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P499 APPLICABILITY OF 2022 CLASSIFICATIONS OF ACUTE MYELOID LEUKEMIA IN THE REAL-WORLD SETTING

Topic: 4. Acute myeloid leukemia - Clinical

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Background:

The increasing knowledge of molecular characterization in acute myeloid leukemia (AML) led to the necessity to fully evaluate the genetic profile also for clinical purposes. These efforts resulted in the release of 2022 new editions of AML classification and prognostication systems, including the 5th edition of The World Health Organization (WHO) classification, the International Consensus Classification (ICC), and the European LeukemiaNet (ELN) recommendations for AML prognosis.

Aims:

We aimed to provide a real-world application of the WHO 2022, ICC and ELN 2022 classifications in the real-world setting, to unravel differences and similarities, and to test their implementation in clinical AML diagnosis. We particularly focused on secondary AML, myelodysplasia (MDS) related.

Methods:

We selected a cohort of 1001 cases diagnosed with AML according to the WHO 2016 and the ELN 2017 classifications. Where available (44.9% of cases), information concerning a previous history of an antecedent MDS or MDS/Myeloproliferative neoplasm (MPN), as well as a previous exposure to cytotoxic therapies were considered for defining secondary AML (s-AML) and therapy-related AML (t-AML), respectively. Survival outcome was available for 84.4% patients.

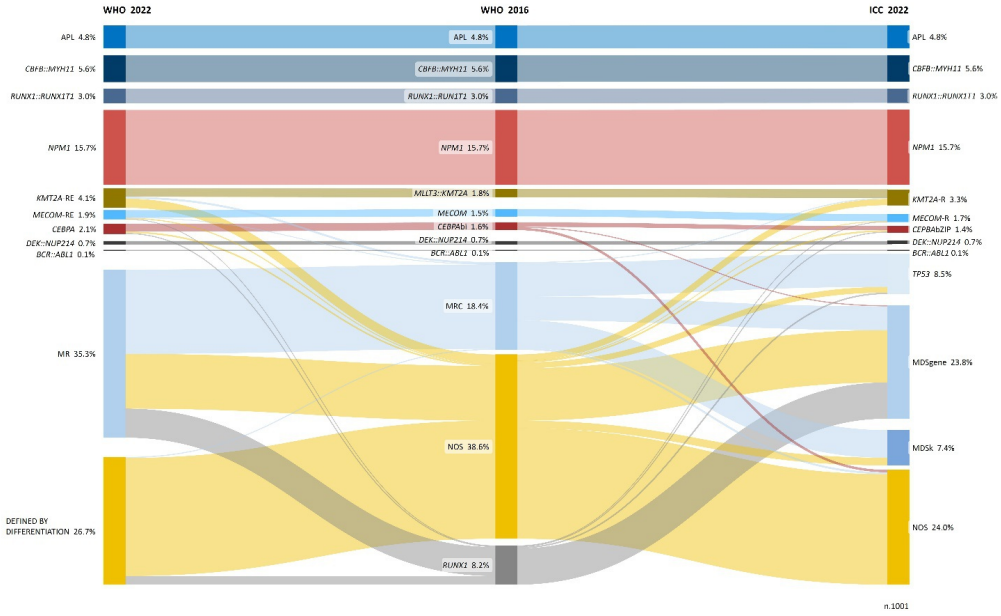
Results:

The overall diagnostic changes between the WHO 2016, compared to WHO 2022 and ICC classifications were 22.8% and 23.7% respectively, with a 13.1% difference in patients' distribution between ICC and WHO 2022. The "not otherwise specified" (NOS) by ICC and "defined by differentiation" by WHO 2022 categories shrank compared to WHO 2016 (24.1% and 26.8% respectively, vs 38.7%), particularly due to an expansion of MDS-related categories. The 92.7% and the 74.4% of *RUNX1*-mutated AML were re-classified respectively by the ICC into AML with MDS-related gene mutations and by WHO 2022 into the AML myelodysplasia related (MR) category, although the latter considers *RUNX1* mutations lacking of sufficient unifying characteristics. Of 397 cases with a MDS-related AML according to ICC, 55.9% were definable by the presence of a MDS-related karyotype. More than 75.0% of s-AML and t-AML cases presented a MDS-related genetic profile according to both new 2022 diagnostic classifications. The overall re-stratification between ELN 2017 and 2022 accounted for

12.9% (4.0% favorable to intermediate and 8.1% intermediate to adverse risk). The majority of s-AML and t-AML (83.1%) fell into the ELN 2022 adverse risk group. Stratifying the 213 AML classified as favorable risk by ELN 2017, the difference in OS between ELN 2022-defined favorable and intermediate risk groups was statistically significant (p<0.01). We also focused on the heterogeneous group of patients with normal karyotype and adverse risk mutations according to the ELN 2022: the survival outcome was significantly inferior in patients with multiple versus single MDS-related gene mutations (p<0.05).

Summary/Conclusion:

The 2022 revisions of AML classification led to a significant improvement of diagnostic schemes. In the real-world setting, conventional cytogenetics, usually easily available and less expensive than molecular characterization, correctly stratified 56% of AML MDS-related, thereby maintaining a diriment diagnostic role. Although the secondary nature of AML (prior MDS or MDS/MPN and therapy-related) is now applied as “diagnostic qualifiers”, it maintains a predictive role for defining an adverse outcome according to the ELN 2022. Considering the similarities between WHO and ICC diagnostic schemes, a tentative to generate a unified model taking into account practical and socio-economic issues is desirable.



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