Article

Dilatatsion kardiomiopatiya bilan og‘rigan bemorlarda kasallik kechishining og‘irlik darajasi va tizimli yallig‘lanish o‘rtasidagi bog‘liqlik

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Annotatsiya:
Maqsad. Dilatatsion kardiomiopatiya bilan og‘rigan bemorlarda klinik-gemodinamik ko‘rsatkichlar va yallig‘lanish markerlari (C-reaktiv oqsil, IL-6, O‘NO-α) o‘rtasidagi bog‘liqlikni o‘rganish.
Materiallar va usullar. Tadqiqotga dilatatsion kardiomiopatiya bilan og‘rigan hamda SYuYe NYHA bo‘yicha II-IV FS bilan asoratlangan 42 nafar (38,5±1,2 yil) bemor kiritildi. Bemorlar ikki guruhga ajratildi: I guruh – FS II (n=12) va II guruh – FS III-IV (n=30).
Natijalar. SYuYe og‘irlik darajasi ortishi bilan (FS III-IV) bemorlar qon zardobida C-reaktiv oqsil (7,6±1,1 mg/l va 4,1±0,6 mg/l, p<0,05), IL-6 (7,5±0,8 pg/ml va 4,6±0,2 pg/ml, p<0,01) va O‘NO-α (8,1±0,9 pg/ml va 5,6±0,7 pg/ml, p<0,05) miqdori oshgan, bu esa chap qorincha dilatatsiyasi (YaSO‘ 58±1 , p<0,05) va otish fraktsiyasining pasayishi (34,7±1,8%, p<0,05) bilan bog‘liq bo‘lgan.
Xulosa. Yallig‘lanish markerlari DKMP og‘irligi va prognozini baholashda muhim diagnostik ahamiyatga ega.

Kalit so’zlar: Dilatatsion katdiomiopatiya, surunkali yurak yetishmovchiligi, yallig‘lanish, C-reaktiv oqsil, interleykin-6, o‘sma nekrozi omili-α, kolxitsin.

Association between disease severity and systemic inflammation in patients with dilated cardiomyopathy

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Abstract:
Aim. The aim of this study was to investigate the relationship between clinical-hemodynamic parameters and inflammatory markers (C-reactive protein, interleukin-6, tumor necrosis factor-α) in patients with dilated cardiomyopathy.
Materials and methods. The study included 42 patients (mean age 38.5±1.2 years) with dilated cardiomyopathy and chronic heart failure classified as NYHA functional class II–IV. The patients were divided into two groups: Group I – class II (n=12) and Group II – class III–IV (n=30).
Results. As heart failure severity increased (class III–IV), serum levels of C-reactive protein (7.6±1.1 mg/L vs. 4.1±0.6 mg/L, p<0.05), IL-6 (7.5±0.8 pg/mL vs. 4.6±0.2 pg/mL, p<0.01), and TNF-α (8.1±0.9 pg/mL vs. 5.6±0.7 pg/mL, p<0.05) were significantly elevated. These changes were associated with left ventricular dilatation (LVEDD 58±1 mm, p<0.05) and reduced ejection fraction (34.7±1.8%, p<0.05).

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Conclusion. The findings suggest that inflammatory markers play a crucial role in assessing the severity and prognosis of dilated cardiomyopathy and chronic heart failure.

Keywords: Dilated cardiomyopathy, chronic heart failure, inflammation, C-reactive protein, interleukin-6, tumor necrosis factor-α, colchicine.

Kirish

2023-yilda Yevropa Kardiologiya Jamiyati (ESC) tomonidan ishlab chiqilgan kardiomiopatiyalarni davolash bo‘yicha yangi klinik tavsiyalar so‘nggi 15 yil mobaynida tibbiyotning turli sohalari hamkorligida olib borilgan jadal ilmiy faoliyat natijasida yaratilgan bo‘lib, kardiologik jamiyatning klinik amaliyotiga joriy qilinmoqda [1]. Ushbu xujjat ESC tomonidan kardiomiopatiyalarni tasniflashning yangi bayonotini e’lon qilish bilan boshlangan bo‘lib, unga shuningdek genetik maslahat va genetik testlash, kardiomiopatiyalarni aniqlash bo‘yicha klinik-diagnostik yondashuvlar, gipertrofik kardiomiopatiya bo‘yicha klinik tavsiyalar, gipokinetik nodilatatsion kardiomiopatiya bo‘yicha takliflar, yurak amiloidozi bo‘yicha bayonot hamda genetik variantlarni interpretatsiya qilish va ularni klinik amaliyotda qo‘llash imkoniyatlarini qamrab olgan muhim hujjatlar hamrohlik qildi [2,8]. Ishlab chiqilgan yangi tasnifga ko‘ra kardiomiopatiyalar 5 ta fenotipga ajratilgan — gipertrofik kardiomiopatiya (GKMP), dilatatsion kardiomiopatiya (DKMP), restriktiv kardiomiopatiya (RKMP), aritmogen o‘ng qorincha kardiomiopatiyasi (AO‘QKMP) va chap qorinchaning nodilatatsion kardiomiopatiyasi (ChQNDKMP).

Kardiomiopatiya fenotiplari orasida dilatatsion kardiomiopatiya chap qorincha otish fraksiyasi pasaygan yurak yetishmovchiligi (ChQOFpasayganYuYe) rivojlanishiga olib keluvchi eng keng tarqalgan sabablaridan biri sifatida tan olingan bo‘lib, butun dunyoda yurak transplantatsiyasi bajarilishiga asosiy ko‘rsatma hisoblanadi [9]. Dilatatsion kardiomiopatiya — asosan chap qorinchaning (ChQ) dilatatsiyasi hamda uning global yoki regional sistolik disfunktsiyaning mavjudligi bilan tavsiflanib, ushbu holatni faqatgina yuklama sharoitlarining buzilishi (masalan, gipertoniya, yurak qopqoqlari kasalliklari, tug‘ma yurak nuqsonlari) yoki yurak ishemik kasalligi bilan izohlab bo‘lmaydi [10]. So‘ngi ma’lumotlarga ko‘ra DKMP ning tarqalish darajasi har 100 000 aholiga 36 holatni tashkil etadi, yillik kasallanish esa har 100 000 aholiga 7 ta holat deb baholanadi [9,11]. Kasallik prognozi uning kelib chiqish sababi, klinik bosqichi va qo‘llanilgan davolash choralarining samaradorligiga bog‘liq holda jiddiy farq qiladi. Standart terapiya sharoitida 5 yillik yashab qolish ko‘rsatkichi taxminan 50–60% atrofida bo‘lsa-da, refrakter yurak yetishmovchiligi yoki qorinchalar aritmiyasi mavjud bemorlarda o‘lim xavfi ortadi [12].

Surunkali yurak yetishmovchiligini (SYuYe) davolashning zamonaviy strategiyalari medikamentoz terapiya, elektr qurilmalar (CRT-D, implantatsiya qilinadigan kardioverter-defibrillyator) va ChQ yordamchi qurilmalarini o‘rnatish yoki yurak transplantatsiyani o‘z ichiga oladi [13]. Hozirgi kunda surunkali yurak yetishmovchiligiga olib kelgan etiologik omillardan qat’iy nazar ChQ OF pasaygan YuYe ni medikomentoz davolashda to‘rt komponentli standart terapiya qo‘llanilmoqda. Bular angiotenzin-aylantiruvchi fermenti ingibitorlari (iAAF)/angiotenzin retseptor va neprilizin ingibitorlari (ARNI), beta-blokatorlar (BB), mineralokortikoid retseptorlari antagonistlari (MRA), 2-tip natriy-glyukoza kotransporteri ingibitorlari (iSGLT-2), shuningdek shish sindromi bo‘lganda qovuzloq diuretiklaridir [13]. Biroq optimal medikamentoz terapiya qo‘llanilishiga qaramasdan DKMP bilan og‘rigan bemorlarning hayot prognozi xali ham noxushligicha saqlanib qolmoqda, bu esa kasallik patogenezini yanada chuqurroq o‘rganishni hamda yangi davolash usullarini ishlab chiqishni talab etadi.

So‘nggi yillarda SYuYe rivojlanishining yangi kontseptsiyasi taklif etilgan bo‘lib, unga ko‘ra tizimli yallig‘lanish yurak yetishmovchiligining noxush kechishi va yuqori yurak-qon tomir xavfining prediktori sifatida qaralmoqda [14]. SYuYe natijasida yuzaga keladigan mikrotsirkulyatsiyadagi jiddiy buzilishlar to‘qimalardagi makrofaglar va monotsitlarning nospetsifik faollashuviga, ular esa o‘z navbatida yallig‘lanisholdi sitokinlari — o‘sma nekrozi omili-alfa (O‘NO-α), interleykin-1 (IL-1), interleykin-6 (IL-6) va boshqalar sintezinining kuchayishiga olib keladi. Ushbu sitokinlar ChQ disfunktsiyasining rivojlanishiga ta’sir etuvchi muhim patogenetik mexanizmlardan biri sifatida qaralmoqda [15].

Maqsad

Dilatatsion kardiomiopatiya bilan og‘rigan bemorlarda klinik-gemodinamik ko‘rsatkichlar va qon zardobidagi yallig‘lanish markyori – C-reaktiv oqsil (CRO) va yallig‘lanisholdi sitokinlari (IL-6, O‘NO-α) miqdori o‘rtasidagi bog‘liqlikni o‘rganish.

Materiallar va usullar

Tadqiqot Xelsinki deklaratsiyasi tamoyillariga muvofiq ravishda amalga oshirildi. Protokol RIKIATM huzuridagi Etik qo‘mita tomonidan ma’qullandi. Tadqiqotga jalb etilishidan oldin barcha ishtirokchilardan yozma ravishda rozilik olindi. Tadqiqotga RIKIATM 7-Miokardning nokoronarogen kasalliklari va pulmonologiya bo‘limidagi DKMP tashxisi qo‘yilgan hamda SYuYe NYHA bo‘yicha II-IV FS bilan asoratlangan 42 nafar (25 erkak va 17 ayol) 18 yoshdan 57 yoshgacha bo‘lgan (o‘rtacha yosh 38,5 ± 1,2 yil) bemorlar olindi. Kardiomiopatiyalarni davolash bo‘yicha ESC 2023 tavsiyalariga muvofiq bemorlarga DKMP tashxisi qo‘yildi. Barcha bemorlardan anamnestik ma’lumotlar yig’ildi, KHBSh shkalasi yordamida klinik holat baholandi, 6 daqiqalik yurish testi (6DYuT) o‘tkazildi va uning asosida NYHA tasnifiga ko‘ra yurak yetishmovchiligi funktsional sinfi aniqlandi. Barcha bemorlar SYuYe funktsional sinfiga ko‘ra ikki guruhga bo‘lindi: I guruh – FS II bo‘lgan bemorlar (n=12); II guruh – FS III- IV bo‘lgan bemorlar (n=30). Shuningdek, barcha bemorlarda umumklinik tekshiruvlar: standart 12 tarmoqli EKG tekshiruvi, transtorakal ExoKG tekshiruvi bajarildi. Bundan tashqari barcha bemorlar qon zardobida yallig‘lanish markyori (CRO) va yallig‘lanisholdi sitokinlari (IL-6, O‘NO-α) miqdori aniqlandi. Tadqiqotga infektsion, allergik, onkologik va immun tizim kasalliklari, shuningdek, o‘pkalar surunkali obstruktiv kasalligi bilan og‘rigan bemorlar qo‘shilmadi, negaki ushbu kasalliklarda yallig‘lanish markyorlari va sitokinlar miqdori yuqori bo‘ladi.

Olingan ma’lumotlarning statistik tahlili MedCalc dasturiy ta’minoti yordamida amalga oshirildi. Aniqlangan ko‘rsatkichlar orasida arifmetik o‘rtacha qiymat (M), standart og’ish (SD) va arifmetik o‘rtacha qiymatning standart xatosi (m) hisoblab chiqildi. Ahamiyatli farqlar Styudentning t-kriteriysi asosida aniqlandi. p0,05 bo‘lgan holatlar statistik jihatdan ishonchli deb hisoblandi. Ma’lumotlar M±m ko‘rinishida keltirildi.

Natijalar

Ikkala guruhdagi bemorlarning boshlang‘ich klinik va demografik ko‘rsatkichlari taqqoslanganda ular o‘rtasida ishinochli farqlar aniqlanmadi. I va II guruhdagi bemorlarning KHBSh shkalasi bo‘yicha to‘plangan ballar yig’indisi mos ravishda 7,3±0,7 ball va 8,9±0,3 ballni tashkil etdi. Shuningdek, 6DYuT davomida bosib o‘tilgan masofa I va II guruhlarda mos ravishda 350,4±19,7 metr va 248,8±13,2 metrni tashkil etdi (Jadval 1).

Table 1. Initial clinical and demographic parameters (M±m) in patients with DCM according to the severity of HF

Jadval 1. DKMP bilan og‘rigan bemorlarda SYuYe og‘irlik darajasiga ko‘ra boshlang‘ich klinik va demografik ko‘rsatkichlar (M±m)

Ko‘rsatkich	I guruh FS II (n=12)	II guruh FS III-IV (n=30)	p
Yosh, yil	41,4±2,6	41,5±2,1	p>0,05
Kasallikning davomiyligi, oy	9,4±3,8	8,7±1,6	p>0,05
YuQS, daqiqa	87,2±3,3	93,7±2,7	p>0,05
YuQS, daqiqa	87,2±3,3	93,7±2,7	p>0,05
SAB, mm.sim.ust.	110,8±4,3	108,4±2,9	p>0,05
DAB, mm.sim.ust.	72,5±3,3	69,2±1,9	p>0,05

Izoh: n – bemorlar soni; p - I guruhga nisbatan ishochlilk darajasi; KHBSh – klinik holatni baholash shkalasi; 6DYuT – 6 daqiqalik yurish testi; YuQS – yurak qisqarishlari soni; SAB – sistolik arterial bosim; DAB – diastolik arterial bosim.

Ikkala guruhdagi bemorlarning ExoKG tekshiruv natijalari taqqoslanganda quyidagilar aniqlandi (Jadval 2). II guruhdagi bemorlarning (FS III-IV) ExoKG ko‘rsatkichlari I guruhdagi bemorlarniki (FS II) bilan taqqoslanganda deyarli barcha ko‘rsatkichlarda yaqqol salbiy o‘zgarishlar aniqlandi, biroq faqatgina YaSO‘, YaSH, OF va ChB o‘lchami ko‘rsatkichlari orasidagi farq ishonchli deb baholandi (p0,05). Jumladan, YaSO‘ ko‘rsatkichlari I va II guruhlarda mos ravishda 52±2 mm

va 58±1 mm ni tashkil etdi; YaSH ko‘rsatkichlari I va II guruhlarda mos ravishda 134,5±13,4 ml va 170,1±10,7 ml ni tashkil etdi; ChQ OF ko‘rsatkichlari I va II guruhlarda mos ravishda 43,1±3,5 % va 34,7±1,8 % ni tashkil etdi; ChB o‘lchami ko‘rsatkichlari I va II guruhlarda mos ravishda 41±2 mm va 54±5 mm ni tashkil etdi. Qolgan ko‘rsatkichlar o‘rtasida ishonchli farqlar aniqlanmadi.

Table 2. Cardiac hemodynamic parameters (M±m) in patients with DCM according to the severity of HF
Jadval 2. DKMP bilan og‘rigan bemorlarda SYuYe og‘irlik darajasiga yurakichi gemodinamikasi ko‘rsatkichlari (M±m)

Ko‘rsatkich	I guruh FS II (n=12)	II guruh FS III-IV (n=30)	p
QAT, mm	9,7±0,5	8,9±0,3	p>0,05
ChQOD, mm	9,8±0,5	9,5±0,3	p>0,05
YaDO‘,mm	67±2	70±1	p>0,05
YaSO‘,mm	52±2	58±1*	p<0,05
YaDH, ml	236,1±15,9	261,8±14,9	p>0,05
YaSH, ml	134,5±13,4	170,1±10,7*	p<0,05
OF, %	43,1±3,5	34,7±1,8*	p<0,05
ChB, mm	41±2	54±5*	p<0,05
O‘Q, mm	28±3	35±3	p>0,05

Izoh: n – bemorlar soni; p - I guruhga nisbatan ishochlilk darajasi; YaDO‘ – yakuniy diastolik o‘lcham; YaSO‘ – yakuniy sistolik o‘lcham; YaDH – yakuniy diastolik hajm; YaSH – yakuniy sistolik hajm; OF – otish fraktsiyasi; ChB – chap bo‘lmacha; O‘Q – o‘ng qorincha; QAT – qorinchalar aro to‘siq; ChQOD – chap qorincha orqa devori.

Biz shuningdek bemorlar qon zardobidagi yallig‘lanisholdi sitokinlari (IL-6, O‘NO-α,) va CRO miqdorini tekshirdik va ikkala guruh o‘rtasida taqqoslama tahlil o‘tkazildi. Bemorlarda yurak yetishmovchiligining og‘irlik darajasi ortib borishi bilan yallig‘lanish markyori va sitokinlar miqdori ham ishonchli darajada ko‘tarilib borganligi aniqlandi. Xususan, I guruhdagi bemorlarda (FS II) CRO miqdori 4,1±0,6 mg/l ni tashkil etgan bo‘lsa, II (FS III-IV) guruhdagi bemorlar qon zardobidagi CRO miqdori 7,6±1,1 mg/l ni tashkil etdi hamda ushbu ko‘rsatkich II guruh bemorlarida I guruhdagi bemorlarnikiga nisbatan 85,4% ga yuqori bo‘ldi (p<0,05). Ikkala guruhdagi bemorlar qon zardobidagi IL-6 miqdorining taqqoslama tahlili o‘tkazilganda, I guruhdagi bemorlar qon zardobida IL-6 miqdori 4,6±0,2 pg/ml ni tashkil etdi, II guruhdagi bemorlarda esa 7,5±0,8 pg/ml ni tashkil etdi hamda II guruh bemorlarida I guruhdagi bemorlarnikidan ishonchli ravishda 63 % ga yuqori ekanligi aniqlandi (p<0,01). YuE funktsional sinfi ortib borishi bilan bemorlar qon zardobidagi O‘NO-α miqdori ham ortib borgan hamda I va II guruhlarda mos ravishda 5,6±0,7 pg/ml va 8,1±0,9 pg/ml ni tashkil etdi. II guruhdagi bemorlar qon zardobidagi O‘NO-α miqdori I guruhdagi bemorlarnikiga nisbatan 44,6% ga yuqori ekanligi aniqlandi (p<0,05).

Table 3. Serum pro-inflammatory cytokines (IL-6, TNF-α) and CRP levels (M±m) in patients with DCM according to the severity of HF
Jadval 3. DKMP bilan og‘rigan bemorlarda SYuYe og‘irlik darajasiga ko‘ra qon zardobidagi yallig‘lanisholdi sitokinlari (IL-6, O‘NO-α) va CRO miqdori (M±m)

Ko‘rsatkich	I guruh FS II (n=12)	II guruh FS III-IV (n=30)	p
CRO, mg/l	4,1±0,6	7,6±1,1*	p<0,05
IL-6, pg/ml	4,6±0,2	7,5±0,8**	p<0,01
O‘NO-α, pg/ml	5,6±0,7	8,1±0,9*	p<0,05
O‘NO-α > 6,0 pg/ml	5 (41,6%)	21 (70%)	

Izoh: n – bemorlar soni; p - I guruhga nisbatan ishochlilk darajasi; CRO – C-reaktiv oqsil; O‘NO-α – o‘sma nekrozi omili-α; IL-6 – interleykin-6.

Keltirilgan ma’lumotlar SYuYe og‘irlik darajasi hamda qon zardobidagi C-reaktiv oqsil va IL-6, O‘NO-α kabi yallig‘lanisholdi sitokinlari o‘rtasida yaqqol musbat bog’liqlik borligini ko‘rsatadi.

Munozara

Etiologiyasidan qat'iy nazar, yurak yetishmovchiligining rivojlanishi ham mahalliy, ham tizimli yallig'lanish kaskadlarining faollashuvi bilan bog'liq [16]. Miokardit yoki yallig'lanishli kardiomiopatiya bilan og'rigan bemorlarda yallig'lanish yurak yetishmovchiligining asosiy sababi hisoblanadi [17]. Bundan tashqari, sitokinlar ta'sirida yuzaga kelgan yallig'lanish o'tkir stress-indutsirlangan "Takotsubo" kardiomiopatiyasi rivojlanishida ham ishtirok etishi aniqlangan [18]. Yurak shikastlanishiga javoban yallig'lanish reaktsiyasi dastlab adaptiv xarakterga ega bo'ladi, biroq ortiqcha va uzoq davom etuvchi yallig'lanish javobi noadaptiv jarayonga aylanib, yurak yetishmovchiligi patogenezida hal qiluvchi omillardan biri bo'lib qoladi. Bir qator tadqiqot natijalariga ko'ra, yurak yetishmovchiligi mavjud bemorlar qon zardobida o'sma nekrozi omili-α (O'NO-α), interleykin-6 (IL-6), interleykin-8 (IL-8) kabi yallig'lanisholdi sitokinlari, hamda C-reaktiv oqsil (CRO) miqdori yuqori bo'lgan [19,20]. Uzoq muddatli subklinik tizimli yallig'lanish yurak mushagidagi yallig'lanish javobining shakllanishida hal qiluvchi o'rin egallashi aniqlangan [21]. Faollashgan to'qima makrofaglari ham yallig'lanisholdi sitokinlari va xemokinlarni sintezlab, miokardda yallig'lanish jarayonini kuchaytiradi hamda miokard fibrozlanishi va kardiomiopatiya rivojlanishi uchun sharoit yaratadi [22]. Jumladan, idiopatik DKMP rivojlangan bemorlarning deyarli yarmida biopsiya materiallarida yallig'lanisholdi sitokinlari miqdorining oshganligi va miokardda limfotsitar infiltratsiya aniqlangan [23].

DKMP bilan og'rigan bemorlar miokard to'qimasida doimiy ravishda O'NO-α ekspressiyasining oshishi qayd etilgan [24]. Belenkov Yu.N. va hammualliflarning tadqiqotida kardiomiotsitlarning o'zi O'NO-α ni ishlab chiqarish qobiliyatiga ega ekanligi va bunda sitokin miqdori to'g'ridan-to'g'ri miokardning zo'riqish darajasiga bog'liq ekanligi isbotlangan [25]. Yurak yetishmovchiligi bo'lgan bemorlar qon zardobida O'NO-α ning yuqori darajasi ChQ OF pasaygan va ChQ OF saqlangan subpopulyatsiyalarda o'lim ko'rsatkichlarining oshishi bilan bog'liq bo'lgan [26].

Qon zardobidagi IL-1 miqdori turli etiologik omillarga (miokard infarkti, chap qorinchaga ortiqcha bosim yuklamasi va kardiomiopatiyalarga) bog'liq yurak yetishmovchiligining eksperimental modellarida doimiy ravishda oshganligi kuzatiladi [27–29]. Yurak yetishmovchiligida immun hujayralari, fibroblastlar, endoteliy hujayralari va kardiomiotsitlar IL-1 sintezi va faollashuviga hissa qo'shishi aniqlangan [30–32]. IL-1 tizimining faollashuvi turli mexanik yo'llar orqali yurakning sistolik va diastolik faoliyatining buzilishiga olib keladi hamda YuE patogenezida muhim ahamiyat kasb etishi mumkin [33]. Masalan, IL-1 siklik AMF ga bog'liq bo'lmagan mexanizm orqali L-tipdagi kaltsiy kanallarining beta-adrenergik reaksiyasini pasaytirishi isbotlangan [34]. Bundan tashqari, IL-1 kardiomiotsitlarda azot oksidi sintezlovchi ferment ekspressiyasini oshiradi, bu esa azot oksidi faolligining ortishiga va miokard qisqaruvchanlik qobiliyatining pasayishiga olib keladi [35]. 2017 yilda italiyalik olimlar tomonidan DKMP bilan og'rigan bemorlarda inflammasomalar va tizimli yallig'lanish biomarkerlari ahamiyatini o'rganishga qaratilgan tadqiqot o'tkazilgan. Bu tadqiqot doirasida 156 nafar ambulator bemor tekshirilgan (o'rtacha yosh — 58 yosh, 77% — erkaklar, ChQ OF medianasi — 35%, NUP medianasi — 189 pg/ml, IL-1 — 1,08 pg/ml, IL-6 — 1,7 pg/ml, IL-10 — 2,7 pg/ml). 89,6 oylik kuzatuv davomida 35 nafar bemor (22%) vafot etgan yoki yurak transplantatsiyasi amaliyoti bajarilgan bo'lib, ularning ko'pchiligida NYHA bo'yicha III FS, bo'lmachalar fibrillyatsiyasi (BF), ChQ OF ancha past va BNP kontsentratsiyasi ancha yuqori ekanligi qayd etilgan. IL-1, IL-6 va IL-10 miqdori yaxshi va yomon prognozli guruhlar o'rtasida sezilarli farq qilmagan. Shuningdek, IL-1 miqdori NYHA sinflari yoki ChQ OF kvartillari orasida ham ahamiyatli farq ko'rsatmagan. Biroq, ko'p omilli tahlilda IL-1 barcha sabablar natijasida yuzaga kelgan o'limning mustaqil va kuchli prediktori ekanligi aniqlangan [36].

Bir nechta klinik tadqiqotlar shuni ko'rsatdiki, yurak yetishmovchiligi bilan og'rigan bemorlarning miokard to'qimasida sog'lom odamlarnikiga nisbatan IL-6 ekspressiyasi yuqori bo'lgan [37]. Simptomsiz sistolik disfuntsiya bilan kechuvchi kasalliklarda IL-6 miqdorining ortishi aniqlangan, shuningdek, simptomsiz keksa bemorlar populyatsiyasida IL-6 va C-reaktiv oqsil (CRO) miqdorining ortishi yurak yetishmovchiligi holatlarini bashorat qilishda qo'llanilishi ko'rsatilgan [38,39]. Interleykin-6 gepatotsitlarda CRO ishlab chiqarilishining kuchli induktori bo'lib, u gipoksiyaga javoban bir necha turdagi hujayralar, shu jumladan, kardiomiotsitlar tomonidan ham ishlab chiqariladi [40]. TIME-CHF tadqiqoti turg'un surunkali yurak yetishmovchiligi bilan og'rigan

chap qorincha otish fraktsiyasi saqlangan va pasaygan bemorlar qon zardobida yuqori sezgirlikka ega C-reaktiv oqsil miqdorining oshganligi ko‘rsatilgan [41].

Bizning tadqiqotimizda DKMP bilan og‘rigan bemorlarning qon zardobida yallig‘lanisholdi sitokinlari (IL-6, O‘NO-α) va yallig‘lanish markeri (CRO) miqdori ishonchli darajada oshgani aniqlandi. Tadqiqotimizda yurak yetishmovchiligining og‘irlik darajasi ortishiga bog’liq ravishda yurakning patologik remodellanish darajasi hamda qon zardobidagi sitokinlar miqdori va C-reaktiv oqsil miqdori oshganligi ko‘rsatildi.

Yurak yetishmovchiligi patogenzida yallig‘lanisholdi sitokinlari muhim o‘rin egallashi, tizimli yallig‘lanishga qarshi yo‘naltirilgan maxsus terapiya usullarini qo‘llashni taqozo etadi. An’anaviy tarzda yallig‘lanish kasalliklarini davolashda qo‘llanilgan kolxitsin, yurak-qon tomir kasalliklarini davolashda o‘zining xavfsizligini isbotlagan hamda hozirgi kunga kelib istiqbolli terapevtik dori vositasi sifatida o‘rganilmoqda. Kolxitsin mikronaychalarni nishonga olib, ularning yig’ilishini va ma’lum yallig‘lanish markerlarining ishlab chiqarilishini ingibirlaydi, shuningdek neytrofillar faoliyatiga ta’sir ko‘rsatib, aterosklerotik pilakchalar shakllanishiga to‘sqinlik qilishi mumkin [42]. Shu sababli kolxitsin yurak ishemik kasalligi (YuIK), yurak ritmi buzilishlari (bo‘lmachalar fibrillyatsiyasi), so‘nggi yillarda esa yurak yetishmovchiligi va insult kabi holatlarni davolashdagi imkoniyatlari o‘rganilmoqda.

2014 yilda Deftereos va hammualiflar tomonidan o‘tkazilgan tadqiqotda va 2024 yildagi COLICA tadqiqotida yurak yetishmovchiligi bilan og‘rigan bemorlarda kolxitsinni qo‘llash imkoniyatlari o‘rganilgan. Deftereos tadqiqotida kolxitsinning turg’un yurak yetishmovchiligi bo‘lgan bemorlarning klinik holatiga ta’siri o‘rganilgan [43]. Bu tadqiqotda kolxitsin terapiyasi bemorlar qon zardobidagi yallig‘lanish markerlarini kamaytirgan bo‘lsada, biroq bemorlarning NYHA bo‘yicha funktsional sinfiga, o‘lim ko‘rsatkichiga yoki gospitalizatsiyalar soniga ijobiy ta’sir ko‘rsatmagan. COLICA tadqiqotida o‘tkir dekompensatsiyalangan yurak yetishmovchiligi bo‘lgan bemorlarda kolxitsinning klinik samaradorligini baholangan [44]. Asosiy yakuniy nuqta — 8 haftadan so‘ng NT-proBNP miqdorining pasayishi bo‘lib, bu ko‘rsatkich kolxitsin va platsebo guruhlari o‘rtasida farq qilmagan. Kolxitsin qabul qilgan bemorlarda yallig‘lanish markerlari, jumladan CRO va IL-6 miqdori kamaygan bo‘lsada, ammo yurak yetishmovchiligining zo‘rayishi yoki qayta dekompensatsiya holatlari bo‘yicha guruhlar o‘rtasida statistik farq aniqlanmagan.

Shunga qaramay yurak yetishmovchiligini davolashda kolxitsinning ta’sirini o‘rganishga qaratilgan yangi tadqiqotlar olib borilmoqda. Xuan Sun va hammualliflarining 2022-yilda AHA jurnalida chop etilgan tadqiqotida eksperimental sichqonlar modelida doksorubitsin yordamida chaqirilgan DKMP ni davolashda kolxitsinning kuchli yallig‘lanishga qarshi ta’siri ko‘rsatilgan [45]. Ushbu ta’sir SIRT2 orqali amalga oshirilib, NLRP3 inflammasomasining faollashuvini susaytirish natijasida DKMP rivojlanishini sekinlashtirgan. Tadqiqotdan quyidagi natijalar olingan: - kolxitsin miokarddagi yallig‘lanishni, neytrofillar infiltratsiyasini va yallig‘lanish sitokinlari (IL-1, IL-6, O‘NO-α) miqdorini kamaytirgan; - kolxitsin SIRT2 ni inaktivatsiya bo‘lishdan himoya qilgan va shu orqali NLRP3 ni deatsetillab, uning faollashuvini cheklagan; - kolxitsin yurak faoliyatini yaxshilagan, miokard remodellanishining oldini olgan, vazn yo‘qotish va doksorubitsin orqali chaqirilgan o‘lim darajasini kamaytirgan. Tadqiqotchilarning xulosasiga ko‘ra kolxitsin DKMP rivojlanishini sekinlashtirishda samarali natija ko‘rsatgan bo‘lib, uni yallig‘lanish etiologiyali yurak yetishmovchiligini davolashda arzon, xavfsiz va istiqbolli vosita sifatida qo‘llash imkoniyatini ilmiy asoslaydi.

Xulosa

Ko‘plab ilmiy tadqiqot natijalari shundan dalolat beradiki, etiologiyadan qat’iy nazar, yurak yetishmovchiligining rivojlanishi sitokinlar va yallig‘lanish markyorlari induktsiyasi bilan bog’liq bo‘lib, ular yurakning salbiy remodellanishi hamda sistolik va diastolik disfunktsiyasi patogeneziga hissa qo‘shishi mumkin. Bizning tadqiqotimizda ham DKMP bilan og‘rigan bemorlarda SYuYe og‘irlik darajasi bilan qon zardobidagi C-reaktiv oqsil va IL-6, O‘NO-α kabi yallig‘lanisholdi sitokinlari o‘rtasida yaqqol musbat bog’liqlik borligi ko‘rsatildi.

Olingan natijalar dilatatsion kardiomiopatiya bilan og‘rigan bemorlarda yallig‘lanisholdi sitokinlari (IL-6, O‘NO-α) va CRO kasallik kechishining og‘irlik darajasiga baxo berishda muhim ahamiyatga ega ekanligini, hamda kelgusida bunday guruh bemorlarda yurak yetishmovchiligini

davolashda qo‘llanilayotgan optimal medikamentoz terapiya tarkibiga kolxitsin dori vositasini qo‘shish istiqbolli ekanligini ko‘rsatadi.

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Authors’ contribution.

Conceptualization, T.A. Abdullaev; methodology, M.M. Rakhmatov; software, M.M. Rakhmatov; validation, T.A. Abdullaev; formal analysis, T.A. Abdullaev; investigation, M.M. Rakhmatov; resources, M.M. Rakhmatov; data curation, T.A. Abdullaev; writing—original draft preparation, M.M. Rakhmatov; writing—review and editing, M.M. Rakhmatov, Kh.A. G‘ulomov; visualization, M.M. Rakhmatov, Kh.A. G‘ulomov; supervision, T.A. Abdullaev; project administration, T.A. Abdullaev; funding acquisition, T.A. Abdullaev. All authors have read and agreed to the published version of the manuscript.

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Ethics approval.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Republican Specialized Scientific-Practical Medical Center of Cardiology.

Nashrga xabardor qilingan rozilik.

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Data Availability Statement

All data sources used are listed in the references section.

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Conflict of interest

The authors declare that they have no conflict of interest

Qisqartmalar

DKMP	Dilatatsion kardiomiopatiya
GKMP	Gipertrofik kardiomiopatiya
RKMP	Restriktiv kardiomiopatiya
AO'QKMP	Aritmogen o'ng qorincha kardiomiopatiyasi
ChQNDKMP	Chap qorincha nodilatatsion kardiomiopatiyasi
SYuYe	Surunkali yurak yetishmovchiligi
ChQ	Chap qorincha
OF	Otish fraksiyasi
CRO	C-reaktiv oqsil
IL-6	Interleykin-6
O'NO-α	O'sma nekrozi omili-α
NUP	Natriyuretik peptid
YuIK	Yurak ishemik kasalligi

Adabiyot

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