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Commentary

Prediction of Prognosis in Myelodysplastic Syndromes

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DESCRIPTION

The majority of acquired bone marrow failure syndromes in adults fall into the category of Myelodysplastic Syndromes (MDS). MDS are becoming easier to understand biologically, with the discovery of more than 40 MDS-associated recurrently mutated genes in the last 7 years being just one example, but improved pathological understanding has not yet resulted in highly effective or curative therapies for the majority of patients who suffer from these disorders. MDS refers to a broad category of clonal diseases of hematopoietic stem or progenitor cells that are characterised by impaired hematopoiesis, disproportional "dysplastic" cell shape, and the capacity for clonal evolution. The World Health Organization (WHO) currently arbitrarily defines secondary Acute Myeloid Leukaemia (AML) as having less than 20% of myeloid blasts in the blood or bone marrow or having one of several karyotypic abnormalities regardless of blast proportion. Increasing failure of cellular differentiation is associated with the evolution to secondary Acute Myeloid Leukaemia (AML). Up to 30% of MDS cases receive an AML diagnosis in the end.

Even though MDS and secondary AML are categorized as separate entities, they reflect a continuum of diseases that go through genetic clonal development. The finding that Age-Related Clonal Hematopoiesis (ARCH), also known as Clonal Hematopoiesis of Indeterminate Potential (CHIP) and myeloid malignancies share comparable gene mutations raises the possibility that MDS or AML can develop from clonal hematopoiesis. Studies have demonstrated that mutant cells in this group of clonal myeloid disorders progress clonally and pick up new mutations. Due to space restrictions, this study will mainly concentrate on the genetic transition from MDS to secondary AML and discuss monitoring for disease response and progression utilising sequencing could be adopted in the clinic.

Prognosis

Clinical care includes estimating the prognosis of MDS patients in order to set expectations for patients and guide clinicians' treatment choices. The Revised International Prognostic Scoring System (IPSS-R), which was initially published in 1997, is currently the most often used technique for estimating the likelihood of developing MDS illness. This straightforward model was used to create treatment guidelines for MDS and identify patient populations in clinical studies. Despite serving as the clinical gold standard for MDS risk assessment, the IPSS had a number of flaws, including a tendency to underestimate risk in some patients who did not have an excess of blasts or aberrant karyotypes. The WHO classification-based prognostic scoring system, the Anderson comprehensive scoring system, and the Anderson lower risk MDS were developed as complementary risk models as a result.

To address a number of the shortcomings of its predecessor, the IPSS was updated in 2012 (IPSS-R). First, the IPSS-R increases the amount of chromosomal abnormalities that are expressly taken into account by the model and gives unfavourable cytogenetic lesions more weight than excessive blasts. Second, the IPSS's revision of the bone marrow blast proportion risk group cutoffs. Third, each case of cytopenia is handled separately and given a severity score. The IPSS-R model also has a more thorough approach to taking patient age into account. The IPSS-R score can be calculated with the use of an online tool, however despite these changes making it more difficult than the IPSS, no new clinical data is required.

The IPSS-R, like the IPSS, is based on a study of MDS patients who were assessed at the time of diagnosis and censored if they received disease-modifying medication. It also excludes patients with therapy-related diseases or proliferative Chronic Myelomonocytic Leukemia (CMML). The IPSS-R has since been validated in other scenarios, including following therapy, in spite of these restrictions.

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