence of pulmonary hypertension in 94 patients (90.4%). During the diagnosis, 67% of patients with pulmonary hypertension had functional class III and 8% — functional class IV, 75% of patients had functional class III or IV. 67 patients underwent right heart catheterization before administering specific therapy for pulmonary hypertension, and the remaining 27 patients had already received specific therapy without confirmation of diagnosis. Our experience has shown that the lack of accurate hemodynamic measurements leads to a misleading diagnosis or inappropriate use of drugs specific to pulmonary hypertension, which can lead the patient to seek alternative treatments that have no proven efficacy.*
Conclusions. *Catheterization of the right heart is the only way to reliable diagnosis of pulmonary hypertension and the risk of serious complications. It is necessary for the diagnosis of pulmonary hypertension, assessment of pulmonary hemodynamic condition and estimation of further prognosis.*

Ключевые слова: *легочная гипертензия, катетеризация правых отделов сердца, тест 6-минутной ходьбы.*

Буковинский медицинский вестник. Т.21, № 4 (84). Р. 114-119.

КАТЕТЕРИЗАЦИЯ ПРАВЫХ ОТДЕЛОВ СЕРДЦА ДЛЯ ОЦЕНКИ ГЕМОДИНАМИКИ ЛЕГОЧНОЙ ГИПЕРТЕНЗИИ

Ю.Н. Сиренко, И.А. Живило, А.Ю. Сиренко

Цель работы *— описание клинических характеристик пациентов, их физиологических и гемодинамических параметров при катетеризации правых отделов сердца в центре легочной гипертензии в Украине.*
Материал и методы. *Проведено процедуру катетеризации правых отделов сердца в соответствии с национальными и международными протоколами в 108 пациентов с промежуточной или высокой вероятностью легочной гипертензии в соответствии с экспертной эхокардиографией. Физиологическая оценка на момент диагностики включает в себя тест 6-минутной ходьбы,*

уровень NTpro-BNP и экспертную эхокардиографию с расширенным протоколом и оценкой функции правого желудочка.

Результаты. *Мы подтвердили наличие легочной гипертензии у 94 пациентов (90,4%). При установлении диагноза 67% пациентов с легочной гипертензией имели III ФК и 8% — IV ФК, 75% пациентов имели III или IV ФК. Катетеризацию правых отделов сердца перед назначением специфической терапии для легочной гипертензии проведено 67 пациентам, а остальные 27 пациентов уже получали специфическую терапию без подтверждения диагноза. Наш опыт показал, что отсутствие точных гемодинамических измерений приводит к ошибочному диагностированию или нецелесообразному применению препаратов, специфических для легочной гипертензии, которые могут привести пациента к поиску альтернативных методов лечения, которые не имеют доказаной эффективности.*

Выводы*. Катетеризация правых отделов сердца остается единственным способом надежной диагностики легочной гипертензии. Катетеризация сердца необходима для установления диагноза легочной гипертензии, оценки легочной гемодинамики и оценки дальнейшего прогноза.*

Ключові слова: *легенева гіпертензія, катетеризація правих відділів серця, тест 6-хвилинної ходьби.*

Буковинський медичний вісник. Т.21, № 4 (84). Р. 114-119.

КАТЕТЕРИЗАЦІЯ ПРАВИХ ВІДДІЛІВ СЕРЦЯ ДЛЯ ОЦІНКИ ГЕМОДИНАМІКИ ЛЕГЕНЕВОЇ ГІПЕРТЕНЗІЇ

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Мета роботи *— опис клінічних характеристик пацієнтів, їх фізіологічних та гемодинамічних параметрів під час катетеризації правих відділів серця в центрі легеневої гіпертензії в Україні.*

Матеріал і методи. *Проведено процедуру катетеризації правих відділів серця відповідно до національного та міжнародного протоколів у 108 пацієнтів з проміжною або високою імовірністю легеневої гіпертензії відповідно до експертної ехокардіографії. Фізіологічна оцінка на момент діагностики включає 6-хвилинний тест, рівень NTpro-BNP та експертну ехокардіографію з розширеним протоколом та оцінкою функції правого шлуночка.*

Результати. *Ми підтвердили наявність легеневої гіпертензії у 94 пацієнтів (90,4%). Під час встановлення діагнозу 67% пацієнтів із легеневою гіпертензією мали III ФК та 8% — IV ФК, 75% пацієнтів мали III чи IV ФК. Катетеризацію правих відділів серця перед призначенням специфічної терапії для легеневої гіпертензії проведено 67 пацієнтам, а інші 27 пацієнтів вже отримували специфічну терапію без підтвердження діагнозу. Наш досвід продемонстрував, що відсутність точних гемодинамічних вимірювань призводить до помилкового діагностування або недоцільного застосування препаратів, специфічних для легеневої гіпертензії, які можуть призвести пацієнта до пошуку альтернативних методів лікування, які не мають доведеної ефективності.*

Висновки. *Катетеризація правих відділів серця залишається єдиним способом надійної діагностики легеневої гіпертензії. Катетеризація серця необхідна для встановлення діагнозу легеневої гіпертензії, оцінки легеневої гемодинаміки та оцінки подальшого прогнозу.*

Background. Pulmonary arterial hypertension (PAH) is a group of rare chronic progressive diseases with a very poor prognosis. According to all international guidelines currently a catheterization of the right heart and the pulmonary artery (RHC) is the only reliable method of confirmation of the diagnosis of PAH [1,2]. Besides a direct measuring of the mean pressure in the pulmonary artery (mPAP) and pulmonary artery wedge pressure (PAWP) during RHC procedure it is possible to measure a level of cardiac output by the direct method (most often with thermodilution) and calculate the level of pulmonary vascular resistance (PVR) and evaluate the mixed venous blood oxygen saturation (SvO2) [2,3]. The degree of PVR alongside with the level of mPAP are keys for PAH diagnosis verification and the levels of cardiac output (CO) and SvO2 are the important prognostic markers of disease [4,5]. The incomplete RHC assessment is linked to a higher likelihood of misdiagnosis and inappropriate treatment in PAH.

In recent decades, due to the technical difficulties (lack of Swan-Ganz Catheter registration, centralized state purchases of medical equipment etc.) in Ukraine RHC procedure has been performed in reduced practice without measuring PAWP, direct determination of the cardiac output and the correct calculation of the systemic and pulmonary hemodynamics. Vast majority of patients in Ukraine had not undergone RHC even with reduced protocol. Considering the features of PAH patients in Ukraine (delay in the referral, errors in diagnosis, lack of drugs for specific therapy for most patients, the lack of follow-up, etc.), we could expect that those patients are basically different from the EU countries and the USA. The aforementioned conditions challenge the data accumulated during RHC in this group of patients in Pulmonary Hypertension Center in NSC "Institute of cardiology n.a. Acad. M.D. Strazhesko" over the past 3 years. We did no found information on similar domestic research in the available literature.

Objective. The aim of this study was to describe patients' clinical characteristics and physiological and hemodynamic parameters at the time of RHC in a pulmonary hypertension center in Ukraine.

Methods. We performed RHC procedure according to the National and international guidelines protocol in symptomatic 108 patients with intermediate or high probability of PH according to the expert echocardiography [1,2,3,6]. In 4 cases we repeated procedure of RHC after 4 and 10 months because clinical worsening and confirm this by hemodynamic data. Physiological assessment at the time of diagnosis includes six-minute walk test (6MWT), NTpro-BNP level, and expert EchoCG with extended protocol with evaluation for pericardial effusion and right ventricular function (TAPSE score). Proportion of patients in subgroups of pulmonary hypertension and without PH is displayed in the Fig. Majority of our patients were with IPH (39,4%), CTEPH (24,1%) and CHD (14,4%). We did not performed RHC in patients with open ventricular septum defects or similar conditions when presence of PAH was clear and therefore several proportion of patients with CHD referred to our center did not underwent RHC procedures.

Descriptive statistics in terms of mean, standard deviations and percentages were used to describe characteristics of the studied patients. After assessment of normality distribution of variables, Student t-test and ANOVA test were used if data had normal distribution. A P-value less than 0,05 was considered a significant test. SPSS version 17 was used for all statistical analysis.

Results and discussion. Table demonstrates demographic, clinical and RHC data. The mean age at diagnosis was 45,8±1,5 years, and there was a female preponderance of 72%. The mean duration between symptoms onset and diagnosis was 11,7±0,4 months. We confirmed presence of PH in 94 patients (90,4%) and rejected diagnosis of PH in 10 cases (9,6%). In half of them was a suspicion of IPAH and in others was a suspicion of CTEPH. At the time of establishing of diagnosis, 67% of patients with PH were in functional class III and 8% were in functional class IV; totally more that 75% of patients had III or IV WHO class.

Only in 67 patients RHC was performed before prescription of specific PAH therapy and other 27 patients already received PAH specific therapy without confirmation of PAH diagnosis. In 4 cases after RHC this type of very expensive treatment was withdrawn and in almost other cases was corrected: calcium channel blockers were administrated in patients with positive test with vasodilator or we did escalation of specific therapy in proper conditions.

All our patients with confirmed PH had signs of poor physiological conditions: low distance in 6MWT, markedly elevated mRAP, SPAP, DPAP and mPAP, decreased cardiac output and compromised right ventricular function (low TAPSE) with dramatically elevated PVR. We noted that the difference between measured mPAP and calculated by EchoCG data more than 10 mm Hg in both sides was in 75 (79,8%) patients.

In comparison with international registers our data show more severe level of PH and more profound changes of hemodynamic parameters that are typical for late stages of disease [7,8,9,10].

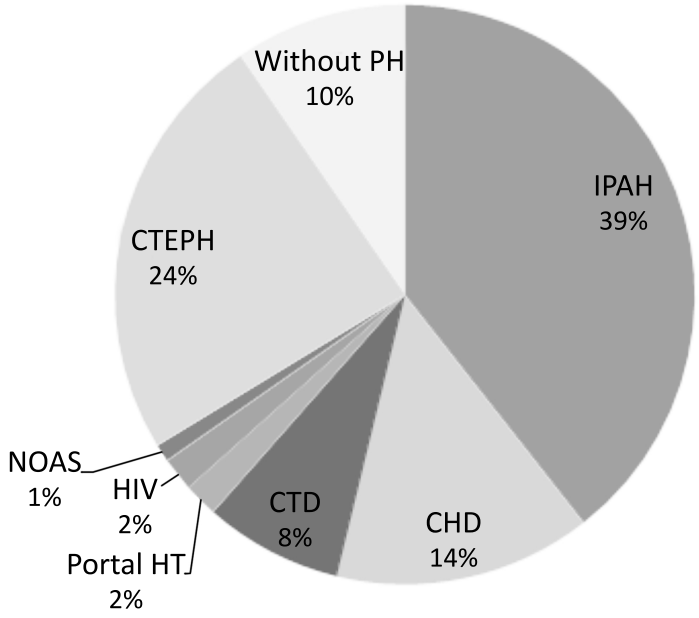

Fig. Proportion of patients in subgroups of pulmonary hypertension (%):
IPAH – idiopathic pulmonary arterial hypertension; CTD - connective tissue disease associated PAH; CHD – congenital heart disease associated PAH; CTEPH – chronic thromboembolic pulmonary hypertension; HIV – human immunodeficiency virus associated PAH, NOAS – nocturnal obstructive apnea syndrome

The safety profile of right heart catheterization in patients with pulmonary vascular disease is well documented: from the largest dataset (n=7,218) analyzing complications in association with RHC studies, the procedural fatality rate was 0,055% and serious adverse event rate was 1,1%, which, aside from the fatalities, were generally mild to moderate in severity and largely confined to localized hematoma at the vascular access site [7]. In our series of patients in 5 patients (5,3%) was wrong carotid puncture without further clinical consequences. None of our patients needed blood transfusion or infusion therapy. We also did not observe temperature reactions and infectious complications and catheter introducer was removed immediately after the procedure. In addition to carotid puncture during catheterization was observed a small hematoma around the site of puncture in 8 patients (8,5%), despite that in all patients receiving oral anticoagulants we canceled them at least 48 hours before the procedure. Thus, the number of complications in the performance of PCC in this series of patients was comparable to mentioned above international registry.

The present study describes the characteristics of PAH in the largest population of patients in Ukraine to date. In comparison with other countries our patients still present very late in the course of the disease, and the majority of them display severe physiological and hemodynamic compromise. Despite clear recommendations on the use of RHC, best practice differs from guidelines. Importantly, the consequences of not performing a right heart catheterization to diagnose the etiology and initiate treatment of the pulmonary vascular disorder can have a significant impact on patient care and perpetuate health care providers misunderstanding of the natural course of the disorder. Our experience demonstrated that the absence of accurate hemodynamic measurements lead to a misdiagnosis with overprescribing or in some cases underprescribing PAH-specific medications that may lead a patient to search for alternative therapies lacking demonstrated efficacy that can produce physical harm, emotional distress and economic hardship [1,3,11]. Our data demonstrated that steps to improve the quality of care of patients with PAH are being implemented by the Pulmonary Hypertension Association through patient and physician education and designation of pulmonary hypertension care centers.

Table

Demographic, Clinical, and Hemodynamic Characteristics of Patients With and Without Pulmonary Hypertension (M±m)

Characteristics	Patients with PH	Patients without PH
Subjects, No	94	10
Age, years	45,8±1,5	48,6±3,7
Women/men, No (%)	68/26 (72/28)	7/3 (70/30)
Symptoms duration, months	37,4±5,7	9,2±1,8*
FC I/II, No (%)	23 (24,5)	-
FC III, No (%)	63 (67,0)	-
FC IV, No (%)	8 (8,5)	-
SBP, mm Hg	118,3±1,6	125,0±6,0
DBP, mm Hg	78,3±1,0	81,0±2,8
Baseline NT-proBNP,	1669,3±263,4	64,6±18,4*
6MWT, m	330,5±11,5	420,3±19,4*
TAPSE, EchoCG, mm	14,5±0,4	23,9±1,8*
mRAP, mm Hg	9,8±0,6	6,2±0,8*
SPAP, mm Hg	87,3±2,9	27,4±1,7*
DPAP, mm Hg	38,1±1,6	11,2±0,9*
mPAP, mm Hg	59,3±2,1	17,7±1,2*
PAWP, mm Hg	9,6±0,5	7,8±1,1
Cardiac index, l/min/m^2	2,24±0,06	3,07±0,30*
PVR, dyn × c × cm^{-5} (Wood units)	1125,1±62,9 (14,1±0,8)	130,1±15,4* (1,6±0,2)
$SvO_{2,\%}$	62,4±1,0	77,3±2,8*

FC – functional class; mRAP – mean right atrium pressure; SPAP – systolic pulmonary arterial pressure; DPAP – diastolic pulmonary arterial pressure; mPAP – mean pulmonary arterial pressure; PAWP – pulmonary artery wedge pressure; PVR - pulmonary vascular resistance; TAPSE – Tricuspid annular plain systolic excursion; SvO2 - mixed venous blood oxygen saturation, * - p < 0,05 in comparison between groups.

Conclusion. RHC remains the only technique for reliably and definitively diagnosing PAH, and in adult patients is associated with a low risk of serious complications. Cardiac catheterization remains necessary to establish the diagnosis of PH and to assess pulmonary hemodynamic state and evaluate the prognosis. Furthermore, there is a clear need to follow the standardized protocols and in further improve regulation to achieve optimal application of RHC, with resulting positive implications for diagnosis and earlier intervention for patients with PAH in routine clinical practice in reference centers.

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Надійшла до редакції 25.10.2017
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