

Infections were the cause of death in 9.8% of patients and in 39% of those with severe infections ($p < 0.001$). **Discussion:** Infectious complications were associated with decreased OS of patients treated with azacitidine. Infection rates in the first three cycles were consistent with existing literature. Despite bacterial prophylaxis, no bacterial resistance was found. Thrombocytopenia was the main variable associated with higher infection risk, as previously described in previous studies. **Conclusion:** In this unicentric outpatient study, patients with MDS and thrombocytopenia are at greater risk of developing infection, especially in the first cycles and should be monitored cautiously. Although infection is associated with reduced survival, death generally occurs due to other causes, such as disease progression.

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NOVEL KEY VARIABLES IN THE SURVIVAL OF PATIENTS WITH MYELODYSPLASTIC NEOPLASMS: A PRACTICAL APPROACH USING MACHINE LEARNING

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Introduction: Prognostic models like the IPSS-R play a crucial role in assessing outcomes for patients with myelodysplastic neoplasms (MDS). However, recent advancements in machine learning (ML) offer the potential to uncover novel predictive variables and enhance prognostic accuracy. Models like ElasticNet are particularly adept at handling multidimensional data, thereby expanding the scope beyond the variables considered in IPSS-R. **Objectives:** Assessing the performance of ML in predicting overall survival in MDS patients by incorporating clinical and hematological variables not traditionally included in prognostic models. **Methods:** We conducted a retrospective cohort study at a single reference center involving patients diagnosed with MDS between 2004 and 2024. We included patients with available clinical outcomes, missing data was handled using the 'cart' multiple imputation, following confirmation of non-random missingness through Little's test. The dataset was then randomly split into a training group (70%) and a testing group (30%). Utilizing group elastic net machine learning, an artificial intelligence model capable of selecting relevant variables and assessing their discriminative power, we constructed 3 receiver operating characteristic (ROC) curves to predict 1, 3, and 5-year survival, extracting the area under the curve (AUC) and identifying variables with non-zero coefficients. Based on these coefficients, we categorized our dataset into "High Risk" and "Low Risk" groups. Subsequently, we

conducted a multivariate Cox proportional hazard regression analysis, adjusting for the new risk variable, age at diagnosis, sex, and transfusion burden. All statistical analyses were performed using R, with the involvement of packages such as 'mice', 'ggplot', 'gplasso', and 'survfit'. **Results:** 162 patients were included in this study. Using the group ElasticNet model, we identified 10 critical variables with notable predictive power: hemoglobin count, mean corpuscular volume, platelet count, presence of dysgranulopoiesis, presence of dysmegakaryopoiesis, serum iron, transferrin saturation, bone marrow cellularity, percentage of blasts in bone marrow, and percentage of ring sideroblasts. ROC curve analysis utilizing these variables' coefficients yielded AUCs of 0.863, 0.822, and 0.719 for predicting 1-year, 3-year, and 5-year survival, respectively. The coefficients were then extracted and used for risk stratification. 5-year survival rates were 24.3% for the High Risk group and 70.4% for the Low Risk group ($p < 0.001$, log-rank test). In multivariable Cox regression analysis, the risk group variable was the most discriminative predictor (HR = 3.56, $p < 0.001$), with sex, age at diagnosis, and transfusion burden also being significant ($p = 0.01$, 0.009, and 0.002, respectively). **Discussion:** The strong performance of the model, as evidenced by the ROC curve analysis, suggests that the selected variables offer substantial discriminative power. ML models offer more refined risk stratification than traditional methods, which may be useful in identifying occult relationships between variables. Validation in independent datasets may be necessary to strengthen the relationships herein exhibited. **Conclusion:** ML is a valuable tool for risk classification and survival prediction, offering significant insights for clinical decision-making and patient management that may be overlooked by other methods.

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BLASTING BEYOND THE OBVIOUS: IDENTIFICATION OF OVERLOOKED PREDICTIVE FACTORS FOR LEUKEMIC CONVERSION IN MYELODYSPLASTIC NEOPLASMS

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Introduction: Myelodysplastic neoplasms (MDS) are a group of clonal hematopoietic disorders characterized by dysplasia in one or more myeloid cell lines, ineffective hematopoiesis, and an increased risk of progression to acute myeloid leukemia (AML). The transition from MDS to AML is a pivotal event that significantly impacts patient outcomes. While the blast

percentage in bone marrow is a well-established predictor of leukemic conversion, it often overshadows other potentially significant prognostic factors. **Objective:** This study aims to identify independent predictive factors for leukemic conversion in patients with MDS, adjusting for the blast percentage in the bone marrow. **Methods:** We conducted a retrospective cohort at a single reference center, involving patients diagnosed with MDS between 2004 and 2024. We included patients with available data on survival and leukemic conversion outcomes. Missing data for other variables were handled using the 'cart' multiple imputation method, following confirmation of non-completely at random missingness through Little's test. We performed multivariate Cox proportional hazards (PH) regression to model leukemic conversion, adjusting for multiple relevant clinical parameters, including blast percentage, allowing for the evaluation of the independent effects of other variables. All statistical analyses were conducted using R software, utilizing the 'mice' package for imputation and the 'survival' package for survival analysis. **Results:** 162 patients were included in this study. In the multivariable Cox PH regression, we adjusted for blast percentage, sex, age at diagnosis, cytogenetic prognostic, presence of dysplasia in specific lineages in bone marrow, complete hemogram parameters, iron-related parameters, and transfusion burden. Optimal cut-offs were defined based on clinical relevance. In our analysis, only blast percentage, male sex, transfusion burden, hemoglobin count lower than 10 g/dL and serum iron higher than 65 μ g/dL were significant ($p < 0.001$, < 0.001 , 0.03, 0.012, and 0.03, respectively). Other than blast percentage, the most discriminative variable was sex, with males having a HR of 10.46 (95% CI: 3.31-33.08) for AML conversion in comparison to females. Transfusion burden (HR = 6.16, 95% CI: 1.85 - 20.52) and hemoglobin higher than 10 ng/dL (HR = 4.31, 95% CI: 1.36 - 13.65) were also relevant predictors for leukemic conversion, while serum iron higher than 65 μ g/dL (HR = 0.28, 95%CI: 0.09-0.86) was a protective factor. **Discussion:** Male sex has been associated with worse outcomes in MDS, such as a higher incidence of transformation to AML, which is partly due to a higher prevalence of high-risk somatic mutations in men. Transfusion burden has also been associated with AML conversion, as iron overload can contribute to leukemic transformation due to the accumulation of free iron radicals, which can cause DNA damage and promote leukemogenesis. However, the protective impact of high serum iron may relate to premature death, as these patients may be less susceptible to AML conversion. Similarly, although higher hemoglobin levels have been associated with better survival, its impact on leukemic transformation in our study may be due to death as a competing risk. **Conclusion:** Our study identified important discriminative factors for AML transformation in MDS patients when adjusting for blast percentage. These factors will allow for a more refined risk stratification in this population.

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LEUCEMIAS MIELOIDES: AVALIAÇÃO EPIDEMIOLÓGICA NO BRASIL

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Introdução: Leucemias mieloides correspondem a 1,48% do total de óbitos decorrentes de neoplasia no Brasil. Tanto a leucemia mieloide crônica (LMC) quanto a leucemia mieloide aguda (LMA) podem resultar em fase blástica com comprometimento sistêmico, que reduz drasticamente a sobrevida dos acometidos. O estabelecimento de perfil epidemiológico permite identificar a parcela da população mais acometida e suscetível à doença e fornece subsídios para maiores esclarecimentos em relação à etiopatogenia. **Objetivo:** Levantar dados epidemiológicos provenientes do Atlas de Mortalidade por Câncer do Instituto Nacional de Câncer (INCA), com enfoque em pacientes diagnosticados com Leucemia Mieloide. **Metodologia:** O presente estudo é de caráter retrospectivo descritivo, embasado por análise de dados digitais. Os registros adotados sobre a mortalidade da Leucemia Mieloide (LM) foram coletados através do Atlas de Mortalidade por Câncer - Instituto Nacional de Câncer (INCA), considerando-se dados no período de 1979 a 2022. Os dados são de domínio público e, portanto, não se fez necessária submissão do projeto à avaliação do comitê de ética em pesquisa. A análise foi realizada pelo Google Planilhas. Para a avaliação da mortalidade causada pela LM, os dados foram agrupados conforme a Classificação Internacional de Doenças, 10ª Revisão (CID-C92). Inicialmente, foram selecionados CIDs de interesse no Atlas de Mortalidade por Câncer (Modelos 1, 2 e 10). **Resultados e discussão:** Entre 1979 e 2022, foram registrados 97.550 óbitos por LM. A porcentagem de óbitos em relação ao total de mortes por neoplasias diminuiu 19,57%, de 1,84% (1,8% dos homens e 1,89% das mulheres) para 1,48% (1,51% e 1,45%, respectivamente). A maioria dos pacientes era do sexo masculino, concentrando, em números absolutos, 51.049 pacientes, ou 52,33%. A faixa etária mais acometida, também em números absolutos, foi de 70 a 79 anos. Os únicos intervalos de idade em que a quantidade de óbitos femininos ultrapassou os masculinos foram de 40 a 49 anos e com 80 anos ou mais. Nota-se diminuição na porcentagem de óbitos por LM em relação ao total de mortes por neoplasias a partir de 2003 (de 1,84% no período entre 1979 e 1983; 1,85% entre 1999 e 2003; e decréscimos nos anos seguintes que resultaram em 1,48% entre 2018 e 2022). Apesar da diminuição em termos relativos, foi observado aumento substancial na quantidade absoluta de óbitos por LM ao longo do tempo. Adotando o intervalo de 20 anos, compreende-se aumento de 106,8% entre 1982 e 2002 e de 50% entre 2002 e 2022. Já para intervalo de 40 anos (1982 a 2022), houve um aumento de 210%. **Conclusão:** Ainda que a porcentagem de mortes por LM tenha diminuído quando comparada com o total de mortes por neoplasias, cerca de 100 mil óbitos por LM são registrados anualmente. Portanto, campanhas de doação de sangue que avaliam hemograma e favorecem descoberta precoce da doença são essenciais para obter maiores chances de sucesso no tratamento. Estudos que analisam população mais afetada e identificam fatores de riscos associados, são de fundamental importância, visto que fornecem maiores esclarecimentos em relação à