MDS-specific comorbidity index is useful to identify myelodysplastic patients who can have better outcome with 5-azacitidine

Recently Della Porta and colleagues[1] reported on the importance of evaluation of comorbidities at baseline in myelodysplastic syndrome patients (MDS) in order to better tailor treatment strategies according to WPSS stratification. They proposed a prognostic score, the so-called MDS-CI, which was validated in a German cohort. It was proved that this score, which identified three risk groups of patients, was able to provide information about overall survival and risk of non-leukemic mortality. We also recently applied this score to a series of 450 patients and confirmed the feasibility and validity of this stratification, in particular in low and intermediate WPSS risk categories.[2] In the original report by Della Porta *et al.*[1] patients considered in the learning cohort had not received disease modifying therapy and none had been treated with hypomethylating agents. Prognostic factors associated to the probability of response in patients treated with azacitidine have not yet been defined. Itzykson *et al.*[3] recently reported on a large analysis of prognostic features at baseline in 282 MDS patients treated with azacitidine and found that a performance status of more than 2, presence of peripheral blasts, transfusion dependency of more than 4 units every eight weeks, and intermediate and poor risk karyotype, independently predicted poorer overall survival (OS). The authors created a prognostic score able to stratify patients into 3 risk groups (low, intermediate and high) and identify differences in OS; no mention of evaluation of comorbidities at baseline in these patients was made. We applied the MDS-CI score to 60 patients consecutively treated with azacitidine outside clinical trials at our institution. Our cohort was made up of 44 males and 16 females, median age 69 years (range 44-83). According to WHO classification, 35 patients were classified as refractory anemia with excess of blasts type 2 (RAEB-2), 13 patients as RAEB-1, 8 patients as refractory cytopenia with multilineage dysplasia (RCMD) and 4 patients as chronic myelomonocytic leukemia type 2 (CMML-2). IPSS stratification revealed an intermediate-2 risk in 51 patients and a high risk in 9 patients. Cytogenetic analysis revealed aberrations in 30 patients and a normal karyotype in the remaining 30; the most common karyotypic abnormality was monosomy 7 (10 patients, 20%) isolated or associated to complex changes. Seven patients were t-MDS: 5 of them had received chemotherapy for non-Hodgkin's lymphoma, one had been treated with chemotherapy for chronic lymphocytic leukemia and one for another neoplasia. Application of the MDS-CI score stratified patients into low risk with score 0 (32 patients), intermediate risk with score 1-2 (14 patients) and high risk with score over 2 (13 patients). In our series of patients, MDS-CI was able to retrospectively identify different overall survival from diagnosis: a median of 21 months for low risk, 11.9 months for intermediate risk and eight months for high risk (P=0.01). Independently from comorbidities, all patients were treated with the drug at the standard dose of 75 mg/m^2 with a 5+2+2 schedule. After a median of four cycles, according to 2006 IWG criteria,[4] 15 patients (25%) achieved a complete response (CR), 3 patients (5%) a partial remission (PR), 20 patients (33%) hematologic improvement (HI) and 7 patients (12%) stable disease. Fifteen patients (25%) experienced progression of disease. We applied the MDS-CI as a time-dependent score in patients who were still alive at one year (n=44) who had received at least four cycles of azacitidine. The score was again able to identify statistical differences in OS in spite of the use of the drug (23 months for low risk, 9.5 months for intermediate risk and six months for high risk, P=0.01). Apart from deaths from progression to acute leukemia, 6 patients died due to other causes during treatment: 4 patients for cardiac disease (3 patients with high risk and one with intermediate risk according to the MDS-CI), one patient for solid tumor relapse (intermediate risk) and another patient for chronic renal failure (high risk). As previously shown,[1,2] MDS-CI stratification at baseline is able to identify patients with worse outcome: our results demonstrate that also in patients treated with hypomethylating agents this score might be useful to identify at baseline subjects who have a greater chance of benefitting from this type of treatment.

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