and progression-free-survival (HR 2,15, CI 1,23–4,11). There was no significant association between high molecular risk by NGS and OS (HR 1.45, 0.59-3.58) or PFS (HR 1.43, CI 0.65-3.13). Progressive age has discreetly impacted in OS (HR 1,05, CI 1,02-1,08), PFS (HR 1,03CI 1-1,05) and NRM (HR 1,06, CI 1,02-1,11; p = 0,002). No differences in outcomes were found between sex, ELN 2022 risk groups, and treatment with bone marrow transplantation. **Conclusions:** NGS and cytogenetic analysis have improved precision in prognosis prediction of AML patients of each patient, allowing safe implementation of appropriate individualized therapy. This study showed association between high-risk cytogenetics and worse prognosis in AML, but no association was observed between molecular risk and AML morbimortality. Further studies with a bigger population and longer follow-up should be conducted in order to better clarify and delve deeper into the results reported in this cohort.

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DESENVOLVIMENTO DE ÍNDICE PROGNÓSTICO PARA PACIENTES ADULTOS COM LEUCEMIA LINFOBLÁSTICA AGUDA NA REALIDADE NACIONAL

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A Leucemia linfoblástica aguda (LLA) está associada a menor sobrevida global (SG) e livre de progressão (SLP) em adultos devido a múltiplos fatores de risco e menor tolerância aos protocolos de quimioterapia. A estratificação prognóstica influencia a escolha terapêutica, incluindo a indicação do transplante alogênico de células tronco hematopoiéticas (alo-TCTH). Com objetivo de determinar um índice prognóstico integrando os fatores de risco para sobrevida em LLA, foi realizada análise multicêntrica aplicando escore prognóstico estabelecido internacionalmente. **Material e métodos:** Estudo multicêntrico, retrospectivo, com revisão de 115 prontuários de adultos com LLA, incluindo variáveis de risco: idade, leucometria, classificação citogenética, DRM, alo-TCTH, desfechos clínicos e seguimento. O índice prognostico foi calculado individualmente e através de análise multivariada foram calculados os coeficientes odds ratio/ hazard ratio (HR/OR) com inclusão da idade e alo-TCTH. Posteriormente, os casos foram classificados em 3 categorias de risco prognóstico. Os métodos de regressão logística, modelo de Cox, Kaplan meier, logrank e regressão risco competitiva foram utilizados nas análises. **Resultados:** Dos 115 pacientes, 53,0% eram LLA-B; 21,7% LLA-T; 3,5% LLA-bifenotipica e 21,7%LLA-B Ph-positivo; média idade 41.6 anos; mediana leucometria 13.200/mm^3; 19% com infiltração de sistema nervoso central; 38% citogenética de alto risco. Em relação ao tratamento, 56,4% (62/110) foram com protocolos inspirados pediatria, 21,8% não inspirados e 21,8% com inibidores de tirosina-quinase. Quanto a resposta, 44,1% (30/68) atingiram DRMneg pós indução e 65,6% (40/61) pós consolidação; 42% dos casos fizeram alo-TCTH em primeira remissão. Com mediana de seguimento de 1,7 anos, SG em 2 anos foi de 49% (95%IC 38-59%) e SLP de 41% (95%IC 30-51%). Incidências estimadas de recidiva e óbito por tratamento foram: 26% e 33%, respectivamente. Conforme índice prognóstico, pacientes foram estratificados em 3 grupos de risco, 26,7% (28/105) baixo, 34,3% intermediário e 39,0% alto. SLP 2 anos foi significativamente maior no grupo de baixo risco (68.2% - 95%IC 83.6-44.3%) em relação ao intermediário (46.8% - 95%IC 63.9-27.7%) e alto (20.9% - 95%IC 37.7-8.8%), p: 0.0001. Comparando tratamento, SLP 2 anos grupo tratado protocolos inspirados pediatria foi 45,4% versus outros 18,4%, p < 0.001. Nas categorias de risco intermediário e alto, SLP 2 anos no grupo alo-TCTH foi 52.4% (95%IC 71.8-33.4%) versus grupo quimioterapia: 13.9% (95%IC 32.1-3.2%), p: 0,004. **Discussão:** O índice de prognóstico modificado foi capaz de refinar a SLP esperada em cada categoria de risco, auxiliando no tratamento e indicação de alo-TCTH. Como limitações, trata-se de um estudo com amostra heterogênea, com centros de realidades distintas e seguimento relativamente curto. Os dados referentes a SLP no grupo alo-TCTH versus quimioterapia precisam ser interpretados com cautela, pois estão sujeitos a viés, uma vez o transplante seleciona um grupo mais favorável. É indicado validação em amostra maior e prospectivamente. **Conclusão:** A incorporação dos principais fatores de risco na LLA e o papel do alo-TCTH na realidade nacional, em um índice prognóstico para adultos pode estratificar de forma significativa a SLP dos pacientes em 3 categorias de risco e auxiliar na tomada de decisão clínica.

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COMPARATIVE ANALYSIS BETWEEN 2010, 2017 AND 2022 EUROPEAN LEUKEMIA NET RISK STRATIFICATION RESULTS IN PATIENTS WITH AML

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Acute myeloid leukemia (AML) is a heterogenous hematologic neoplasm characterized by recurrent cytogenetic and molecular abnormalities resulting in arrested differentiation and proliferation of immature hematopoietic precursors. Risk stratification in AML remains the principle in survival prognostication and treatment selection. Prognostication of AML

has relied mostly on cytogenetics for a long time. In recent years, many gene mutations have emerged as prognostic relevant, initially in patients with normal karyotype and then regardless of cytogenetics. The most relevant cytogenetic and molecular abnormalities are included within the current European LeukemiaNet (ELN) guidelines. The approach to AML in 2023 differs greatly from that of 10 years ago. Improved pathophysiological and genomic understanding has led to newly approved therapies. This study evaluated outcomes between the 2010, 2017 and 2022 ELN criteria in twelve patients aged ≥18 years with newly diagnosed AML. The age patients ranged from 18 to 76 years (median, 33 years). Our data set included results of karyotype analyses and next-generation sequencing (NGS) assays targeting recurrently mutated genes in myeloid malignancies and gene fusions. Karyotype analysis identified abnormalities in five patients (41.7%) and normal karyotype in two patients (16.6%). Five patients did not have a karyotype result, due to culture failure or lack of medical request. Molecular abnormalities occurred in 100% of patients (mutations in 16 genes, fusions involving *RUNX1* and *KMT2A*). Overall survival ranged from 0.2 to 28.3 months (mean, 10.6 ± 8.4 months). ELN 2010 categorized as adverse three patients (25.0%). ELN 2017 and ELN 2022 categorized as risk adverse seven (58.3%) and five (41.7%) patients, respectively. Most patients with ELN 2022 adverse-risk disease were older 60 years. Compared with ELN 2017 criteria, the ELN 2022 changed the assigned risk in 16.7% of patients from adverse to intermediate risk. Updates to the ELN 2022 guidelines include removal of *FLT3-ITD* allelic ratio and *NPM1* comutation status with subsequent allocation of *FLT3-ITD* into the intermediate-risk group. These changes were responsible for these risk reclassifications. There was consensus on the favorable risk classification for the three versions of the ELN. The ELN 2010, 2017 and 2022 guidelines categorized as risk intermediate 50%, 16.7% and 33.3% of patients, respectively. Patients with ELN 2022 adverse–risk AML had genetic abnormalities associated to poor prognosis, as complex karyotype, -7, *KMT2A* rearranged and, mutations in *RUNX1*, *EZH2* and *U2AF1*. Advances in AML biology have led to an increasing complexity in prognostic estimation. This study showed the contribution of genetic abnormalities to risk stratification in AML. Consistent with prior analyses, certain ELN defining mutations and cytogenetic abnormalities were correlated with adverse prognosis.

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ACUTE MYELOID LEUKEMIA IN COMPLETE RESPONSE FOR 2 YEARS WITH AZACYTIDINE ASSOCIATED WITH HIGH-DOSE VITAMINS

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Acute Myeloid Leukemia (AML) is an uncommon neoplasia, and its treatment is challenging. The AZAVIT-ABCEF protocol (Plataforma Brasil-CAAE: 53015421.0.0000.5463) is of low intensity and reasonably well-tolerated. **Objective:** To report a clinical case of a patient with AML in complete remission (CR) with the protocol, cycles of 7 days every 28 days. **Materials and methods:** Descriptive work carried out through data collection from medical records. **Clinical case:** A 62-year-old woman, whose mother died from AML and did not wish to undergo intensive chemotherapy. Hb was 6.5 g/dL, leukocytes 33,800/mm^3 with 43% blasts, and platelets 107,000/mm^3. Myelogram was refused, and peripheral blood immunophenotyping was positive for: CD11b, CD13, partial CD14, CD15, CD33, CD36, CD64, partial CD117, weak CD123, HLA-DR, and MPO. Diagnostic AML with monocytic component in December 2020. In the first cycle, she presented non-pruritic hyperemic lesions on her face and upper limbs, and vespertine fever. Skin biopsy showed neutrophilic infiltrate, sweet syndrome. The patient left the hospital and returned 1 month later with anemia and thrombocytopenia. She complained of significant pain in the hip joint, and MRI showed soft tissue edema with moderate joint effusion. Corticosteroid therapy was initiated, resolving the inflammatory condition. Marrow examination in March 2021 and April 2022 showed CR. In April 2023, she decided to stop the protocol, and 3 months later she presented with pancytopenia, marrow with dysplastic changes and 15% blasts (CD13, CD123, CD33, CD38, CD117, TdT, and MPO). **Discussion:** The possible mechanism of action: Azacitidine - reactivation of tumor suppressor genes, transcription of differentiating genes, action on protein metabolism and microRNA inhibition, increased VDR (vitamin D receptor) expression in primitive hematopoietic cells promoting differentiation, transcription of genes related to autoimmunity, making leukemic cells visible to the immune system, reactivation of antiviral activity, and differentiation of mesenchymal cells. Vitamin B1 - cofactor in the pyruvate dehydrogenase enzyme complex, as thiamine triphosphate, which prevents the transformation of pyruvate into lactate and favors respiration through the Krebs cycle, cofactor in the metabolism of alpha-ketoglutarate, and decreases the formation of 2-hydroxyglutarate (DNA methylation), activation of the immune system, and increased neoplastic cell death via P53 (non-canonical pathway, PUMA and NOXA). Vitamin C - cofactor in the Krebs cycle reaction involving the TET2 and IDH2 genes, promoting DNA demethylation, immunomodulatory effects activating antiretroviral reactions, and increased VDR expression in primitive hematopoietic cells. Vitamin D - decreases the function of myeloid suppressor cells, increases T cell immune response, modifies the tumor microenvironment, and favors autoimmunity. It promotes differentiation by binding to VDR, which interacts with nuclear proteins that bind to vitamin A. Erythropoietin and filgrastim are differentiating agents for the erythroid and granulocytic lineages, respectively. **Conclusion:** The patient achieved CR with the treatment, and its discontinuation may have favored the appearance of previously unreported dysplasia, as well as an increase in the number of blasts. Prospective studies are needed to assess the effectiveness of the protocol.

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