

VERIFICATION OF MYOCARDITIS BY MULTISPIRAL COMPUTED TOMOGRAPHY OF THE HEART IN DILATED CARDIOMYOPATHY SYNDROME

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Annotation.

Dilated cardiomyopathy (DCMP) remains one of the most common diagnoses in patients with chronic heart failure (CHF), which is established by clinicians on the basis of typical structural and functional changes of the heart (dilation of the chambers of the heart with reduced contractility), regardless of the nature of such a condition. In many cases, this diagnosis, established at the first stage of the examination, means only a "big heart". At the same time, the issue of the nosological nature of DCMP is key in choosing treatment tactics and determining the prognosis of the patient.

Purpose – To investigate whether intravenous contrast-enhanced multislice spiral computed tomography (computed tomography) (MSCT) versus myocardial morphological examination can diagnose myocarditis and the non-inflammatory causes of dilated cardiomyopathy (DCM) and evaluate prognosis in patients with the latter.

Material and methods – A study group consisted of 130 patients, including 95 men (46.8±11.9 years), with DCM (mean left ventricular (LV) end-diastolic dimension (EDD), 6.6±0.8 cm; mean LV ejection fraction (EF), 29.8±9.3%; NYHA functional class (FC) III (II; III)). All the patients underwent intravenous contrast-enhanced 320-slice CT of the heart; myocardial morphological examination was made in 48 patients (endomyocardial biopsy in 29 patients, intraoperative biopsy in 7, and autopsy in 9, and study of the explanted heart in 3). In addition, cardiotropic viral DNA in the blood and myocardium and the level of anticardiolipin antibodies were determined; echocardiography (in all the patients), scintigraphy ($n = 45$), magnetic resonance imaging (MRI) ($n = 21$), and coronary angiography (CG) ($n = 46$), and a genetic consultation were performed. A comparison group comprised 20 patients, including 14 men (69.3±9.2 years), with coronary atherosclerosis (40% or more stenoses) according to MSCT findings in the absence of criteria for DCM (mean LV EDD, 4.8±0.5 cm; mean LV EF, 59.4±4.6%).

Results – Morphological/comprehensive examination showed that myocarditis as a cause of DCM was diagnosed in 76 (65%) patients; its concurrence with genetic cardiomyopathies was in 17 more patients (17%). MSCT of the heart revealed lower accumulation areas in 2 (1.5%) patients (type 1 based on the proposed rating scale), delayed myocardial contrast agent accumulation (DMCAA) in 81 (62.3%): subendocardial accumulation (type 2) in 8, intramyocardial accumulation in 4 (type 3), subepicardial accumulation in 52 (type 4), and transmural accumulation in 15 (type 5); DMCAA was not noted in 49 patients. DMCAA was not found in the comparison group. As compared with biopsy, the sensitivity, specificity, predictive value of positive and negative results of the tests in detecting active myocarditis for all the types of DMCAA were 77.4, 47.1, 72.7, and 53.3%, respectively; those for types 3-5 of DMCAA were 77.4, 52.9, 75.0, and 56.3%; those in detecting all the morphological types of myocarditis were 68.3, 28.6, 84.8, and 13.3%, and those for types 3-5 were 65.9, 28.6, 84.4, and 12.5%, respectively. Comparison of the data of MSCT and those of comprehensive ex-

amination in all the patients with DCM, the diagnostic significance in detecting myocarditis for all the types of DMCAA was 70.6, 67.9, 88.9 and 38.8%, respectively; that for DMCAA types 3-5 was 60.8, 67.9, 87.3, and 32.3%. In the study group, MSCT also identified the non-compacted myocardium ($n = 31$ (23.8%)), coronary atherosclerosis ($n = 31$ (23%)), which is confirmed by CG findings in 15 patients. The patients with DMCAA significantly more frequently showed a relationship with previous infection, acute onset, significantly higher NYHA FCs, end-diastolic and end-systolic LV volumes, and insignificantly lower LV EF. During a mean follow-up periods of 12 (6; 37.25) months, the overall mortality rate was 17.7% (23 deaths); the death + transplantation index was 20% ($n = 26$). All the types of DMCAA were found to be significantly related to prognosis: in the DMCAA group, the mortality rate was 21.5% versus 7.8% in the non-DMCAA group (odds ratio 3.22; 95% confidence interval, 1.02 to 10.21; $p < 0.05$).

Conclusion – MSCT with the assessment of delayed contrast enhancement (and simultaneous CT coronary angiography) can be used for the non-invasive diagnosis of myocarditis in patients with DCM, including that in the presence of contraindications to MRI. DMCAA correlates with the presence of myocarditis, its activity, the degree of functional disorders, and prognosis.

Keywords: dilated cardiomyopathy; myocarditis; intravenous contrast-enhanced multislice spiral computed tomography; delayed myocardial contrast agent accumulation; chronic heart failure

ВЕРИФИКАЦИЯ МИОКАРДИТА МУЛЬТИСПИРАЛЬНОЙ КОМПЬЮТЕРНОЙ ТОМОГРАФИЕЙ СЕРДЦА ПРИ СИНДРОМЕ ДИЛАТАЦИОННОЙ КАРДИОМИОПАТИИ

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Аннотация.

Дилатационная кардиомиопатия (ДКМП) остается у больных с хронической сердечной недостаточностью (ХСН) одним из наиболее частых диагнозов, который устанавливают клиницисты на основании типичных структурно-функциональных изменений сердца (дилатация камер сердца со снижением сократимости), независимо от природы такого состояния. Во многих случаях этот диагноз, установленный на первом этапе обследования, означает лишь «большое сердце». Вместе с тем вопрос нозологической природы ДКМП является ключевым в выборе тактики лечения и определении прогноза у больного.

Цель исследования – Изучение возможности мультиспиральной компьютерной томографии (МСКТ) сердца с внутривенным контрастированием у больных с синдромом дилатационной кардиомиопатии (ДКМП) в диагностике миокардита (в сопоставлении с морфологическим исследованием миокарда), невоспалительных причин ДКМП и оценке прогноза.

Материал и методы – В основную группу вошли 130 пациентов (95 мужчин, средний возраст $46,8 \pm 11,9$ года) с синдромом ДКМП: средний конечный диастолический размер (КДР) левого желудочка (ЛЖ) $6,6 \pm 0,8$ см, средняя фракция выброса (ФВ) $29,8 \pm 9,3\%$; III (II; III) функциональный класс (ФК) по классификации NYHA. Всем проведена 320-срезовая МСКТ сердца с внутривенным контрастированием; 48 пациентам выполнено морфологическое исследование миокарда (эндомиокардиальная биопсия у 29, интраоперационная у 7, аутопсия у 9, исследование эксплантированного сердца у 3). Кроме того, определяли ДНК кардиотропных вирусов в крови и миокарде, уровень антикардиальных антител, проводили эхокардиографию (всем пациентам), сцинтиграфию (у 45), магнитно-резонансную томографию – МРТ (у 21), коронарографию – КГ (у 46), консультацию генетика. Группу сравнения составили 20 пациентов (14 мужчин, средний возраст $69,3 \pm 9,2$ года) с коронарным атеросклерозом (стенозы 40% и более) по данным МСКТ в отсутствие критериев ДКМП (средний КДР ЛЖ $4,8 \pm 0,5$ см, средняя ФВ $59,4 \pm 4,6\%$).

Результаты – По данным морфологического комплексного обследования, миокардит как причина синдрома ДКМП диагностирован у 76 (65%) пациентов, его сочетание с генетическими кардиомиопатиями – у 17 (17%). При МСКТ сердца участки пониженного накопления выявлены у 2 (1,5%) больных (1-й тип по предложенной шкале оценки), отсроченное накопление контрастного препарата (ОНКП) в миокарде – у 81 (62,3%): у 8 субэндокардиальное (2-й тип), у 4 интрамиокардиальное (3-й тип), у 52 субэпикардиальное (4-й тип), у 15 трансмуральное (5-й тип); у 49 больных ОНКП не отмечено. В группе сравнения ОНКП не выявлено. В сопоставлении с биопсией чувствительность, специфичность, прогностическая ценность положительного и отрицательного результатов тестов всех типов ОНКП в выявлении активного миокардита составили 77,4, 47,1, 72,7 и 53,3%, 3–5-го типа ОНКП – 77,4, 52,9, 75 и 56,3%, в выявлении всех морфологических типов миокардита – 68,3, 28,6, 84,8 и 13,3%, 3–5-го типов 65,9, 28,6, 84,4 и 12,5% соответственно. При сопоставлении данных МСКТ и комплексного обследования у всех больных с ДКМП диагностическая значимость всех типов ОНКП в выявлении миокардита составила 70,6, 67,9, 88,9 и 38,8%, 3–5-го типа ОНКП – 60,8, 67,9, 87,3 и 32,3%. При МСКТ в основной группе выявлены также некомпактный миокард ($n=31$, или 23,8%), коронарный атеросклероз ($n=31$, или 23%), который подтвержден данными КГ у 15 пациентов. У больных с ОНКП достоверно чаще определялись связь дебюта с перенесенной инфекцией, острое начало, достоверно более высокие ФК по классификации NYHA, конечный диастолический и конечный систолический объемы ЛЖ, недостоверно более низкая ФВ ЛЖ. Общая летальность при среднем сроке наблюдения 12 (6; 37,25) мес составила 17,7% (умерли 23 больных), показатель смерть + трансплантация – 20% (26 больных). Выявлена достоверная связь всех типов ОНКП с прогнозом: в группе ОНКП летальность составила 21,5% по сравнению с 7,8% в группе без ОНКП (отношение шансов 3,22 при 95% доверительном интервале от 1,02 до 10,21; $p < 0,05$).

Заключение – МСКТ с оценкой отсроченного контрастирования (и одновременной КТ-ангиографией коронарных артерий) может использоваться для неинвазивной диагностики миокардита у пациентов с синдромом ДКМП, в том числе при наличии противопоказаний к проведению МРТ. ОНКП в миокарде коррелирует с наличием миокардита, его активностью, степенью функциональных нарушений и прогнозом.

Ключевые слова: синдром ДКМП, миокардит, МСКТ сердца с внутривенным контрастированием, отсроченное накопление контрастного препарата, хроническая сердечная недостаточность

METABOLIK SINDROMLI BEMORLARDA GASTROEZO-FAGIAL REFLYUKS KASALLIGINING XUSUSIYATLARI

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Annotatsiya.

Kengaygan kardiomyopatiya (DCMP) surunkali yurak etishmovchiligi (CHF) bo'lgan bemorlarda klinisyenlar tomonidan yurakning tipik strukturaviy va funktsional o'zgarishlari (kontraktillikning pasayishi bilan yurak kameralarining kengayishi) asosida o'rnatiladigan eng keng tarqalgan tashxislardan biri bo'lib qolmoqda. bunday holatning tabiati. Ko'pgina holatlarda, tekshiruvning birinchi bosqichida aniqlangan ushbu tashxis faqat "katta yurak" degan ma'noni anglatadi. Shu bilan birga, DKMPNING nozologik tabiati masalasi davolash taktikasini tanlash va bemorda prognozni aniqlashda muhim ahamiyatga ega.

Maqsad – Miokarditni tashxislashda (miokardning morfologik tekshiruvi bilan taqqoslaganda) kengaygan kardiomyopatiya sindromi (DKMP) bo'lgan bemorlarda tomir ichiga kontrastli yurakning multispiral kompyuter tomografiyasi (MSCT) imkoniyatlarini o'rganish, dkmpning yallig'lanishsiz sabablari va prognozni baholash.

Material va usullar – Asosiy guruhga DCMP sindromi bo'lgan 130 bemor (95 erkak, o'rtacha yoshi $46,8 \pm 11,9$ yosh) kirdi: chap qorincha (LV) ning o'rtacha terminal diastolik hajmi (KDR) $6,6 \pm 0,8$ sm, o'rtacha ejeksiyon fraktsiyasi (FV) $29,8 \pm 9,3\%$; III (II; III) funktsional sinf (FC) NYHA tasnifi bo'yicha. Vena ichiga kontrastli 320 qismli yurak MSCT o'tkazildi; 48 bemor miyokardning morfologik tekshiruvini o'tkazdi (29-da endomiyokard biopsiyasi, 7-da intraoperativ biopsiya, 9-da otopsi, 3-da eksplantatsiya qilingan yurak tekshiruvi). Bundan tashqari, qon va miyokarddagi kardiotrop viruslarning DNKsi, antikardial antikorlarning darajasi aniqlandi, ekokardiografiya (barcha bemorlarda), sintigrafiya (45 da), magnit-rezonans tomografiya – MRI (21 da), koronarografiya – kg (46 da), genetika bo'yicha maslahat o'tkazildi. Taqqoslash guruhi 20 bemorni (14 erkak, o'rtacha yoshi $69,3 \pm 9,2$ yosh) koronar ateroskleroz bilan (stenozlar 40% va undan ko'p) MSKT ma'lumotlariga ko'ra, DKMP mezonlari bo'lmagan taqdirda (o'rtacha KDR LV $4,8 \pm 0,5$ sm, o'rtacha FV $59,4 \pm 4,6\%$) tashkil etdi.

Natijalar – Morfologik kompleks tekshiruv ma'lumotlariga ko'ra, miokardit DKMP sindromining sababi sifatida 76 (65%) bemorda tashxis qo'yilgan, uning genetik kardiomyopatiyalar bilan kombinatsiyasi 17 (17%) da tashxis qo'yilgan. Yurak MSCT bilan 2 (1,5%) bemorda (tavsiya etilgan baholash shkalasi bo'yicha 1-toifa), miyokardda kontrastli preparatning (ONKP) kechiktirilgan to'planishi aniqlandi – 81 (62,3%): 8 subendokardial (2-toifa), 4 intramiokardiyak (3-toifa), 52 ta subepikardial (4-tip), 15 ta transmural (5-tip); 49 ta ONKP bilan og'rigan bemorlarda qayd etilmagan. Taqqoslash guruhida ONKP aniqlanmagan. Biopsiya bilan taqqoslaganda, faol miokarditni aniqlashda barcha turdagi ONKP testlarining ijobiy va salbiy natijalarining sezgirliigi, o'ziga xosligi, prognostik qiymati 77,4, 47,1, 72,7 va 53,3% ni tashkil etdi, 3-5 turdagi ONKP-77,4, 52,9, 75 va 56,3%, miokarditning barcha morfologik turlarini aniqlashda – 68,3, 28,6, 84,8 va 13,3%, 3-5 turdagi 65,9, 28,6, 84,4 va 12,5%. MSCT ma'lumotlarini va DKMP bilan kasallangan barcha bemorlarda keng qamrovli tekshiruvni taqqoslashda miyokarditni aniqlashda barcha turdagi ONKPLARNING diagnostik ahamiyati 70,6, 67,9, 88,9 va 38,8%, 3-5 turdagi ONKP-60,8, 67,9, 87,3 va 32,3% ni tashkil etdi. MSCT bilan asosiy guruhda 15 bemorda kg ma'lumotlari bilan tasdiqlangan ixcham bo'lmagan miokard ($n = 31$ yoki 23,8%), koronar ateroskleroz ($n = 31$ yoki 23%) ham

aniqlandi. ONKP bilan og'rigan bemorlarda debyutning o'tgan infeksiya bilan bog'liqligi, o'tkir boshlanishi, NYHA tasnifiga ko'ra ishonchli darajada yuqori FC, cheklangan diastolik va cheklangan sistolik LV hajmlari, ishonchsiz darajada past FV LV aniqlandi. O'rtacha kuzatuv muddati 12 (6; 37,25) oy bo'lgan umumiy o'lim darajasi 17,7% ni tashkil etdi (23 bemor vafot etdi), o'lim + transplantatsiya ko'rsatkichi 20% (26 bemor). Barcha turdagi ONKPLARNING prognoz bilan ishonchli aloqasi aniqlandi: ONKP guruhida o'lim darajasi 21,5% ni tashkil etdi, ONKP bo'lmagan guruhda esa 7,8% (1,02 dan 10,21 gacha bo'lgan 95% ishonch oralig'ida 3,22 koeffitsient nisbati; $p < 0,05$).

Xulosa – Kechiktirilgan kontrastni baholash (va koronar arteriyalarning bir vaqtning o'zida KT angiografiyasi) bilan MSCT DCMP sindromi bo'lgan bemorlarda, shu jumladan MRGGA qarshi ko'rsatmalar mavjud bo'lganda, miyokarditni invaziv bo'lmagan tashxislash uchun ishlatilishi mumkin. Miyokarddagi NKP miyokarditning mavjudligi, uning faolligi, funktsional buzilishlar darajasi va prognozi bilan bog'liq.

Kalit so'zlar: DCMP sindromi, miokardit, IV kontrastli yurak MSCT, kontrastli preparatning kechiktirilgan to'planishi, surunkali yurak etishmovchiligi

Introduction/The relevance of research. Dilated cardiomyopathy (DCMP) remains one of the most common diagnoses in patients with chronic heart failure (CHF), which is established by clinicians on the basis of typical structural and functional changes of the heart (dilation of the chambers of the heart with reduced contractility), regardless of the nature of such a condition. In many cases, this diagnosis, established at the first stage of the examination, means only a "big heart". At the same time, the issue of the nosological nature of DCMP is key in choosing treatment tactics and determining the prognosis of the patient.

In 2011, the concept of "DCMP syndrome" was introduced [1], which was considered as an "entrance diagnosis" (by analogy with acute coronary syndrome, for example), stated the etiological heterogeneity of this condition, the impossibility of making a diagnosis of true DCMP without excluding myocarditis and a number of other etiological factors, and accordingly the need for an in-depth nosological examination. Despite some internal inconsistency, the term itself and the view of DCMP that it reflects have "caught on" and have spread both in the work of cardiologists and in scientific publications.

In 2016, the agreed opinion of a group of leading European experts on the problem of DCMP was published [2]: in this document, the term "DCMP syndrome" is used from the first pages, and the main part of the text is devoted to various aspects of nosological diagnosis. European experts, as well as Russian ones [3], retain the idea of true DCMP as a myocardial disease of unknown (primary, idiopathic) or genetic nature – it is in this understanding that the diagnosis DCMP and can be set as final.

However, in many patients with DCMP syndrome, it is possible to determine its secondary nature – first of all, this concerns chronic, latent myocarditis, the timely detection of which is a cornerstone diagnostic task. To this day, endomyocardial biopsy (EMB) remains the "gold standard" and the only absolute method of diagnosing myocarditis, with which all other methods are compared [4]. According to the most reputable European specialists with experience in conducting EMB in several thousand patients, the frequency of detection of myocarditis in the syndrome DCMP reaches 83%, including in 59% of patients it is viral-negative myocarditis, which is subject to immunosuppressive treatment [5]. The idea that genetic defects and myocarditis are often combined in one patient is becoming increasingly recognized, as has been repeatedly reported in domestic works [1, 6, 7].

Unfortunately, the possibilities of EMB are limited in patients with DCMP syndrome, which makes it especially important to search for the most informative noninvasive techniques and criteria for the diagnosis of latent myocarditis. Magnetic resonance imaging (MRI) of the heart with contrast is recognized as one of these methods. The phenomenon of "delayed contrast" of the myocardium is used to diagnose infectious and inflammatory diseases of the myocardium, cardiomyopathies (CMP), and genetic diseases [8]. However, in comparison with myocardial biopsy, the possibilities of MRI are not absolute: if in acute, infarct-like myocarditis, the sensitivity of MRI is 80%, then in "cardiomyopathic" and arrhythmic variants of myocarditis - only 47 and 57%, respec-

tively [9]. Similar data have been obtained recently by domestic authors [10]. In addition, patients with DCMP often have contraindications to MRI: implanted devices (37% according to the European registry [11], 34% according to Russian data [12]) or indications for their implantation (inability to control dynamics), difficulty of prolonged lying down, claustrophobia, etc.

In this situation, it certainly seemed promising to study the diagnostic and prognostic capabilities of multispiral computed tomography (MSCT) of the heart with contrast, which can not only be used in the presence of implanted devices, but at the same time allows you to assess the condition of the coronary arteries (CA), which is necessary for all patients with DCMP syndrome. Until recently, the possibilities of MSCT in assessing the condition of the myocardium, especially in non-coronary diseases, have not been practically studied. There are several studies on the phenomenon of "delayed contrast" of the myocardium in cardiac MSCT with intravenous contrast to diagnose myocardial viability in patients with coronary heart disease (CHD) [13], as well as myocardial fibrosis in patients with various heart diseases in comparison with MRI data [14], which have shown good diagnostic capabilities of this method. However, studies of the possibilities of MSCT with intravenous contrast in the diagnosis of myocarditis, especially in comparison with myocardial biopsy, have never been conducted, which makes this work highly relevant. In the pilot work [15], the MSCT data were compared for the first time with the results of EMB in patients with DCMP and myocarditis: the undoubted diagnostic capabilities and advantages of the method were established, which made it possible to conduct this study in full. Objective: to study the possibilities of cardiac MSCT with intravenous contrast in patients with the syndrome DCMP in the diagnosis of myocarditis (in comparison with morphological examination of the myocardium), non-inflammatory causes of DCMP and prognosis assessment.

Research materials and methods. Patients included in the study. The main group included 130 patients from 20 to 77 years old (95 men and 35 women, average age 46.8 ± 11.9 years), with DCMP syndrome.

Inclusion criteria: age over 18 years, the final diastolic size (CDR) of the left ventricle (LV) is more than 5.5 cm, the ejection fraction (LV) is less than 45%, the written consent of the patient. The exclusion criterion was the patient's refusal to participate. Criteria for refusal of inclusion: LV CDR of 5.5 cm or less, LVEF of 45% or more, contraindications to the procedure MSCT (iodine allergy, glomerular filtration rate less than 40 ml/min), myocardial infarction (MI)/acute coronary syndrome less than 6 months old, rheumatic and congenital heart defects (with the exception of DMPP without hemodynamically significant relief), infectious endocarditis, hypertrophic CMR, thyrotoxic, hypertensive heart, diffuse connective tissue diseases, verified systemic vasculitis, lymphoproliferative diseases, heart surgery less than 2 months old, pregnancy.

All patients had CHF, the average functional class (FC) according to the NYHA classification was III (II; III). Most patients have dilated all chambers of the heart. The average echocardiographic parameters in the main group were: LV CDR 6.6 ± 0.8 cm, LV final diastolic volume (CDR) 186 (146; 235) ml, LV final systolic volume (CSR) 128 (92; 173) ml, LV LV $29.8 \pm 9.3\%$, left atrium volume (LP) 110.9 ± 41.5 ml, right atrium volume (PP) 88.8 ± 40.8 ml, the size of the right ventricle (RV) 3.1 ± 0.7 cm, systolic pressure in the pulmonary artery (SDLA) 41.6 ± 13.2 mmHg. Various devices (stimulants, defibrillators, etc.) were implanted initially or during follow-up in 44 (34%) patients.

The comparison group included 20 patients aged 45 to 84 years (14 men and 6 women, average age 69.3 ± 9.2 years), with presumably non-inflammatory, coronary myocardial lesion. Inclusion criteria: age over 18 years, presence of coronary atherosclerosis (stenosis of 40% or more according to MSCT), regardless of the presence of ischemia, absence of criteria DCMP (LV CDR < 5.5 cm, LVEF $> 45\%$), the presence of written consent of the patient. Criteria for re-

fusing to be included in the comparison group: LV CDR >5.5 cm, LVEF <45%, contraindications to MSCT, congenital and rheumatic heart defects, infectious endocarditis, thyrotoxic/hypertensive heart, hypertrophic CMR, diffuse connective tissue diseases, verified systemic vasculitis, lymphoproliferative diseases, heart surgery less than 2 months old, pregnancy. The patient's refusal to participate in the study served as an exclusion criterion. 55% of patients in the comparison group had CHF, on average II FC according to the NYHA classification. The main echocardiographic parameters were within the normal range (mean LV CDR 4.8 ± 0.5 cm, LV CDR 105.0 ± 29.4 ml, LV CSR 41.4 ± 11.2 ml, volume PP 58.5 ± 22.1 ml, pancreatic size 2.6 ± 0.5 cm, PV $59.4 \pm 4.6\%$, SDLA 30.7 ± 7.9 mmHg, only the average volume of LP slightly exceeded the norm (75.0 ± 19.7 ml). The pacemaker was previously implanted in 5 (25%) patients.

Laboratory and instrumental examination of patients in the main group included the determination of DNA of cardiotropic viruses (herpes viruses types 1, 2 and 6, zoster, Epstein-Barr, cytomegalovirus, parvovirus B19, entero/adenoviruses) in the blood and myocardium by polymerase chain reaction, the level of anticardial antibodies in the blood, echocardiography - Echocardiography (for all patients), myocardial scintigraphy (in 45), MRI of the heart (in 21), coronary angiography - KG (in 46), consultation of a geneticist (prof. E.V. Zaklyazminskaya, RNC im. Academician B.V. Petrovsky of the Russian Academy of Medical Sciences) and DNA diagnostics by sequencing Sanger (at 26).

In addition, 48 patients underwent morphological examination of the myocardium (EMB in 29, intraoperative in 7, autopsy in 9, examination of the explanted heart in 3). EMB was performed using the standard method of access through the femoral vein with Cordis Standard 5.5 F 104 Femoral biopsy forceps with sampling from 3-5 sites. Fragments of LV myocardium were taken intraoperatively (during reverse remodeling) (papillary muscle) and LP. They were stained with hematoxylin and eosin, according to Van Gieson, according

to additional indications - RAS reaction, Perls reaction and congo red staining. Myocarditis was diagnosed according to the Dallas criteria.

All patients underwent cardiac MSCT with intravenous contrast on a Toshiba Aquilion ONE device (Toshiba, Japan) with a detector width of 16 cm (320 rows), a tube rotation time of 350 ms. The study was performed in the native phase (to calculate coronary calcium and accurately determine the scanning area) and against the background of the administration of a contrast agent. Contrast agent (iodine content 350-370 mg / ml) in an amount of 60-90 ml (depending on the patient's body weight) was injected using an automatic injector into the ulnar vein, then 30 ml of isotonic sodium chloride solution was additionally injected to reduce artifacts from the contrast agent in the right parts of the heart. Tomography was performed with the following parameters: pitch 0, without moving the table, 120 KV, 150-300 mAs, scanning area along the Z axis 10-16 cm. The delayed phase to assess the accumulation of contrast agent by the myocardium was determined 10 minutes after the arterial phase. Post-treatment included the calculation of coronary calcium, the construction of multiplanar and three-dimensional images, and a qualitative assessment of delayed accumulation of contrast agent (ONCP). The dose of X-ray irradiation did not exceed 10 mSv.

The average follow-up period was 12 (6; 37,25) months. The main evaluation criterion is mortality during the follow-up period, the combined criterion is the number of deaths and heart transplantation (TC).

The study was approved by the local Ethics Committee of the I.M. Sechenov First Moscow State Medical University (Protocol No. 05-15 dated 05/20/2015). Statistical processing of the obtained data was performed using the SPSS 21 program. The normality of the distribution was checked using the Kolmogorov-Smirnov criterion. Quantitative features with a normal distribution are presented as $M \pm SD$ (mean \pm standard deviation), otherwise as a median (Me) indicating the 1st and 3rd quartiles (Q1; Q3). The differences were con-

sidered statistically significant at $p < 0.05$. To assess the diagnostic and prognostic significance of various signs, ROC analysis, construction of Kaplan-Meier survival curves, and logistic regression analysis were used. The risk of developing different outcomes was assessed by calculating the ratio of odds and relative risk.

The results and their discussion. The results of cardiac MSCT with intravenous contrast in patients with DCMP syndrome. In MSCT with intravenous contrast in patients with the syndrome DCMP revealed 4 groups of changes that were important in nosological diagnosis and treatment choice:

1st - signs of atherosclerosis of CA - stenosis more 40% were detected in 31 patients of the main group; their presence was confirmed by the data of KG in 15 patients; 10 patients did not undergo KG, in 5 the degree of coronary atherosclerosis in KG was less pronounced than according to the data MSCT; detection of coronary atherosclerosis as such did not serve as a criterion for exclusion from the study, since its degree correlated with the severity of functional disorders; in some cases, a combination of possible or reliable ischemic heart disease with myocarditis and other causes of DCMP was proven;

2nd - changes in the structure of the myocardium – LV non-compact myocardium syndrome was diagnosed according to generally accepted visual criteria in 31 (23.8%) patients with DCMP syndrome, and in 16 of them a reliable diagnosis was established using MSCT for the first time; in all 6 patients who underwent MRI, the presence of non-compact myocardium was confirmed;

3rd - signs of intracardiac thrombosis were detected in 14 (10.8%) patients, including thrombosis of the LP auricle in 7 patients, parietal LV thrombosis in 9, thrombosis of the PP cavity in 2; the detection of a thrombus in the LP auricle in 4 patients and in PP in one became a diagnostic finding, since transesophageal echocardiography (PE-echocardiography) was not performed by them; in 3 more patients it was possible to detect a blood clot in the LV,

which was not detected by echocardiography; In one case MSCT resolved the doubts that arose after echocardiography, excluding the presence of LP thrombosis, in 3 more patients MSCT was performed against the background of anticoagulant therapy for thrombosis previously detected in emergency echocardiography LP and confirmed thrombus lysis; thrombosis was never "missed" during MSCT;

4th - the presence of ONCP sites was noted in 79 (60.8%) patients, 2 of them had a combination of signs of postinfarction cardiosclerosis (PIC) with chronic myocardial inflammation, in one case confirmed with EMB, 64 patients with intact CA, 13 with CA stenosis >40%. For the convenience of further quantitative analysis, we have developed a scale for evaluating various types of delayed contrast depending on the localization:

Type 1 - reduced accumulation of contrast agent,

Type 2 is subendocardial delayed contrast, type 3 is intramiocardial, type 4 is subepicardial and type 5 is transmural delayed contrast. Most often in patients with DCMP revealed subepicardial (40%) and transmural (11.5%) delayed contrast, which in MRI are considered specific for non-coronary (inflammatory) myocardial damage.

At the same time, the "ischemic" type of accumulation (subendocardial) was detected in 8 patients, of whom only 2 had CA stenosis (in the absence of data confirming IT); 2 more of these patients had non-compact myocardium, which suggests blood supply disorders directly under the non-compact layer. Reduced accumulation of contrast agent in combination with thinning of the LV wall in 2 patients could be interpreted as cicatricial myocardial lesion, however, in one of them the SC was not changed, no focal lesion was detected during scintigraphy, and in the second (a 44-year-old woman) there was 50% stenosis of the anterior interventricular artery in combination with moderate hyperhomocysteinemia, which does not allow exclude the true IM.

In 21 patients, data on various types of cancer were compared with MSCT and MRI of the heart. It should be noted that MRI of the heart was performed in various laboratories and the results of the study were analyzed by different specialists. The presence or absence of ONCP when comparing MRI and MSCT data coincided in 11 patients from 21 main groups: in 3 cases, the absence of ONCP in both studies, in 8 different types of ONCP according to our proposed scale.

The results of cardiac MSCT with intravenous contrast in the comparison group. In the comparison group when MSCT diagnosed a different degree of coronary atherosclerosis (>40% according to the inclusion criteria), confirmed by ECG data in 6 patients; in one patient, the degree of coronary atherosclerosis in KG was less pronounced, which may be associated with severe calcification of the CA. There was no delayed contrast in the comparison group. One patient without signs of DCMP syndrome had a non-compact LV myocardium.

Thus, the absence of the phenomenon of delayed myocardial contrast in patients with and without coronary atherosclerosis in the anamnesis allowed us to regard this phenomenon as specific for inflammatory/ fibrous myocardial damage. Further verification this hypothesis was carried out when comparing the results MSCT with data from morphological examination of the myocardium in patients with DCMP syndrome.

The results of nosological diagnosis according to the morphological examination of the myocardium. According to morphological examination data, myocarditis was diagnosed in 48 patients with DCMP syndrome in 34, its combination with genetic CMPS in 8 more, in 3 the picture of isolated primary DCMP was revealed and in 3 more – postmyocarditis cardiosclerosis – PMCS. The viral genome in the myocardium was found in 50% of patients, with parvovirus B19 prevailed (68%); in addition, Epstein-Barr virus, cytomegalovirus, herpes simplex viruses of types 1, 2 and 6 were detected. There was a pro-

nounced correlation between the viral genome and morphological signs of myocarditis.

Patients with a morphologically verified diagnosis of myocarditis had varying degrees of its histological activity - from an active process with necrosis of cardiomyocytes, their edema and pronounced dystrophic changes in combination with bright lymphocytic infiltration and vasculitis to a predominance PMCS (perimuscular, perivascular) with moderate cellular infiltration. In some cases, PMCS was diagnosed, which testified in favor of the inflammatory nature of the DCMP syndrome: such patients were allocated to a special subgroup, but when analyzing the MSCT data, they were considered as patients with myocarditis. The results of complex nosological diagnosis in patients with DCMP syndrome. Morphological examination of the myocardium was performed in 37% of the patients included in the study, in other cases, differential diagnosis of the causes of DKMP syndrome was carried out using an algorithm developed by us earlier based on the results of a comprehensive examination (anamnesis data, the presence of systemic immune manifestations, viral genome in the blood, titers of anticardial antibodies, etc. [16] The results of complex nosological diagnosis in patients with DCMP syndrome. Morphological examination of the myocardium was performed in 37% of the patients included in the study, in other cases, differential diagnosis of the causes of DKMP syndrome was carried out using an algorithm developed by us earlier based on the results of a comprehensive examination (anamnesis data, the presence of systemic immune manifestations, viral genome in the blood, titers of anticardial antibodies, etc. According to a comprehensive examination, myocarditis as the cause of DCMP syndrome was diagnosed in 82 patients out of 130 in the main group, its combination with genetic CMPs in 22, isolated primary DKMP U 17, toxic (alcoholic) KMP U 4, PMKS in 3 patients; in addition, in 2 patients, despite the lack of initial data, PIC was diagnosed.

Among the genetically determined forms of DCMP syndrome (both isolated and in combination with myocarditis), LV non-compact myocardial syndrome prevailed (in 31); in addition, arrhythmogenic pancreatic dysplasia (in 3), Emery-Dreyfus myodystrophy (in 1) and unspecified systemic myopathies (in 2) were diagnosed. Pathogenic mutations in the genes of myosin-binding protein C Type 3, laminin, dystrobrevin, desmoplakin were detected in 5 patients, and diagnosis continues.

The diagnostic significance of cardiac MSCT in the detection of myocarditis (in comparison with the morphological examination of the myocardium and the data of a comprehensive examination). When comparing the results directly MSCT with data from a morphological study of the myocardium correlated the phenomenon of delayed myocardial contrast with the presence, first of all, of signs of active myocarditis: when using ROC analysis, the AUC for all types of delayed contrast was 0.622, for intramiocardial, subepicardial and transmural (i.e., 3rd-5th) types - 0.652.

At the same time, the diagnostic significance of the role MSCT in detecting any morphological type of myocarditis (not only active) is slightly lower, which seems quite natural - sensitivity, specificity, PCR and PORT of all types of delayed contrast were 68.3, 28.6, 84.8 and 13.3%, respectively, and type 3-5 - 65.9, 28.6, 84.4 and 12.5%, respectively.

The correlation of cancer with the presence and severity of interstitial changes (edema, small- and large-focal sclerosis, and their combination) was also evaluated: ROC analysis revealed a close relationship (AUC 0.674), which confirms the dual nature of the phenomenon of delayed contrast (not only active inflammation, but also fibrosis). There was no direct connection between delayed contrast and the presence of the viral genome in the myocardium.

When comparing the MSCT data with the results of complex nosological diagnostics in patients of the main group (with DCMP syndrome), a correlation was noted with the presence of myocarditis (isolated or in combination with

genetically determined CMPs) of both all 5 types of delayed myocardial contrast (AUC 0.668; $p < 0.05$) and 3-5 types - intramyocardial, subepicardial and transmural (AUC 0.643; $p < 0.01$). Thus, the most significant in the diagnosis of myocarditis, regardless of the degree of its activity, were precisely those types of delayed contrast that are considered specific for inflammation in MRI.

Conclusion. For the first time, the high diagnostic and prognostic significance of cardiac MSCT with intravenous contrast has been studied and proven in patients with the syndrome DCMP in comparison with the results of morphological examination of the myocardium. In MSCT with intravenous contrast NCP in various layers of the myocardium was detected in 62.3% of patients with DCMP syndrome, while in the comparison group (in patients with coronary atherosclerosis without signs of DCMP), ONCP was not detected. The predominant type of cancer was subepicardial accumulation in various LV walls (type 4 according to the scale we proposed; 64.2% of accumulation cases); areas of reduced accumulation (type 1; 2.5%), subendocardial (type 2; 9.9%), intramiocardial (type 3; 4.9%) and transmural accumulation (type 5; 18.5%).

Myocarditis as the cause of DCMP syndrome was diagnosed according to the results of morphological examination of the myocardium in 70.8%, according to the results of a comprehensive examination - in 66.2% of cases; its combination with various genetic CMPs - in 16.7 and 16.8%. The viral genome (mainly parvovirus B19) in the myocardium is marked in 50%. The detection rate of non-compact myocardial syndrome in MSCT in patients with DCMP syndrome was 23.8%, CA stenosis - more than 40% in combination with myocarditis - 23.8%.

MSCT with ONCP assessment has high diagnostic significance in the verification of myocarditis as a cause of DCMP syndrome: sensitivity, specificity, PCRT and PCORT of all types (from 2nd to 5th) Oncological differences in the detection of morphologically active myocarditis were 77.4, 47.1, 72.7 and

53.3%, type 3-5 (intramyocardial, subepicardial and transmural) - 77.4, 52.9, 75 and 56.3%. The ONC phenomenon reflects the presence of inflammation, edema and fibrosis in interstitial tissue. When compared with the data of a comprehensive examination, the prognostic significance of type 2-5 ONC in the diagnosis of myocarditis was 70.6, 67.9, 88.9 and 38.8%, type 3-5 - 60.8, 67.9, 87.3 and 32.3%, differing primarily from PCRT.

The total mortality rate was 17.7% (23 patients died) with an average follow-up period of 12 (6; 37.25) months, the combined assessment criterion (death + TC) was 20%. The presence of all types of delayed contrast when MSCT was accompanied by significantly higher mortality compared with type 0-1 contrast: 21.5 and 7.8%, respectively; $p < 0.05$ (OR 3.22 at 95% CI from 1.02 to 10.21; $p < 0.05$), however, this effect is associated with higher CHF FC and lower LV. Significant correlations of the type of delayed contrast with anamnestic, morphological and functional signs were also noted. MSCT with assessment of delayed myocardial contrast (and simultaneous CT angiography) can be used for noninvasive differential diagnosis of the causes of DCMP syndrome (myocarditis, coronary atherosclerosis with scarring of the myocardium, LV non-compact myocardium syndrome), including in the presence of contraindications to MRI, and to determine its prognosis.

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