somáticas pode fornecer informações cruciais para o prognóstico e para a tomada de decisões terapêuticas. O caso reforça a ideia de que o manejo da SMD deve ser dinâmico e personalizado, adaptando-se à progressão biológica da doença e sempre priorizando o bem-estar do paciente.

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https://doi.org/10.1016/j.htct.2025.104881

ID - 2900

DESENVOLVIMENTO E PADRONIZAÇÃO DE PAINEL CUSTOMIZADO PARA DETECÇÃO DE VARIANTES ONCOGÊNICAS EM NEOPLASIAS MIELOIDES POR SEQUENCIAMENTO EM LARGA ESCALA

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Introdução: Alterações citogenéticas e moleculares definem risco prognóstico e auxiliam na definição terapêutica nas síndromes mielodisplásicas (SMD). **Objetivos:** O objetivo do trabalho foi padronizar um painel de genes para investigação de variantes em 50 genes frequentemente alterados em neoplasia mieloide a partir da metodologia de sequenciamento em larga escala. **Material e métodos:** Foram incluídos 24 pacientes com diagnóstico de SMD, mediana de idade de 68 anos (30 a 92 anos), oito mulheres e 17 homens, classificação IPSS-R: muito baixo 14%, baixo 41%, intermediário 14% e alto 32%. Quatro amostras com variantes previamente conhecidas foram utilizadas como controles positivos. Amostras pareadas de sangue periférico (SP) e medula óssea (MO) foram coletadas dos pacientes com SMD e submetidas à extração de DNA. Os 50 genes do painel foram selecionados pelos pesquisadores considerando a relevância clínica definidas pelas classificações e estratificações de risco atuais (OMS, ICC, IPPS-M). O painel foi customizado pela *Integrated DNA Technologies* (IDT) para cobertura de regiões codificantes (CDS) dos 50 genes, utilização de *Unique Molecular Identifier* (UMI) para alta taxa de correção de erros e captura hibrida. Amostras de SP e de MO dos pacientes com SMD foram submetidas ao sequenciamento em duplicata. O sequenciamento em larga escala foi realizado no *NovaSeq X* com a *flow cell* de 1.5B 300 ciclos, almejando 10.000 vezes de cobertura. As análises de bioinformática foram realizadas no *BaseSpace* e software R. Os filtros aplicados foram de pelo menos 500x de cobertura, sendo pelo menos 30 leituras com a variante considerando-se a análise com *Unique Molecular Identifier* (UMI). Outros filtros incluíram *Variant Allele Frequency* (VAF) acima de 2%, variantes *missense, missense* sitio *de splice, frameshift, stop códon e lost codon*, variante presente nas amostras em duplicata. Os critérios de patogenicidade e oncogenicidade foram aplicados conforme as recomendações AMP/ASCO/CAP considerando variantes apenas aquelas que foram classificadas como provavelmente patogênicas ou patogênicas e com algum critério de oncogenicidade. **Resultados:** Dentre os 24 pacientes com SMD, 13 (54%) pacientes apresentaram pelo menos uma variante e 11 (46%) pacientes não apresentaram variantes em nenhum dos genes investigados. As análises identificaram as variantes esperadas nas amostras utilizadas como controles positivos. Mutações oncogênicas em pacientes com SMD foram identificadas em 11 genes. O gene TET2 foi o mais frequentemente mutado na coorte de SMD (31%), seguido por *ASXL1* (19%), *SRSF2* (10%), *CBL* (8%), *TP53* (8%), *CEBPA* (6%), *IDH2* (6%), *SF3B1* (6%), *NRAS* (4%), *DNMT3A* (2%) e *RUNX1* (2%). Vinte variantes em 9 genes foram detectadas em amostras de SP e MO. Duas variantes foram encontradas apenas no SP (*DNMT3A* e *SF3B1*) e 8 variantes apenas em MO (*CEBPA, ASXL1, RUNX1, TET2*). A frequência alélica da variante (VAF) no SP variou de 3% a 68% e na MO de 2% a 81%. **Discussão e conclusão:** O painel customizado detectou variantes em SMD. Projetos de pesquisas que viabilizam o treinamento de recursos humanos e implementação de metodologias de sequenciamento em larga escala são relevantes no contexto do SUS. O desenvolvimento de painéis customizado com alta sensibilidade é uma poderosa ferramenta na detecção de variantes em baixa frequência alélica e relevantes em neoplasias mieloides.

https://doi.org/10.1016/j.htct.2025.104882

ID - 804

DISPARITIES IN DIAGNOSIS AND MANAGEMENT OF MYELODYSPLASTIC SYNDROMES IN A BRAZILIAN CANCER CENTER: A COMPARISON BETWEEN PUBLIC AND PRIVATE HEALTHCARE SYSTEMS.

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Introduction: Disparities in access to healthcare services are well-documented in Brazil, where a mixed public-private system often leads to unequal resource distribution. Prior studies have demonstrated differences in service utilization and health expenditures between the Brazilian public health system (SUS) and private healthcare providers. However, no studies to date have specifically examined how these

disparities affect patients with myelodysplastic syndromes (MDS). **Objectives:** This study aims to characterize and compare the diagnostic and therapeutic profiles of MDS patients treated within the public and private systems in a Brazilian cancer center. **Material and methods:** We performed a retrospective cohort study of patients diagnosed with MDS between 2014 and 2024 at a tertiary cancer center in Brazil. Patients were categorized by healthcare system. Variables analyzed included time from symptom onset to diagnosis, MDS subtype, cytogenetic and mutational profiles, treatment modalities, and duration of follow-up. **Results:** Among the 96 patients included, 32 (33%) were treated in the public system and 64 (67%) in the private sector, a 2:1 ratio. The overall median age at diagnosis was 70 years. The highest level of education among SUS patients was high school, while within the private group, 50% of patients were college graduates. The median time from cytopenia investigation to diagnosis was 165 days in the SUS group versus 30 days in the private group. None of the SUS patients underwent an NGS molecular panel for more appropriate risk stratification, compared to 35 (54%) of the private sector who did. Of the total number of patients, 53 (55%) were classified as having therapy-related MDS due to a history of oncological treatment with radiotherapy and/or chemotherapy (26 from SUS and 27 from private). The most common mutations in the private sector patient panels were SF3B1 (22%), ASXL1 (14%), RUNX1 (14%), TP53 (11.4%), U2AF1 (11.4%), and TET2 (11.4%). In the M-IPSS risk assessment, 6 (17%) were classified as very low risk, 2 (5%) as low risk, 3 (8.5%) as low-intermediate risk, 5 (14.2%) as high-intermediate risk, 6 (17%) as high risk, 5 (14.2%) as very high risk, and 29 (45%) were at unknown risk. In the R-IPSS analysis, the public sector group showed: 8 (25%) patients as very low risk, 8 (25%) as low risk, 2 (6%) as intermediate risk, 8 (25%) as high risk, 4 (12.5%) as very high risk, and 2 (6%) as unknown. Regarding treatment, 20 (62%) SUS patients received first-line treatment with erythropoietin, and only 2 underwent consolidation with allogeneic transplant. In the private sector group, the median number of lines of treatment was 1 (maximum: 3), with treatments ranging from erythropoietin (31%), azacitidine (20%), a combination of venetoclax and hypomethylating agent (7%), luspatercept (3%), to lenalidomide (1.5%). Sixteen (25%) private sector patients underwent consolidation with allogeneic transplant. During the entire follow-up (median of 15 months), 24 patients presented transformation to Acute Myeloid Leukemia (8 from the SUS and 16 from the private sector). **Discussion and conclusion:** This study highlights significant disparities in the diagnosis and therapeutic management of MDS patients between Brazil's public and private healthcare systems. Although the underlying disease biology appeared similar, reduced access to timely diagnosis, molecular testing, and advanced therapies in the public system may contribute to poorer outcomes. Our findings provide real-world evidence from a developing country context.

https://doi.org/10.1016/j.htct.2025.104883

ID - 1763

IMPACT OF INNATE IMMUNITY-RELATED GENE ON THE SURVIVAL OF PATIENTS WITH MYELODYSPLASTIC NEOPLASMS

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Introduction: Myelodysplastic neoplasms (MDS) are clonal disorders characterized by cytopenias, bone marrow dysplasia, and a risk of progression to acute myeloid leukemia related to myelodysplasia (AML-RM). The accumulation of driver mutations in hematopoietic stem cells (HSCs) leads to clonal expansion and ineffective hematopoiesis. Activation of innate immune pathways, particularly through Toll-like receptors (TLRs), is increasingly recognized as a key contributor to disease progression, fostering inflammation, apoptosis, and abnormal cell proliferation. Dysregulated TLR signaling and chronic inflammation disrupt bone marrow homeostasis and are frequently associated with chromosomal abnormalities and poor prognosis. **Objectives:** This study aimed to evaluate overall survival in relation to the expression of key genes involved in immune and inflammatory signaling. **Material and methods:** Data from 48 patients with either MDS or AML-RM were collected and stored in the RedCap database. RNA was extracted from bone marrow and the following genes had their expression analyzed through RT-PCR: NFKB, TRAF6, MYd88, IRAK1, IRAK2 and IRAK4. 2^−ΔCT was used for this assessment, in which patients were divided into three groups based on the expression level of each gene: low expression, intermediate expression, and high expression. Furthermore, K-means clustering was applied to the 2^−ΔCT values in order to split patients into meaningful groups based on their gene expression. The elbow method was used to determine the ideal number of clusters. Kaplan-Meier estimates were used to plot survival curves, with the log-rank test being used for comparisons. **Results:** After splitting the patients by gene expression, no gene emerged as a moderator of survival ($p = 0.92, 0.63, 0.54, 0.89, 0.36$, and 0.64, respectively for NFKB, TRAF6, MYd88, IRAK1, IRAK2 and IRAK4). Through the elbow method, the ideal number of gene expression clusters was two, defining two clusters that only differed significantly by their expression of IRAK4 ($p = 0.03$, 8 patients in the IRAK4-high cluster). Although the IRAK4-high cluster had lower median survival (1.8 months vs 4 months for the IRAK4-low cluster), no significant differences emerged ($p = 0.32$). **Discussion and conclusion:** Our findings suggest that the isolated expression of innate immune signaling genes does not independently predict survival in patients with MDS or AML-RM. These results underscore the multifactorial nature of MDS