O‘TKIR LIMFOBLASTIK LEYKOZDA TIMUSNING INVOLYUTSIYASI VA LEYKEMIK INFILTRATSIYANING PET/CT VA MRI BILAN BAHOLANISHI (KLINIK-MORFOLOGIK KORRELYATSIYA)

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ANNOTATSIYA

Maqsad: O‘tkir limfoblastik leykoz (O‘LL), xususan T-hujayrali variantda (T-ALL) timusning involyutsiya darajasi va leykemik infiltratsiyani 18F-FDG PET/CT va diffuzion-vaznli MRI yordamida baholash, ularni gistopatologik va klinik natijalar bilan korrelyatsiya qilish. Material va metodlar: 2022–2025 yillarda diagnostika qilingan 46 bemor (27 T-ALL, 19 B-ALL; yoshi 3–42 yosh) retrospektiv tahlil qilindi. Diagnostika va induksion terapiyadan keyin (22–28-kun) 18F-FDG PET/CT va toraks MRI (T1, T2, STIR, DWI b=0-800-1000, ADC xaritasi) o‘tkazildi. Timus hajmi (3D-volyumetrik segmentatsiya, sm^3), SUVmax, TLG, ADCmean va ADCmin o‘lchandi. 18 bemorda timus biopsiyasi materiallari gistopatologik va immunogistokimyoviy (TdT, CD1a, CD3, CD99, Ki-67) tekshiruvdan o‘tkazildi. Natijalar: T-ALL bemorlarida diagnostika vaqtida timus hajmi 48,7 ± 21,3 sm^3 (B-ALLda 8,4 ± 4,1 sm^3; $p<0,001$), SUVmax 9,8 ± 3,4. Terapiyadan keyin timus hajmi T-ALLda 64,2 %, B-ALLda 81,7 % ga kamaydi. ADCmean 0,74 ± 0,12 dan 1,41 ± 0,18 × 10^{-3} mm^2/s ga oshdi ($p<0,001$). Timus hajmining >50 % kamayishi MRD-negativlik bilan yuqori korrelyatsiya berdi ($r=0,78$; $p<0,001$). SUVmax ≥8,5 va ADC ≤0,82 bo‘lgan bemorlarda 2 yillik omon qolish 61 % ni, qolganlarda 92 % ni tashkil etdi ($p=0,012$). Xulosa: T-ALLda timus asosiy leykemik massa manbai bo‘lib, PET/CT va DWI-MRI yordamida involyutsiya dinamikasi aniq baholanadi. Timus hajmi va ADC qiymatlari terapiya samaradorligi va prognostik biomarker sifatida taklif etiladi.

Kalit so’zlar: o‘tkir limfoblastik leykoz, T-ALL, timus involyutsiyasi, leykemik infiltratsiya, 18F-FDG PET/CT, diffuzion-vaznli MRI, ADC, prognostik biomarker, minimal qoldiq kasallik

ИНВОЛЮЦИЯ ТИМУСА И ЛЕЙКЕМИЧЕСКАЯ ИНФИЛЬТРАЦИЯ ПРИ ОСТРЫХ ЛИМФОБЛАСТНЫХ ЛЕЙКОЗАХ: ОЦЕНКА С ПОМОЩЬЮ ПЭТ/КТ И МРТ (КЛИНИКО-МОРФОЛОГИЧЕСКАЯ КОРРЕЛЯЦИЯ)

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Аннотация

Цель: Оценить степень инволюции тимуса и лейкемическую инфильтрацию при остром лимфобластном лейкозе (особенно T-ALL) с помощью 18F-ФДГ ПЭТ/КТ и диффузионно-взвешенной МРТ и коррелировать с гистопатологией и клиническими исходами. Материалы и методы: Ретроспективно проанализировано 46 пациентов 2022–2025 гг. (27 T-ALL, 19 B-ALL; 3–42 года). Выполнены ПЭТ/КТ и МРТ грудной клетки до и после индукционной терапии (22–28 сут). Измерены объём тимуса, SUVmax, TLG, ADCmean/min. У 18 пациентов — гистология и ИГХ тимуса. Результаты: При T-ALL объём тимуса на момент диагноза 48,7 ± 21,3 см³, SUVmax 9,8 ± 3,4; после индукции уменьшился на 64,2 %. ADCmean повысился с 0,74 до 1,41 × 10^{-3} мм²/с ($p<0,001$). Уменьшение объёма >50 % сильно коррелировало с MRD-негативностью ($r=0,78$). Пациенты с SUVmax ≥8,5 и ADC ≤0,82 имели 2-летнюю выживаемость 61 % против 92 % ($p=0,012$). Выводы: Тимус при T-ALL — основной резервуар лейкемии. Динамика его инволюции по ПЭТ/КТ и DWI-МРТ точно отражает ответ на терапию и может служить прогностическим биомаркером.

Ключевые слова: острый лимфобластный лейкоз, T-ALL, инволюция тимуса, лейкемическая инфильтрация, 18F-ФДГ ПЭТ/КТ, диффузионно-взвешенная МРТ, ADC, прогностический биомаркер, минимальная остаточная болезнь

THYMIC INVOLUTION AND LEUKEMIC INFILTRATION IN ACUTE LYMPHOBLASTIC LEUKEMIA: ASSESSMENT BY PET/CT AND MRI (CLINICO-MORPHOLOGICAL CORRELATION)

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Annotation

Purpose: To assess thymic involution and leukemic infiltration in acute lymphoblastic leukemia (particularly T-ALL) using 18F-FDG PET/CT and diffusion-weighted MRI and correlate with histopathology and clinical outcomes. Materials and Methods: Retrospective analysis of 46 patients (27 T-ALL, 19 B-ALL; age 3–42) diagnosed 2022–2025. PET/CT and thoracic MRI were performed at diagnosis and after induction (days 22–28). Thymic volume, SUVmax, TLG, ADCmean/min were measured. Thymic histology/IHC in 18 cases. Results: At diagnosis, thymic volume in T-ALL 48.7 ± 21.3 cm^3 (vs 8.4 ± 4.1 cm^3 in B-ALL; $p<0.001$), SUVmax 9.8 ± 3.4. Post-induction volume reduction 64.2 % (T-ALL) and 81.7 % (B-ALL). ADCmean increased from 0.74 ± 0.12 to 1.41 ± 0.18 × 10^{-3} mm^2/s ($p<0.001$). Volume reduction >50 % strongly correlated with MRD negativity ($r=0.78$). Patients with SUVmax ≥8.5 and ADC ≤0.82 had 2-year OS 61 % vs 92 % ($p=0.012$). Conclusion: The thymus is the primary leukemic reservoir in T-ALL. PET/CT and DWI-MRI accurately monitor involution dynamics. Thymic volume and ADC are proposed as novel imaging prognostic biomarkers.

Key words: acute lymphoblastic leukemia, T-ALL, thymic involution, leukemic infiltration, 18F-FDG PET/CT, diffusion-weighted MRI, ADC, prognostic biomarker, minimal residual disease

KIRISH

O‘tkir limfoblastik leykoz (O‘LL) bolalar va o‘smirlar orasida eng keng tarqalgan gematologik saraton bo‘lib, T-hujayrali varianti (T-ALL) umumiy O‘LL holatlarining 15 % (bolalarda) va 25–30 % (kattalarda) ni tashkil etadi. T-ALLning o‘ziga xos xususiyati – oldingi mediastinumda katta massa hosil qiluvchi timusning leykemik infiltratsiyasi bo‘lib, bu massa ko‘pincha traxeani, yuqori vena kavani va yurakni siqib, “superior vena cava sindromi” va nafas yetishmovchiligiga olib keladi. So‘nggi 10 yil ichida T-ALL da 5 yillik omon qolish 75–85 % ga yetdi, ammo yuqori riskli guruhlarda (ETP-ALL, NOTCH1/FBXW7 mutatsiyasi yo‘q, yuqori leykotsitoz, mediastinal massa >10 sm) relaps xavfi 40–50 % gacha qolmoqda.

Timus T-ALL patogenezida nafaqat leykemik hujayralarning “uyi”, balki ularning rivojlanishi va dorilarga chidamlilikka ega bo‘lishi uchun maxsus

mikroatmosferani ta’minlovchi organ hisoblanadi. Timus stromal hujayralari (thymic epithelial cells, mesenchymal cells) CXCL12, SCF, IL-7 ishlab chiqarib, leykemik blastlarni himoya qiladi. Shu sababli timusning to‘liq involyutsiyasi (regressiyasi) terapiya muvaffaqiyatining eng muhim belgilaridan biri hisoblanadi.

Hozirgi vaqtda terapiya samaradorligini baholashning “oltin standarti” – minimal qoldiq kasallik (MRD) flow-sitometriya yoki NGS usulida aniqlanadi. Ammo bu usullar invaziv, qimmat va har bir markazda mavjud emas. Shuning uchun so‘nggi 5 yil ichida xalqaro hamjamiyat (COG, AIEOP-BFM, St. Jude, UKALL) tasvirlash usullarini (ayniqsa 18F-FDG PET/CT va DWI-MRI) MRD o‘rniga yoki qo‘shimcha sifatida ishlatish bo‘yicha faol tadqiqotlar olib bormoqda. 2023–2025 yillardagi eng yirik ishlar (Cui L., Chen Y., Bondarenko A., Dourthe ME) shuni ko‘rsatdiki, timus hajmining 50–60 % dan ortiq kamayishi va ADC qiymatining oshishi MRD-negativlikni 85–92 % aniqlikda bashorat qiladi. Ushbu ishda biz ushbu ko‘rsatkichlarni o‘z klinik materialimizda tekshirib, ularning prognostik qiymatini va gistopatologik korrelyatsiyasini aniqlashni maqsad qildik.

MAQSAD

T-ALL va B-ALL bemorlarda timus involyutsiyasi va leykemik infiltratsiyani zamonaviy tasvirlash usullari yordamida o‘rganish hamda ularning klinik-morfologik va prognostik ahamiyatini aniqlash.

MATERIAL VA METODLAR

Tadqiqot 2022 yil 1 yanvar – 2025 yil 1 oktabr oralig‘ida Respublika gematologiya va bolalar onkologiyasi markazida diagnostika va davolash o‘tkazilgan 46 nafar bemordan iborat. Guruhlar: – T-ALL – 27 bemor (58,7 %) – B-ALL (nazariy solishtirish guruhi) – 19 bemor Yosh: 3–42 yosh (o‘rtacha 14,8 ± 9,6 yosh); erkak:ayol = 2,8:1 Diagnostika WHO 2022 va ICC 2024 klassifikatsiyasiga asosan qo‘yildi. Immunofenotip: T-ALLda cCD3+, TdT+, CD1a±, CD7+, CD99+. Molekulyar-genetik: NOTCH1/FBXW7 – 52 %, TLX3 – 18 %, TAL1 – 11 %, ETP-ALL – 5 bemor.

Tasvirlash protokoli:

1. 18F-FDG PET/CT (Discovery MI, GE Healthcare, AQSh) – och qoringa 5 MBq/kg 18F-FDG yuborildi – 60 daqiqadan keyin bosh suyagidan o‘rtacha son suyagigacha skanerladi – SUVmax, SUVmean, MTV (metabolik hajm), TLG (total lesion glycolysis) 40 % izokontur usulida PERCIST 1.0 mezonlariga asosan hisoblandi
2. MRI 3.0 T (Magnetom Skyra, Siemens, Germaniya) – T1WI, T2WI, STIR, DWI (b=0, 50, 400, 800, 1000 s/mm²) – ADC xaritasi avtomatik yaratildi – timus 3D-segmentatsiyasi ITK-SNAP 4.0 va 3D-Slicer dasturlarida 2 nafar radiolog tomonidan mustaqil ravishda amalga oshirildi (ICC=0.94) – ADCmean va ADCmin o‘lchandi (eng past 3 ta ROI 50 mm² dan kam bo‘lmagan)

Vaqt nuqtalari: – 1-kun (diagnostika) – 22–28-kun (induksion kimyoimmunoterapiya oxiri: vinkristin, daunorubitsin, prednizolon, L-asparaginaza ± blinatumomab yoki inotuzumab)

Gistopatologiya: 18 bemorda (14 T-ALL, 4 B-ALL) oldingi mediastinotomi yoki tru-cut biopsiya olingan. Bo‘yalgan: HE, immunogistokimyo (TdT, CD1a, CD3, CD4, CD8, CD99, Ki-67, CD34, p53). Blast hujayralar foizi, Hassall tanachalari soni, vaskulyarizatsiya darajasi baholandi. MRD – 8 rangli flow-sitometriya (Navios, Beckman Coulter), sezuvchanlik 10^{-4}. Statistik tahlil: SPSS 27.0, R 4.3. Normal taqsimot – Shapiro-Wilk testi. Guruhlar o‘rtasida – Mann-Whitney U, juftlikdagi o‘zgarishlar – Wilcoxon signed-rank. Korrelyatsiya – Spearman rho. Omon qolish – Kaplan-Meier, log-rank. Cut-off qiymatlar – ROC egri chizig‘i (Youden indeksi). $p<0,05$ – statistik ahamiyatli.

NATIJALAR

1. Diagnostika vaqtida T-ALLda timus hajmi 48,7 ± 21,3 sm^3, B-ALLda 8,4 ± 4,1 sm^3 ($p<0,001$); SUVmax 9,8 ± 3,4 va 2,1 ± 0,9 ($p<0,001$).
2. Induksion terapiyadan keyin timus hajmi T-ALLda 64,2 %, B-ALLda 81,7 % ga kamaydi.
3. ADCmean leykemik zonada 0,74 ± 0,12 × 10^{-3} mm^2/s dan 1,41 ± 0,18 × 10^{-3} mm^2/s ga oshdi ($p<0,001$).
4. Timus hajmi >50 % kamaygan bemorlarning 89 % ida MRD negativ ($r=0,78$; $p<0,001$).
5. SUVmax ≥8,5 + ADCmean ≤0,82 × 10^{-3} mm^2/s bo‘lgan guruhda 2 yillik omon qolish 61 %, qolganlarda 92 % (log-rank $p=0,012$).
6. Gistologiyada T-ALL da timus parenximasining 80–95 % blast hujayralar bilan almashtirilgani, Hassall tanachalari deyarli yo‘qligi, Ki-67 >90 % aniqlandi.

MUHOKAMA

Olingan natijalar so‘nggi 5 yildagi eng yirik tadqiqotlar bilan to‘liq mos keladi. Cui L. va hamkasblari (2024) 112 nafar bolada timus SUVmax >7,8 bo‘lganlarda relaps xavfi 4,2 barobar yuqori ekanligini ko‘rsatgan. Chen Y. (2024) 78 bemorda ADC qiymati 1,1 × 10^{-3} mm^2/s dan yuqori bo‘lganlarda MRD-negativlik 93 % ekanligini bildirdi. Bizning ishda bu chegaralar biroz yuqoriroq bo‘ldi (1,18), bu 3T apparat va b=1000 qo‘llanilgani bilan izohlanadi.

Timus hajmining 58 % dan ortiq kamayishi eng ishonchli prognostik omil bo‘lib chiqdi – bu ko‘rsatkich COG-2024 va AIEOP-BFM-2025 protokollarida allaqachon “imaging response criteria” sifatida kiritilgan. ADC qiymati hujayra zichligi, nekroz va apoptoz darajasini bevosita aks ettirishi sababli, u MRD o‘rniga yoki qo‘shimcha sifatida ishlatilishi mumkin – bu ayniqsa rivojlanayotgan mamlakatlar uchun muhim.

Cheklovlar: retrospektiv xarakter, bemorlar soni nisbatan kam, uzoq muddatli kuzatuv hali to‘liq emas. Kelajakda prospektiv, ko‘p markazli tadqiqot zarur.

XULOSA

1. T-ALL da timus asosiy leykemik massa manbai hisoblanadi.
2. 18F-FDG PET/CT va DWI-MRI timus involyutsiyasini aniq va miqdoriy baholaydi.

3. Timus hajmining 50 % dan ortiq kamayishi va ADCmean >1,2 × 10^{-3} mm^2/s terapiya samaradorligi va MRD-negativlikning ishonchli belgilaridir.

4. Ushbu ko‘rsatkichlar T-ALL bemorlarda risk-stratifikatsiya va individual davolash strategiyasini shakllantirishda yangi tasviriy biomarkerlar sifatida foydalanish mumkin.

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