replace splenectomy as a good palliative procedure, especially in elderly patients or those with concomitant disease in whom the risks of this procedure are of concern.

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Multiple Myeloma

Correlation between fatigue and hemoglobin level in multiple myeloma patients: results of a cross-sectional study

This cross-sectional study showed a positive correlation between fatigue-related quality of life, evaluated with the FACT-An questionnaire, and hemoglobin level in 1071 patients with multiple myeloma. Multiple regression analysis adjusting for several covariates was used. Improved FACT-An scores in women and men were associated with hemoglobin increase up to sex-specific normal values.

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Anemia is a very common finding in hematologic malignancies including multiple myeloma (MM), and is especially severe in patients with recurrent disease or during chemotherapy.[1] Improved quality of life (QOL) is correlated with increased hemoglobin concentration,[2-6] independently of tumor response.[2,3] The objective of this cross-sectional study was to further examine the relationship between fatigue-related QOL, hemoglobin level and other characteristics in MM patients.

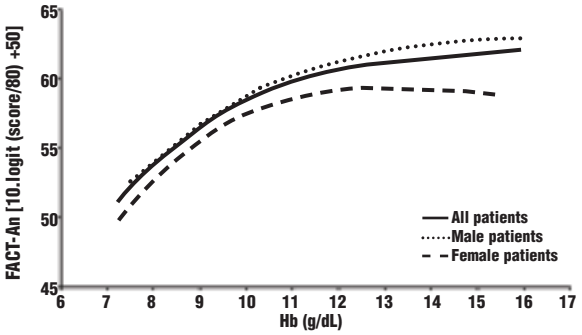

Figure 1. FACT-An scores and hemoglobin levels: multiple logistic regression using third-order polynomials.

All MM outpatients admitted in 24 Italian centers between November 2001 and March 2002 were included. Patients' demographic and clinical data were collected, and the Functional Assessment of Cancer Therapy - Anemia (FACT-An), a 20-item questionnaire measuring fatigue-related QOL,[7] was administered. Raw FACT-An scores were calculated[8] and logit-transformed to obtain approximately normal distributions. The regression of FACT-An scores on hemoglobin was studied using polynomials of increasing order until achieving the maximum adjusted R^2. Other factors, as well as two-way interactions, were tested for addition (if $p<0.05$) into a multiple regression model. Treatment center and its interactions with other model factors (fixed effects) were added as random effects. Data analyses were performed using SAS®.

Of 1071 consecutive patients enrolled, hemoglobin and FACT-An data were available for 1046 (Table 1). The median disease duration was 23 months. MM treatment had previously been administered to 76.6% of the patients and included bone marrow transplant in 31.2%. Treatment was ongoing in 72.0% (chemotherapy with corticosteroids 25.8%, chemotherapy only 11.8%, corticosteroids only 8.5%, interferon 15.7%, thalidomide 10.9%, bisphosphonates 8.4%), while 16.6% were receiving erythropoietin. The mean hemoglobin (Hb) concentration was 11.90 g/dL (SD 1.87, range 6.4-17.0, median 12.0) and 6.1% of the patients were transfusion-dependent. Mean raw FACT-An scores were 56.3 overall (median 60), 36.4 for the fatigue subscale (median 39), and 20.0 for the non-fatigue items (median 21). The FACT-An scale showed good internal consistency (Cronbach's α 0.83). The median raw FACT-An scores increased from 45 for Hb $\geq$ 9 g/dL to 64 for Hb > 14 g/dL. The linear regression coefficient of logit-transformed scores on hemoglobin was 1.36 (standard error 0.135, Pearson's r 0.297, $p=0.0001$). Score improvements per hemoglobin increase were progressively lower, however, and a third-order polynomial best fitted the data (R^2 0.103, i.e. explaining 10.3% of FACT-An score variability versus 8.8% of linear regression). This regression pattern was still observed (Figure 1) after adjusting for other factors (Table 1). The main ($p<0.01$) independent predictors of lower FACT-An scores besides anemia were female sex, older age, unfavorable response, advanced stage and concurrent illness (Table 1). Two-way interactions between factors, including hemoglobin concentration, were not significant. The model R^2

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Table 1. Hemoglobin levels and multivariate-adjusted FACT-An scores according to patients' characteristics.

	Frequency %	Hb (g/dL) Mean±SD	FACT-An score Mean (CI_{95})	*Adjusted for other factors p value
Hb+Hb²+Hb³				0.0001@
Sex				0.0002§
Male	50.8	12.18±1.97	60.5 (58.6–62.3)	
Female	49.2	11.59±1.73	57.2 (55.1–59.2)	
Age (†)				0.011§
				0.0012@
≤65 years	50.8	12.13±1.90	60.0 (58.0–61.9)	
> 65 years	49.2	11.66±1.82	57.8 (55.7–59.8)	
Response phase				0.0029§
Complete remission	11.4	12.83±1.56	62.3 (59.6–64.8)	
Partial or unspecified remission	45.5	12.26 ± 1.64	58.8 (56.5 - 60.9)	
No response	6.4	10.67±2.00	58.4 (54.7–61.8)	
Relapse	15.3	11.20±2.02	55.3 (52.3–58.2)	
New diagnosis	21.4	11.56±1.92	59.7 (57.1–62.0)	
MM Stage (Durie and Salmon)				0.014§
				0.0054@
I	15.6	12.47±1.63	61.3 (58.9–63.6)	
II	26.3	11.93±1.86	59.7 (57.5–61.7)	
III	58.1	11.72±1.91	58.0 (56.0–60.0)	
Concurrent disease				0.0009§
No	62.7	11.90±1.87	60.4 (58.4–62.2)	
Yes (°)	37.3	11.89±1.88	56.7 (54.3–58.9)	
Working status				0.025§
Outside job	27.0	12.38±1.76	60.7 (58.4–62.9)	
No outside job	73.0	11.72±1.90	58.2 (56.3–60.1)	

*SD: standard deviation; CI_{95}: confidence interval with 1-α = 0.95. *transformed as 10.logit(x)+50 when 0<x<1, 0 when x=0, 100 when x=1, x being the ratio between the score and its maximum possible value 80, and converted back to the original FACT-An scale. † range 31-94, mean 64.6, SD 10.1 years. °hypertension 11.4%, other cardiovascular diseases 8.6%. §as categorical variable. @as numerical (continuous or ordered) variable.*

of 0.227 was contributed by hemoglobin 0.046, concurrent disease 0.033; response phase 0.029, sex 0.014, stage 0.008, age 0.006, working status 0.006, and combinations of these factors 0.085. Transfusion dependence, disease duration, creatininemia, marital status, previous bone marrow transplant, and concomitant antineoplastic therapy did not significantly improve the model. WHO performance score (0, 48.5%; 1, 29.2%; 2, 11.5%; 3, 5.2%; 4, 0.4%; missing, 5.3%), although highly correlated with FACT-An score (Spearman's r -0.47, p=0.0001), was considered an independent assessment rather than a predictor of patients' well-being, and was therefore excluded from the model. FACT-An scores in women increased as hemoglobin increased until about 12 g/dL, whereas in men a limited increase was still detected for hemoglobin beyond 14 g/dL (Figure 1), consistent with respective normal values.

Previous cross-sectional regression analyses assumed a linear QOL-Hb relationship.[4,5] In this study non-linear analysis was made possible by the large sample size and the wide range of hemoglobin values. Tumor-type homogeneity removed a major potential confounder while other confounders were controlled by multivariate analysis, and skewed distribution of FACT-An scores, a common ceiling-effect product[9] that can limit model validity, was overcome by transforming the raw data. The results obtained strengthen previous evidence of a positive relationship between fatigue-related QOL and hemoglobin concentration[2-6] and of an attenuated, though continued, QOL improvement for hemoglobin values increasing towards normal,[6,10] while addressing the issue of further characterizing the potential benefit by sex.[10] We recognize that, although strongly correlated with more comprehensive QOL indices,[7] FACT-An scores essentially measure the impact of anemia on the aspects of QOL more closely related to fatigue, while emotional and social aspects are involved indirectly and to a lesser extent. Moreover, as only outpatients were included, symptomatic bone disease was possibly underrepresented, as also suggested by limited bisphosphonate use; the role of hemoglobin in determining FACT-An scores may be reduced by the overwhelming impact of severe bone pain. In spite of these limitations, our results support the hypothesis that correction of anemia until sex-specific normal hemoglobin values are attained is likely to improve fatigue-related QOL in MM patients.

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Platelets

Retrospective analysis of 472 Chinese children with chronic idiopathic thrombocytopenic purpura: a single center experience

We retrospectively analyzed the clinical characteristics and management of 472 Chinese children (age 1~14 years) with chronic idiopathic thrombocytopenic purpura (ITP). The distribution of cases by age showed a maximum at 4 years and more patients below 7 years old than between 7 and 14 years old had ITP (337, 71.4% vs. 135, 28.6%). Variable bleeding signs occurred in this series of patients. Steroids therapy was effective for Chinese children with chronic ITP whether as first- or second-line therapy. Traditional Chinese medicine was less effective than steroids.

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Idiopathic thrombocytopenic purpura (ITP) is a disorder characterized by platelet destruction caused by an anti-platelet antibody that results in platelet phagocytosis via the reticuloendothelial system.[1,2] Several papers involving children with chronic ITP have been reported,[3,4] however, a large-scale experience of Chinese children with chronic ITP has not been reported. To explore the clinical characteristics and management of Chinese children with this condition, we retrospectively analyzed 472 consecutive Chinese children (age 1-14 years) with chronic ITP diagnosed in our hospital from January 1980 to December 2000. The diagnosis of ITP was based on the previously reported criteria[5] except the cut-off age was 14 years in this study. The data were analyzed by SPSS10.0 statistical software. The response to therapy was calculated by the χ^2 test. A p value <0.05 was considered statistically significant. Of the 472 cases, we found a slight predominance of boys (256, 54.2%)over girls (216, 45.8%). The distribution of cases according to age (Figure 1) showed a maximum at 4 years old and more patients below 7 years old than between 7 and 14 years old had chronic ITP (337, 71.4% vs. 135, 28.6%). Our findings

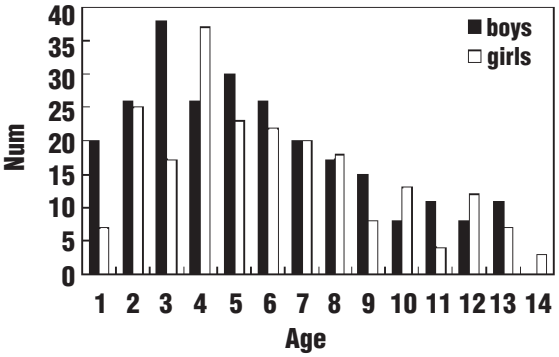

Figure 1. The distribution of chronic ITP in children of different gender and age.

are similar to those reported by Kuhne *et al.*[6] who compared Vietnamese and European cohorts of patients. However, our series showed that the frequency of boys with chronic ITP below one year of age (20 cases) was higher than that of girls (7 cases). This might be due to referral bias, because our hospital is the only one specialized in blood diseases in China, and those patients who were refractory to first-line therapy or who relapsed were usually referred to our hospital. Of the 382 patients for whom data were available, 117(30.6%), 96 (25.1%), 82 (21.5%) and 87 (22.8%) patients had the initial diagnosis made in spring, summer, fall, and winter respectively. At diagnosis, of the 277 patients for whom data were available, there were 147 (53.1%) boys and 130 (46.9%) girls with a mean platelet count of 32.93±21.56×10^9/L (range 2-90×10^9/L) and 34.35±21.15×10^9/L (range 1-90×10^9/L), respectively. Initial platelet counts of <20×10^9/L were found in 50 boys (34.0%) and in 45 girls (34.6%). The difference of platelet counts between boys and girls was not statistically significant (p>0.05). The vast majority of children had mild bleeding symptoms. Purpura and petechiae (430 cases, 91.1%), epistaxis (231 cases, 48.9%) as well as gum bleeding (79 cases, 16.7%) were often seen. No definitive statistical difference was found in the type of bleeding. Intracranial hemorrhage (ICH) occurred in two children (0.4%): one case in a boy 3 months after splenectomy (no platelet count recorded at that time; platelet count 26×10^9/L on the day he was referred to our hospital) who died from a recurrent ICH one year later; the other case in a girl with a platelet count of 6×10^9/L. Our data agree with Iyori's findings on the risk of ICH in Japanese children.[7]

Patients were treated with steroids, intravenous immunoglobulin (IVIG), immunosuppressive agents or traditional Chinese medicine (TCM). Patients who failed the initial therapy received open splenectomy, steroid and/or TCM as a second therapy. Treatment response was defined as follows: complete response (CR): a platelet count ≥100×10^9/L persisting for at least 2 months with no maintenance therapy; partial response (PR): a platelet count between 50-100×10^9/L; and no response (NR): a platelet count < 50×10^9/L. Three-hundred and twenty-four (68.6%) children received first-line therapy (Table 1). Two hundred and thirty-four (72.2%) had been followed up for more than 6 months and 167 (51.5%) for more than 12 months. There were significant differences between steroid treatment and TCM treatment (p<0.005)

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