Comparison of existing prognostic models in chronic myelomonocytic leukemia

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To the Editor: Chronic myelomonocytic leukemia (CMML) is characterized by both myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPNs).[1] The rare incidence of CMML leads to the difficulty to establish the standard criteria of diagnosis and specific treatment paradigms, and the accurate prognostic scores are required for appropriate treatment paradigms.

The existing prognostic scores mainly included: CMML-specific prognostic scores (CPSS), CPSS Model (CPSS-MOL), MD Anderson prognostic scoring system (MDAPS), Global MDAPS (G-MDAPS), Groupe Francophone des Myélodysplasies (GFM), and Mayo molecular model (MMM).[1-3] These scores were based on relatively large samples (range 213–578 cases) and combining characteristics of MDS and MPN. Furthermore, CPSS-MOL, GFM, and MMM incorporating gene mutations may be more accurate. However, the uniform criteria were lacked. There were some shortcomings: First, varied prognosis scores may have a difference in predicting overall survival (OS) and transformation to acute myeloid leukemia (AML). Second, further study for mutations and their prognostic relevance is necessary. Third, whether existing scores apply to some special types like CMML with fibrosis or extramedullary diseases or not.[1,2] To verify the validity of existing prognostic models, different scores were evaluated to explore the correlation of prognostic scores and possible risk factors and verify whether these scores can predict the incidence of extramedullary infiltration.

A total of 45 CMML patients admitted to our hospital from 2008 to 2019 were recruited and provided written consent for study participation. Routine tests included white blood cells (WBCs), hemoglobin (Hgb), and platelets (PLTs), smear morphology, bone marrow staining, lactate dehydrogenase (LDH). The biopsy of spleens, the hematoxylin-eosin staining for skin infiltration or myelofibrosis, CMML-specific molecular risks were also tested. SPSS 22.0 (SPSS Inc, Chicago, IL, USA) statistical software was applied to analyze the data.

Totally, 45 CMML patients with an average age of 65 years (range 18–83 years) were evaluated. One patient just had the result of bone marrow puncture in medical records; however, the specific report was lost. The remaining 44 patients were divided as follows: CMML-0 was diagnosed in 16 patients, CMML-1 in eight patients, and CMML-2 in 20 patients. The median OS was 265 days (range 20–1565 days). The median WBCs, Hgb, PLTs, and LDH were 30.16×10^9/L, 80 g/L, 59×10^9/L, and 345 U/L, respectively. CMML with infiltration of spleen and skin were identified in 16 patients (35.6%) and two patients (4.4%), respectively. Myelofibrosis was observed in one patient (2.2%). Thirteen patients (28.9%) and 23 patients (51.5%) received decitabine and conventional chemotherapy (cytoreductive drugs, HAG/CAG regime including homoharringtonine, cytarabine, granulocyte colony-stimulating factor [G-CSF]/cytarabine, aclarubicin, and G-CSF), respectively. Eleven patients (24.4%) converted to AML during follow-up time and more than half of the patients (23/45, 55.1%) were dead in 1 year.

WBCs ($P = 0.001$), French-American-British sub-type ($P = 0.004$), LDH ($P = 0.013$), and CMML-specific cytogenetic risk ($P = 0.002$) were independently adversely with prognosis. CMML-specific cytogenetic risk ($P = 0.002$), World Health Organization (WHO) sub-types ($P = 0.034$), G-MDAPS ($P = 0.023$), CPSS ($P = 0.008$), and CPSS-MOL ($P = 0.007$) were significantly associated with OS. Multivariate analysis showed WBCs ($P = 0.002$), LDH ($P = 0.016$), CMML-specific cytogenetic risk ($P = 0.005$) caused unfavorable OS. CPSS (area under roc curve [AUC] = 0.668) and CPSS-MOL (AUC = 0.625) were significantly better at predicting the risk of AML transformation, but G-MDAPS (AUC = 0.749) can identify risk of death. There was no significant difference between extramedullary infiltration and prognostic scores,

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000000637

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Chinese Medical Journal 2020;133(4)

Received: 01-10-2019 **Edited by:** Peng Lyu

though the WHO sub-group showed a weak correlation (Spearman correlation coefficient: 0.327, $P = 0.028$).

The traditional prognostic models included both MDS models (like international prognostic scoring system) and specific CMML models (like MDAPS). More recently developed prognostic models of CMML integrating somatic mutations could predict better. Mayo prognostic model integrated absolute monocyte count, presence of circulating immature myeloid cells, Hgb, and PLTs without somatic mutations. GFM found anemia, leucocytosis, thrombocytopenia, age >65 years, and ASXL1 mutation have an inferior OS. To further verify the prognosis of ASXL1 mutations, the original Mayo prognostic model was refined and included ASXL1 mutation to MMM. CPSS identified cytogenetic abnormalities adversely impact OS and risk of AML transformation, and a modified version of CPSS with higher accuracy added mutations of RUNX1, NRAS, SETBP1, and ASXL1. Specific prognostic models of CMML with their relevant components are shown in Table 1.[1,2]

"Proliferative" CMML can be seen as extramedullary infiltration like splenomegaly, which sporadically infiltrates skin, meningeal, gingiva, kidneys, pleuro-pericardic, and so on.[2,4] Splenomegaly leads to the inferior OS after receiving hypomethylating agents. Skin infiltration was diagnosed by skin biopsy and possibly causes AML transformation.[5] Meningeal infiltration can manifest as headache, ocular disorders, and facial numbness. A number of mature and abnormal monocytes can be seen on lumbar puncture and may disappear after remission.[4]

Overall, the study verified the importance of different prognostic models and realized the necessity of biopsy of CMML with extramedullary infiltration and fibrosis, though it was limited by small sample size and retrospective nature. Although CMML identified diagnosis code, there is no satisfactory treatment. Hence, an effective predictive tool to overcome the limitations of the current prognostic models is obviously required.

Table 1: Prognostic models and their specific risk stratification in chronic myelomonocytic leukemia.

Parameters	MDAPS (score)	G-MDAPS (score)	CPSS (score)	GFM (score)	MMM (score)	CPSS-MOL (score)
General						
Age (years)		60–64 (1)/≥65 (2)		>65 (2)		
RBC-TD		Yes (1)	Yes (**1**)			Yes (1)
Complete blood count						
WBC ($\times 10^9$/L)		>20 (**2**)		>15 (**3**)		>13 (1)
Hb ($\times 10^9$/L)	<120 (1)	<120 (**2**)		Anemia (**2**)	<100 (1)	
PLT ($\times 10^9$/L)		<30 (**3**)/30–49 (**2**)/50–199 (**1**)		<100 (**2**)	<100 (1)	
Blasts in BM (%)	≥10 (1)	5–10 (**1**)/11–29 (**2**)				≥5 (1)
Other						
AMC ($\times 10^9$/L)					>10 (1)	
ALC ($\times 10^9$/L)	>2.5 (1)					
Presence of IMCs	Yes (1)				Yes (1)	
Clinical performance		Poor performance (**2**)*				
Gene mutation/ chromosomal abnormalities		Complex karyotype/ Chromosome 7 abnormality (**3**)	L (**0**)/I (**1**)/H (**2**)†	ASXL1 (**2**)	ASXL1 (**1**)‡	L (**0**)/I-1 (**1**)/I-2 (**2**)/H (**3**)§
WHO sub-group			CMML-1 (**0**)/ CMML-2 (**1**)			
FAB sub-group			CMML-MD (**0**)/ CMML-MP (**1**)			
Risk stratification						
L	0–1	**0–4**	**0**	**0–4**	0	**0**
I (I-1/I-2)	2/3	**5–6/7–8**	**1/2–3**	**5–7**	1/2	**1/2–3**
H	4	**≥9**	**4–5**	**8–12**	≥3	**≥4**

* Poor performance means an ECOG performance status of 2. † The risk classification of molecular level in CPSS ranks by CMML-specific cytogenetic risk classification: low risk means normal, and isolated –Y; intermediate risk means other abnormalities; and high risk means trisomy 8, complex karyotype (≥3 abnormalities), and abnormalities of chromosome 7. ‡ MMM scores just included ASXL1 frameshift and nonsense mutation. § Genetic risk group include CPSS cytogenetic risk group and ASXL1, NARS, SETBP1, and RUNX1 mutations. Scores of cytogenetic risk same as CPSS cytogenetic risk, mutation of ASXL1, NARS, and SETBP1 earn one score, RUNX mutation earns two score. MDAPS: MD Anderson Prognostic Scoring System; G-MDAPS: Global MDAPS; PSS: CMML specific prognostic scoring system; GFM: Groupe Francophone des Myélodysplasies; MMM: Mayo molecular model; CCPSS-MOL: CPSS model; RBC-TD: RBC transfusion requirement; WBC: White blood cell count; Hb: Hemoglobin; PLT: Platelet count; BM: Bone marrow; AMC: Absolute monocyte count; ALC: Absolute lymphocyte count; IMCs: Immature myeloid cells; WHO: World Health Organization; FAB: French American British; I: Intermediate risk; I-1: Intermediate-1 risk; I-2: Intermediate-2 risk; L: Low risk; H: High risk; CMML: Chronic myelomonocytic leukemia; CMML-MD: Myelodysplastic CMML; CMML-MP: Myeloproliferative CMML.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s)/or his /her guardian has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients or his /her guardian understand that his/her/their name(s) and initials will not be published and due efforts will be made to conceal his/her/their identity, but anonymity cannot be guaranteed.

Conflicts of interest

None.

References

1. Patnaik MM, Tefferi A. Chronic myelomonocytic leukemia: 2018 update on diagnosis, risk stratification and management. Am J Hematol 2018;93:824–840. doi: 10.1002/ajh.25104.
2. Itzykson R, Fenaux P, Bowen D, Cross NCP, Cortes J, De Witte T, *et al*. Diagnosis and treatment of chronic myelomonocytic leukemias in adults. Hemasphere 2018;2:e150. doi: 10.1097/hs9.0000000000000150.
3. Kantarjian H, O'Brien S, Ravandi F, Cortes J, Shan J, Bennett JM, *et al*. Proposal for a new risk model in myelodysplastic syndrome that accounts for events not considered in the original international prognostic scoring system. Cancer 2008;113:1351–1361. doi: 10.1002/cncr.23697.
4. Aoyama K, Ishikura H, Tsumura H, Watanabe T, Suyama N, Kumakura S, *et al*. Meningeal involvement of chronic myelomonocytic leukemia. J Neurol 2003;250:45. doi: 10.1007/s00415-003-1138-5.
5. Martinez-Leborans L, Victoria-Martinez AM, Torregrosa-Calatayud JL, Alegre de Miquel V. Leukemia cutis: a report of 17 cases and a review of the literature. Actas Dermosifiliogr 2016;107:e65–e69. doi: 10.1016/j.ad.2016.02.015.

How to cite this article: Jian JL, Qiao YH, Zhang SL, Ma HZ, Liu B. Comparison of existing prognostic models in chronic myelomonocytic leukemia. Chin Med J 2020;133:496–498. doi: 10.1097/CM9.0000000000000637