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Commentary

The quest for the perfect MDS scoring system

Much has been said and discussed in the last few years, and discussions have increased in frequency during last months, over the need for optimization of prognostic scoring systems in myelodysplastic syndromes [1,2].

There are indeed some key points that we need to stress about this subject. These observations are shared at present by all MDS experts, but are not jet concretized in any score and not clear to general hematologists:

(1) There is an urgency for an integrated prognostic score including biological and individual patient parameters.
(2) Different weights have to be attributed to different biological and clinical parameters.
(3) The MDS prognostic score has to be applicable to all the therapeutic scenarios available at present for these syndromes.

The work of Pfeilstöcker et al. addresses and dissects very well the first two points, just touching the third one.

At least 20 different prognostic scoring systems have been produced and published [3–15], some in very distinguished international journals, and a plethora of tentative alternative scoring systems presented at meetings. Many Centers have developed a local scoring system and applied home developed parameters, which not always retain universal validity. The paper by Pfeilstöcker et al. published in this issue of the Journal is the first which compares directly, and in a critical manner the applicability of several MDS prognostic scores.

Even if we witnessed an "evolution" within prognostic scoring systems, prompted by the evident practical limitations of the previously published ones, there has never been an effort to technically compare head-to-head the different scores in order to validate their flexibility and their applicability during the course of the disease.

The parameters which retain significance overtime according to Pfeilstöcker et al. seem to be the ones depending directly from the biology of the disease, which are the cytogenetic alterations. We may foresee that the same prognostic value and weight will be attributed to molecular alterations, as recently demonstrated by Bejar et al. [16], which will soon need to be integrated in prognostic scores. This, of course, does not necessarily mean that cytogenetics is the only prognostic key for MDS. Evidently, as has been broadly and robustly demonstrated, percentage of blasts, transfusion dependency (or level of anemia), and co morbidities [17–19] retain their importance.

Nevertheless, it seems plausible that none of the most commonly applied scoring systems holds an absolute "quality supremacy", and the application of different prognostic scores during different phases of MDS looks like a concrete possibility. Not only this, but we should also consider applying one or another scoring system, depending on what we wish to predict: survival, trend to evolve (in terms of severity of cytopenias), progression to AML.

It appears quite clearly from the interesting and challenging analysis conducted by Pfeilstöcker et al. that flexibility and validity over time are not universal characteristics of the prognostic systems we apply at present. Some prognostic scores, in fact, include parameters which mutate during the course of the disease, thus weakening the score itself.

Whenever we read a manuscript presenting a new prognostic scoring system for MDS, we are brought by hand to consider the advantages of the present score over previous ones, the new important parameters included and previously neglected, but we are never presented with an exhaustive critical evaluation of the applicability of several scores in the same context. This is once again, the main novelty of the work of Pfeilstöcker et al.

At present, only a couple of prognostic systems are broadly applied. WHO-based scoring system (WPSS) [12] has been presented as a time-dependent tool, adjustable during the course of the disease, and it has the great advantage of indicating dysplasia (WHO classification) as a key prognostic feature, and transfusion need (now in WPSS-R, the more objective parameter of severity of anemia) [20], but in fact, does not include individual clinical parameters and it seems to lose strength over time. The same is true for IPSS, but, while we wait for future implementation of molecular alterations into MDS prognostic scores, we have to manage with what we have: will IPSS-R [21] lead the way of our therapeutic choice, giving a novel weight to cytogenetic abnormalities and what will be the position of WPSS-R, integrated with co morbidities indexes? [22].

Indeed, the importance of cytogenetics as major prognostic factor over time, during the course of MDS is supported and reinforced by recent evidence [23] and indirectly by the already mentioned evidences on the prognostic weight of mutations of p53, ASXL1, EZH2, ETV6, RUNX1 [16]. Factors intrinsic to the specific type of MDS are determinant for the outcome of the patient.

It is high time to open a broader discussion and work on the prognostic systems proposed until now, in order to develop a common, simple and universally applicable tool with which we should be able to evaluate our MDS patients at diagnosis and during sequential therapy, especially in relation to the different therapeutic options available, parameters which has been considered by few Authors, and still to be included in any MDS prognostic scoring system.

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