Partial and total monosomal karyotypes in myelodysplastic syndromes: Comparative prognostic relevance among 421 patients

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Myelodysplastic syndromes (MDS) include a group of heterogeneous hematological disorders with a variable risk of leukemic evolution and short survival. Around 40–50% of patients show abnormal karyotypes that are mostly characterized by monosomies or deletions. Cytogenetic findings are independent prognostic factors and the International prognostic scoring system (IPSS) differentiates three cytogenetic categories, despite the Intermediate one being heterogeneous. The aim of this study, including 421 Argentinean patients with primary MDS, is to characterize the cytogenetic profile, to test its prognostic value and to compare partial and monosomal karyotypes against other cytogenetic findings. An abnormal karyotype (median survival: 26 months) was observed in 176 patients. The presence of complex karyotypes, number of alterations, and the IPSS cytogenetic groups showed significant differences for predicting outcome. Behavior of patients with isolated deletions (median survival: 49 months) did not differ from those with normal karyotype (56 months, $P = 0.654$) or Good prognostic findings (43 months, $P = 0.371$). However, a worse prognosis was observed when another alteration was added (31 months, $P = 0.043$). Karyotypes with autosomal monosomies (median survival: 16 months) had a prognostic impact similar to other Poor cytogenetic findings (17 months, $P = 0.626$). In our population classified according to French-American-British (FAB) or World Health Organization (WHO), this new categorization of cytogenetic abnormalities, recognizing three different risk groups, showed an independent prognostic impact and a better discriminating power than the IPSS categories. It can be concluded that all isolate deletions (excluding $7q$-) are good prognostic findings and all monosomies (excluding Y chromosome loss) are bad indicators. Am. J. Hematol. 00:000–000, 2011. © 2011 Wiley-Liss, Inc.

Introduction

Myelodysplastic syndromes (MDS) comprise a heterogeneous group of bone marrow (BM) clonal disorders characterized by ineffective hematopoiesis leading to pancytopenia and variable risk of evolution to acute myeloid leukemia (AML) [1–3]. Although MDS has been recognized for more than 50 years, the first criteria for a systematic classification of MDS into five subgroups were defined in 1982 by the French–American–British (FAB) cooperative group on the basis of morphologic characteristics, percentage of BM blasts and peripheral monocye count [4]. In 1999, the World Health Organization (WHO) proposed a revised classification distinguishing nine categories, placing chronic myelomonocytic leukemia (CMML) and refractory anemia with excess of blast in transformation (RAEBt) among “myelodysplastic/myeloproliferative disorders” and AML, respectively [5]. This last classification has been recently reviewed redefining two additional categories [6].

Abnormal karyotypes are usually found in 26–56% of MDS [1–3,7,8]. They are not associated with any particular chromosomal alterations and are most often characterized by total or partial losses of chromosome material from chromosomes 5, 7, 13, 17, 20 or a sex chromosome, as well as a relatively high incidence of genetic gains such as trisomy 8, 19, and 21, while recurrent translocations or other structural abnormalities are rare.

The great variability in the natural history of MDS complicates decision-making regarding therapies. During the last 25 years, since the development of the Bournemouth index [9], different scores have been proposed for the prediction of the clinical outcome in these patients. The karyotype has been recognized as an independent predictor since 1993 when Lille system [1] confirmed that the presence of complex karyotypes (CK) was associated with poor prognosis. In 1997, the International prognostic scoring system (IPSS) [2] recognized three cytogenetic categories of risk including some particular cytogenetic alterations. This categorization was later adopted by the WHO classification-based prognostic scoring system (WPSS) [10]. However, the Intermediate group, including trisomy 8 and other chromosome alterations not specified, is heterogeneous and is matter of debate [3,7,11,12].

Recently, some deletions, which are usually found in a low frequency, have been related with a favorable outcome in MDS, such us deletion $9q$, $11q$, and $12p$ [3,13,14]. Also, monosomal karyotypes have been proposed as a better indicator of poor prognosis in AML, which refers to or more
distinct autosomal chromosome monosomies or one single autosomal monosomy in the presence of structural abnormalities [15]. Therefore, the aim of this study was to characterize the cytogenetic profile, to test its prognostic value and to compare partial and monosomal karyotypes against the rest of the cytogenetic findings characterized by the IPSS in the Argentinean MDS patients.

Methods

Patients. This is a multicenter retrospective analysis of 421 patients with available cytogenetic data at diagnosis evaluated from 1982 to 2010. Of these, 168 patients belong to the pilot study for MDS registry promoted by the Argentinean Society of Hematology. Patients without cytogenetic analysis (n = 20) or with failure of cytogenetic analysis (n = 47) were not included in this study. Hematologists from the participating institutions completed a standard registration form for each patient describing the clinical and hematological features at presentation and during the follow-up. Patients included in this study had a confirmed diagnosis of primary MDS, without documented previous radio- or chemotherapy, and fulfilled prerequisite criteria according to Valent et al., 2007 [16]. Refractory cytopenia was defined as a hemoglobin level of less than 10 g/dL, an absolute neutrophil count of less than 1.5 × 10^9/L, or a platelet count of less than 100 × 10^9/L [16]. Initially, all patients were categorized according to FAB [4] and 401 patients were also evaluated according to WHO [5]. Most patients received supportive care; chemotherapy was administered once the leukemic phase of the disease was diagnosed (62 patients) or for stem cell transplant (14 patients); 44 patients received hypomethylating agents and 8 lenalidomide. Infections, bleeding and leukemic evolution were considered as MDS-related causes of death. BM transplanted patients were excluded from survival analysis.

Cytogenetic analysis. Unstimulated BM cells were short term cultured and G-banding analyses were performed following standard procedures. Whenever possible, 20 metaphases were analyzed and 11 of them karyotyped according to the International System for chromosome nomenclature (ISCN) [17]. The following abnormalities were scored for each chromosome: loss of a chromosome (monosomy), partial loss of a chromosome (deletion), partial or total extra copy of a chromosome (partial or total trisomy), other structural cytogenetic abnormalities (inversion, translocation, addition of chromosomal material, derivative chromosomes from translocations -that frequently also encompassed partial losses and/or trisomies-, dicentrics, isochromosomes, and duplications), marker chromosomes, ring chromosomes and double minutes. Aberrations were counted following the International Working Group on MDS Cytogenetic Study (IWGMC) consensus guidelines [18].

Statistical analysis. The Kaplan-Meier estimates of survival were calculated from the day of diagnosis for each variable and compared using the log-rank test (Mantel-Cox) provided by SPSS software version 15.00 (SPSS, Chicago) and curves were plotted using GraphPad Prism version 4.00 (GraphPad Software, San Diego). The Cox proportional hazards model was applied to multivariate analysis using the enter method provided by SPSS software. The level of statistical significance was fixed at 0.05.

Results

Description of the population and clinical data

Table I provides a summary of the 421 patients demographic and clinical data at diagnosis: age, sex, % BM blast, number of cytopenias, FAB and WHO classification, IPSS and WPSS prognostic systems. The median age was 69 (17–93) years with a gender ratio of 1.3 (M/F: 238/183). During the follow-up (mean: 28 months, range: 1–266 months), 101 (24.1%) died from survival analysis.

Cytogenetic analysis

Among the overall 421 patients, 176 (42%) patients showed deletions or monosomies in their karyotypes and 104 (59%) cases involved, at least, one chromosome #5, #7, #8, or #20 (Supporting Information Table 1s). Abnormal karyotypes showed one, two, ≥3 aberrations in 121 (69%), 26 (15%), and 29 (16%) cases, respectively. In our series, it was observed that all chromosomes were involved and different cytogenetic alterations were found. From the overall 322 identified altered chromosomes: 109 (34%) showed deletions, 27 (18%) monosomies [total + partial losses = 166 (52%)], 78 (24%) total or partial trisomies, 78 (24%) other structural alterations. The most frequently involved chromosomes were #5 (41 cases), #7 (32), #8 (38), #11 (14), #17 (13), #20 (26), and Y (14). The most common cytogenetic aberrations were: del(5q) (29 cases, 17.0% of patients with abnormal karyotype), –7/del(7q) (28, 16.0%), +8 (38, 22%), del(20q) (16, 9%), +21 (8, 5%), Y chromosome loss (4, 8%) and other structural anomalies that involved chromosomes #1 (7, 4%), #3 (7, 4%), and #11 (5, 9%) (Fig. 1; Supporting Information Table 2s) It is remarkable that chromosome 8 was only implicated in total trisomies. Also, marker chromosomes, ring chromosomes and doubles minutes were observed in 16, 2, and 1 cases, respectively.

Analysis of prognostic factors and cytogenetic groups of risk

Almost all analyzed variables, gender, number of cytopenias and percentage of BM blast, FAB and WHO classifications, IPSS and WPSS systems showed significant differences for predicting survival (Table I).

Cytogenetic findings had a clear impact on the outcome of our patients (Table II, Fig. 2). Patients with an abnormal karyotype showed a significant worse outcome than those with a normal karyotype either including or excluding 11 patients with Y chromosome loss (P < 0.001). Among patients with an abnormal karyotype (not including Y chromosome losses), those involving ≥3 altered chromosomes [1], the presence of ≥2 aberrations [19] and cytogenetic category of risk according to IPSS [2] (Fig. 2A) showed significant differences for predicting survival (Table II).

Seven patients showed an isolated autosomal monosomy, all of them were losses of chromosome 7 (Supporting Information Table 2s), with a median survival of 15 months. Monosomalous karyotype, as was defined by Breems et al. [15], was observed in 23 patients with a median survival of 16 months. Due to the reduced number of cases with an isolated monosomy 7 and the lack of differences between them in terms of survival (P = 0.890), they were later analyzed as one group of monosomal karyotype (MK+). Patients without monosomal karyotypes (MK−) and non complex karyotypes (CK−) showed better outcome (median survival: 32 months) than the rest of the patients (P < 0.001). Patients with MK+ exhibited a similar behavior than those with CK+ (P = 0.866) (Fig. 2B). Also when MK+ group (median survival: 16 months) was compared against other poor findings according to the IPSS (median survival: 17 months) no differences were observed in terms of survival (P = 0.626; Fig. 2C). A statistical comparison (Fisher’s exact test) of the distribution of both groups according to WHO (P = 0.3451), FAB (P = 0.5471), IPSS (P = 1.000), and WPSS (P = 0.8026) was performed showing similarities (Table I). Therefore, MK+ was grouped together with other Poor prognostic findings.

In the Intermediate risk group, 30 patients presented deletions in their karyotypes (median survival: 42 months) and showed no difference in terms of survival when compared against other Intermediate findings according to the IPSS (27 months, P = 0.504). However, 19 patients who presented isolated deletions exhibited a better outcome...
Variables | Normal + Y Lost | Good | Deletions, NC | Other intermediate | Monosomalous karyotype | Poor nonsomalous | Total (%) | Events # | Median (months) | P value
---|---|---|---|---|---|---|---|---|---|---|---|
Age (years) | 71 | 71 | 62 | 65 | 65 | 64 | 69 | | | |
Median | 67 ± 16 | 66 ± 14 | 60 ± 14 | 65 ± 12 | 61 ± 14 | 58 ± 19 | 65 ± 16 | | | |
>60 | 189 (74) | 22 (62) | 18 (60) | 35 (63) | 19 (63) | 13 (59) | 296 (70) | 131 | 34 | =0.180 |
<60 | 67 (26) | 5 (19) | 12 (40) | 21 (38) | 11 (37) | 9 (41) | 125 (30) | 62 | 32 | |
Sex | Female | 113 (44) | 13 (48) | 15 (50) | 19 (36) | 13 (43) | 10 (46) | 183 (44) | 67 | 60 | <0.001 |
Male | 143 (56) | 14 (52) | 15 (50) | 37 (66) | 17 (57) | 12 (55) | 238 (56) | 126 | 29 | |
BM Blast (%) | <5 | 180 (70) | 21 (78) | 14 (47) | 39 (70) | 8 (27) | 10 (46) | 272 (65) | 92 | 62 | <0.001 |
5–9 | 34 (13) | 4 (15) | 6 (20) | 9 (16) | 4 (13) | 5 (23) | 62 (15) | 36 | 26 | |
10–19 | 32 (13) | 2 (7) | 6 (20) | 5 (9) | 12 (43) | 5 (23) | 62 (25) | 45 | 17 | |
>19 | 10 (4) | – | 4 (13) | 4 (12) | 6 (20) | 2 (9) | 25 (6) | 20 | 8 | |
N' Cytopenias | 0–1 | 155 (61) | 16 (59) | 16 (53) | 34 (61) | 8 (27) | 6 (27) | 235 (56) | 87 | 59 | <0.001 |
2–3 | 101 (40) | 11 (41) | 14 (47) | 21 (38) | 22 (73) | 16 (73) | 185 (44) | 106 | 25 | |
FAB | RA | 137 (54) | 20 (74) | 11 (37) | 28 (50) | 7 (23) | 5 (23) | 208 (49) | 62 | 75 | <0.001 |
RARS | 23 (9) | 1 (4) | 1 (3) | 7 (13) | – | 4 (18) | 36 (9) | 13 | 64 | |
RAEB | 54 (21) | 5 (19) | 10 (33) | 12 (21) | 14 (47) | 8 (36) | 103 (25) | 68 | 19 | |
RAEBI | 10 (4) | – | 4 (13) | 3 (5) | 6 (20) | 2 (9) | 25 (6) | 20 | 9 | |
CMMI | 32 (12) | 1 (4) | 4 (13) | 6 (11) | 3 (10) | 3 (14) | 49 (12) | 30 | 25 | |
WHO | RA/RARS|Sq-CMML | 15 (7) | 12 (48) | 2 (10) | 4 (11) | 2 (11) | 1 (6) | 36 (11) | 14 | 64 | <0.001 |
RCMD/–RS | 116 (47) | 8 (36) | 6 (30) | 26 (59) | 3 (16) | 8 (50) | 167 (51) | 49 | 70 | |
RAEB-I | 24 (12) | 4 (16) | 4 (20) | 7 (16) | 3 (16) | 2 (13) | 44 (13) | 28 | 26 | |
RAEB-II | 31 (15) | 1 (8) | 6 (30) | 6 (14) | 11 (6) | 5 (31) | 60 (18) | 41 | 18 | |
MDS-U | 18 (8) | – | 2 (10) | 1 (2) | – | – | 19 (6) | 4 | 121 | |
IPSS | Low | 121 (49) | 13 (50) | – | – | – | – | 134 (33) | 26 | 80 | <0.001 |
Intermediate-I | 92 (36) | 12 (46) | 17 (57) | 39 (72) | 4 (13) | 2 (10) | 166 (41) | 76 | 43 | |
Intermediate-II | 26 (10) | 1 (4) | 7 (23) | 9 (16) | 9 (30) | 14 (67) | 66 (16) | 44 | 20 | |
High | 9 (4) | – | 6 (20) | 6 (11) | 17 (57) | 5 (24) | 43 (11) | 36 | 10 | |
WPSS | Very low/Low | 85 (48) | 14 (64) | 1 (6) | 2 (5) | – | – | 102 (35) | 15 | 126 | <0.001 |
Intermediate | 50 (28) | 3 (14) | 5 (28) | 10 (26) | 3 (16) | – | 71 (25) | 31 | 51 | |
High | 42 (24) | 5 (23) | 9 (50) | 22 (58) | 3 (16) | 8 (57) | 89 (31) | 52 | 23 | |
Very high | – | – | 3 (17) | 4 (11) | 13 (68) | 6 (33) | 26 (9) | 22 | 14 | |

NR: Not reached; NC: noncomplex; *: Log-Rank test (Mantel-Cox); RA: Refractory Anemia; RARS: RA with Ringed Sideroblasts; RAEB: RA with Excess of Blast; RCMD: refractory cytopenia with multilinear dysplasia; RCMD-RS: RCMD with Ringed Sideroblasts; MDS-U: MDS unclassifiable.

aData on dysplasia was not available in 20 patients diagnosed as RA according to FAB.

deletions were placed together with Good prognostic findings when deletions plus other alteration remained into the Intermediate ones.

This new categorization of karyotypes, where all isolated deletions were placed into good prognostic findings and monosomalous karyotypes among the worse ones, allowed us to better discriminate three groups of risk than the original IPSS distributions (Tables II and III, Fig. 2D). Multivariate analysis confirmed that the new characterization of cytogenetic findings was an independent predictor for survival when tested versus % BM blast. Also, when analyzed versus the IPSS categorization it showed significant differences for the overall FAB classified population [*P = 0.024, exp(B) 1.452] and a borderline difference for the population classified by WHO [P = 0.063, exp(B) 0.1499] (Table III).

Discussion

Cytogenetic studies have been recognized as an independent prognostic factor in MDS since 1993 [1] and their inclusion among different prognostic systems has contributed to the improvement in assessing prognosis.

In our population, the observed frequency of normal karyotypes was 58%, similar to other reports [2,10,12,20,21]. This frequency varied in a wide range of 44–74% in different published MDS series and this may be related to difficulties in assessing and discriminating between regional variations,
differences in classification, and the inclusion/exclusion of therapy-related MDS, AML, or of pediatric cases. Several differences have been reported between western and Asian groups, but, little is known about the epidemiological patterns of MDS in Latin American regions [8,12,21–23]. Most series usually include patients classified according to FAB. The proportion of normal karyotypes in each FAB subgroup decreased according to worsening prognosis FAB subgroup from 64% in RA to 36% in RAEBt patients. However, the low frequency of 6% of RAEBt patients in our series is remarkable, being less than half of the usually observed percentages in other reports. From the time the WHO classification was published, Argentinean clinicians generally choose to classify RAEBt patients as having AML. The prevalence of IPSS in 2007 [10]. However, the Intermediate group according to the IPSS is heterogeneous, including chromosome alterations not specified that are usually found in a

patients (%) Median (months) *P value

Karyotypes
Normal + Y lost 256 (61) 102 56 *<.001
Abnormal 165 (39) 91 26

Abnormal karyotypes N = 165
N’ Altered chromosomes (Lille, 1993) 172 (63) 74 28 *=0.037
1 + 2 chromosomes 38 (27) 28 19
> 3 chromosomes 110 (67) 61 32 *=0.002
1 aberration 55 (33) 41 17
IPSS (International Prognostic Scoring System, 1997) Good risk findings 27 (16) 12 43 <.001
Intermediate risk findings 90 (55) 53 31
Poor risk findings 48 (29) 37 16
Monosomal karyotype (Breems et al., 2008) MK – CK– 123 (75) 68 32 <.001
MK – CK+ 12 (7) 10 18
MK + CK– 13 (8) 11 15
MK + CK+ 17 (10) 13 16
Abnormalities Good 27 (16) 12 43 =0.141
Intermediate
Deletions (Isolated) 19 (12) 8 49
Deletions + Other alteration 11 (7) 7 31
Other intermediates 56 (34) 34 27
MK 30 (18) 24 16
Poor non MK 22 (13) 17 17
Re-categorization of cytogenetic findings
IPSS Good risk findings + isolate deletions 46 (28) 20 50 <.001
Other Intermediates risk findings 67 (41) 41 27
IPSS Poor risk findings + MK 52 (32) 41 16
Overall Population N = 421
Cyto genetic group of risk according to the IPSS
Good risk findings 283 (67) 103 56 =.009
Intermediate risk findings 90 (21) 53 31
Poor risk findings 48 (11) 37 16
Re-categorization of cytogenetic findings
IPSS Good risk + isolate deletions 302 (72) 111 54 <.001
Other Intermediates risk findings 67 (16) 41 27
IPSS Poor risk findings + MK 52 (12) 41 16

MK: Monosomal karyotype, CK: Complex karyotype.
* 11 patients with Y chromosome lost were considered together with 245 cytogenetically normal MDS patients.

The number of cytopenias, percentage of BM blast, gender, FAB and WHO classifications, IPSS and WPSS prognostic systems showed significant differences for predicting outcome in our population (Table I). Also, the subdivision of karyotypes into risk subgroups according to three systems exhibited significant differences stratifying patients with abnormal karyotypes into cytogenetic groups of risk with different life expectancies (Table II) [1,2,19]. Lille system [1] divided the presence CK versus other alterations while Lausanne-Bournemouth index [19] includes among bad prognostic karyotypes the presence of two aberrations. The above mentioned studies did not explain the predictive significance of the types of cytogenetic abnormalities, considering that deletions and monosomies usually affect more than 50% of abnormal karyotypes in MDS, as was observed in our series. In 1997, the IPSS [2] recognized that some deletions (5q-, 20q-, and 7q-) and monosomy 7 were associated with specific prognosis allowing us to differentiate three different cytogenetic categories of risk. This modality of grouping karyotypes was adopted for the WPSS in 2007 [10].
very low frequency while other authors tried to determine the significance of some of these findings [3,7,11,13,14].

In our series, patients with deletions from the Intermediate group shared the same prognosis as the rest with Intermediate findings. However, when they were divided, isolated deletions showed a similar behavior than in patients with normal karyotype and than those with del(5q) or del(20). These findings are in agreement with recent reports suggesting that del(12p), del(9q), del(11q) isolated are associated with good prognosis [3,13,14]. Although most of these deletions were found in a very low frequency in our series, patients with del(12p) showed a good outcome (median survival of 60 months), similar to these other reports [3,13,14]. Monosomal karyotypes have been proved to be a better prognostic indicator of poor prognosis in a series of 1975 AML patients [15]. When we tried to ascertain whether the presence of a monosomal karyotype had a worse prognostic impact, the behavior of this group was similar to the presence of a CK with or without monosomies, indicating a comparable prognostic impact.

**Figure 2. Cytogenetic Group of Risk of all abnormal Karyotypes not including Y chromosome losses (Survival plots, Kaplan–Meier curves Mantel Cox) [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]**

**TABLE III. Multivariate Analyses for Survival**

<table>
<thead>
<tr>
<th>Categories</th>
<th>Degree of freedom</th>
<th>$P$ value</th>
<th>Exp (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FAB</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPSS good risk findings + Isolate deletions</td>
<td>2</td>
<td>&lt;0.001</td>
<td>0.401</td>
</tr>
<tr>
<td>Other intermediate risk findings</td>
<td>1</td>
<td>&lt;0.001</td>
<td>0.522</td>
</tr>
<tr>
<td>IPSS poor risk findings + MK</td>
<td>1</td>
<td>&lt;0.001</td>
<td>0.119</td>
</tr>
<tr>
<td>BM blast (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>3</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>5–9</td>
<td>1</td>
<td>&lt;0.001</td>
<td>0.293</td>
</tr>
<tr>
<td>10–19</td>
<td>1</td>
<td>&lt;0.001</td>
<td>0.503</td>
</tr>
<tr>
<td>&gt;19</td>
<td>1</td>
<td>&lt;0.014</td>
<td></td>
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<tr>
<td>New categories of risk</td>
<td>1</td>
<td>&lt;0.024</td>
<td>1.452</td>
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<tr>
<td>IPSS categories of risk</td>
<td>1</td>
<td>&lt;0.951</td>
<td>0.991</td>
</tr>
<tr>
<td><strong>WHO</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>New cytogenetic categories of risk</td>
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<td></td>
<td></td>
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<tr>
<td>IPSS good risk findings + Isolate deletions</td>
<td>2</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>Other intermediate risk findings</td>
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<td>&lt;0.001</td>
<td>0.353</td>
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<td>IPSS poor risk findings + MK</td>
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<td>&lt;0.027</td>
<td>0.546</td>
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<tr>
<td>BM blast (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;5</td>
<td>2</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>5–9</td>
<td>1</td>
<td>&lt;0.001</td>
<td>0.237</td>
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<td>10–19</td>
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<tr>
<td>IPSS categories of risk</td>
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<td>&lt;0.919</td>
<td>0.978</td>
</tr>
</tbody>
</table>

BM: Bone marrow; MK: Monosomal karyotype.
findings that all isolate deletions (excluding 7q-) are good prognostic findings and that all monosomies (excluding Y chromosome loss) are bad indicators. This new categorization of cytogenetic alterations, where three groups of risk have been identified, showed an independent prognostic assessment and a better discriminating power that the original IPSS categories of risk in our population classified according to FAB or WHO.

It can be concluded that cytogenetic findings had a clear impact on the clinical outcome and that the data analyzed in the present series, the largest in Latin America, are coincident with recently published data suggesting that the intermediate cytogenetic group according to the IPSS should be redefined.

Acknowledgments

The authors thank the investigators of the Argentinean MDS’s Study Group organized by the Argentinean Society of Hematology for the use of the Pilot Study for MDS Registry database and Dr. Christine Dosne de Pasqualini, PhD for revising the manuscript.

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