Original article

Concordance between bone marrow aspiration and bone marrow biopsy to evaluate response after induction chemotherapy in acute myeloid leukemia at Siriraj Hospital

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Abstract:

Background: *The standard treatment for acute myeloid leukemia (AML) is chemotherapy, together with stem cell transplantation if indicated. Bone marrow study, comprising bone marrow aspiration and bone marrow biopsy, is the current method to evaluate treatment response. While many guidelines recommended evaluating treatment response with only bone marrow aspiration, it has still been a routine practice at Siriraj Hospital to perform both bone marrow aspiration and biopsy. Confirming the concordance of the two methods would help decrease the need to perform bone marrow biopsy, reducing patient discomfort, procedure time, and cost.* ***Objectives:*** *The study aimed to determine the concordance between bone marrow aspiration and bone marrow biopsy in evaluating treatment response among patients with AML receiving the '3+7 regimen'.* ***Method:*** *The data of patients receiving a diagnosis of AML were evaluated for response after standard '3+7' induction therapy by both bone marrow aspiration and biopsy, between January 1, 2012 and December 31, 2021 were retrospectively reviewed. Results from both bone-marrow-study methods were interpreted as either 'complete remission' or 'residual disease' and then were analyzed as either 'concordance' or 'discordance'. The primary outcome was percentage of patients with 'concordance' bone marrow study.* ***Results:*** *A total of 725 individuals were identified as patients receiving a diagnosis of AML receiving inpatient care, of which the bone marrow studies of 233 were analyzed. Overall, 181 patients (77.7%) had concordant result. Of the 52 patients with discordant result, 14 patients (26.9%) had inadequate bone marrow aspirate specimen while 3 patients (5.8%) had inadequate bone marrow biopsy specimen.* ***Conclusion:*** *Among patients receiving a diagnosis of AML receiving '3+7 regimen', 77.7% had concordant results between bone marrow aspiration and bone marrow biopsy. The identifiable cause of discordant result was mostly from inadequate bone marrow aspirate specimens.*

Keywords : ● *Acute myeloid leukemia* ● *Bone marrow biopsy* ● *Bone marrow aspiration* ● *Response assessment*

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นิพนธ์ต้นฉบับ

การศึกษาเพื่อประเมินความสอดคล้องระหว่างผลของการเจาะไขกระดูกเพื่อส่งเสมียร์ไขกระดูกกับการตัดชิ้นเนื้อไขกระดูกเพื่อประเมินการตอบสนองต่อการรักษาในผู้ป่วยมะเร็งเม็ดเลือดขาวชนิดฉับพลันแบบมัยอีลอยด์ในโรงพยาบาลศิริราช

เกตน์สิรี สนิท และ ยิ่งยง ชินธรรมมิตร์
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บทคัดย่อ

หลักการและเหตุผล *การรักษามาตรฐานของโรคมะเร็งเม็ดเลือดขาวชนิดฉับพลันแบบมัยอีลอยด์ คือการให้ยาเคมีบำบัดและ/หรือร่วมกับการปลูกถ่ายเซลล์ต้นกำเนิดถ้ามีข้อบ่งชี้ การประเมินผลตอบสนองต่อการรักษาในปัจจุบันคือการตรวจไขกระดูก ซึ่งประกอบด้วยการเจาะไขกระดูกเพื่อส่งเสมียร์ไขกระดูกและการตัดชิ้นเนื้อไขกระดูก ทั้งนี้หลายแนวทางปฏิบัติแนะนำให้ทำการตรวจเฉพาะการเจาะไขกระดูกเพื่อส่งเสมียร์ไขกระดูกเพียงอย่างเดียว แต่ในโรงพยาบาลศิริราช ยังมีการทำทั้งสองวิธีควบคู่กัน ดังนั้น ถ้าสามารถทราบถึงความสอดคล้องระหว่างผลของการตรวจทั้งสองวิธี อาจสามารถลดการตัดชิ้นเนื้อไขกระดูก ทำให้ผู้ป่วยได้รับความเจ็บปวดลดลง และลดระยะเวลาการทำหัตถการรวมถึงลดค่าใช้จ่ายลง* ***วัตถุประสงค์*** *เพื่อศึกษาความสอดคล้องระหว่างผลของการเจาะไขกระดูกเพื่อดูเสมียร์ไขกระดูกกับการตัดชิ้นเนื้อไขกระดูก ในการประเมินผลตอบสนองต่อการรักษาด้วยยาสูตร 3+7 ในผู้ป่วยโรคมะเร็งเม็ดเลือดขาวชนิดฉับพลันแบบมัยอีลอยด์* ***วิธีการศึกษา*** *ทบทวนเวชระเบียนผู้ป่วยโรคมะเร็งเม็ดเลือดขาวชนิดฉับพลันแบบมัยอีลอยด์ ที่ได้รับการรักษาด้วยยาเคมีบำบัดสูตรชักนำ 3+7 และได้รับการเจาะไขกระดูกเพื่อประเมินการตอบสนองต่อการรักษาที่โรงพยาบาลศิริราช ในระยะเวลา 10 ปี ตั้งแต่วันที่ 1 มกราคม 2555 ถึง 31 ธันวาคม 2564 เพื่อศึกษาถึงผลของการตรวจไขกระดูกแต่ละวิธีว่าให้ผลเป็น Complete remission หรือ Residual disease แล้วนำมาแปลผลเป็น Concordance หรือ Discordance คิดเป็นร้อยละของผู้ป่วยทั้งหมด รวมถึงศึกษาปัจจัยด้านอายุ เพศ ระยะเวลาตั้งแต่เริ่มการให้ยาเคมีบำบัดจนถึงระยะเวลาการเจาะไขกระดูก และผลตรวจเม็ดเลือดก่อนการเจาะไขกระดูก โดยคำนวณเป็นค่าเฉลี่ยของผู้ป่วยทั้งหมด* ***ผลการศึกษา*** *ในผู้ป่วยโรคมะเร็งเม็ดเลือดขาวชนิดฉับพลันแบบมัยอีลอยด์จำนวนทั้งหมด 725 รายที่ได้รับการรักษาในหอผู้ป่วยโรงพยาบาลศิริราช มีผู้ป่วยจำนวน 233 รายที่ถูกนำมาวิเคราะห์ พบว่าผู้ป่วย 181 ราย (ร้อยละ 77.7) ให้ผล Concordance ในขณะที่ 52 รายให้ผล Discordance โดยในกลุ่มนี้ 14 ราย (ร้อยละ 26.9) ได้สเมียร์ไขกระดูกที่มีคุณภาพไม่ดี ในขณะที่อีก 3 ราย (ร้อยละ 5.8) ได้ชิ้นเนื้อจากการตัดชิ้นเนื้อไขกระดูกที่ด้อยคุณภาพ* ***สรุป*** *จากการศึกษานี้พบว่าการประเมินการตอบสนองต่อการรักษาด้วยยาเคมีบำบัดระยะชักนำด้วยยาสูตร 3+7 ในผู้ป่วยโรคมะเร็งเม็ดเลือดขาวชนิดฉับพลันแบบมัยอีลอยด์ พบว่า ได้ผล Concordance ร้อยละ 77.7 ในส่วนกลุ่มที่ได้ผล Discordance พบว่าสาเหตุส่วนใหญ่เกิดจากการได้สิ่งส่งตรวจที่ไม่ได้คุณภาพ*

คำสำคัญ : ● *โรคมะเร็งเม็ดเลือดขาวชนิดฉับพลันแบบมัยอีลอยด์* ● *การตัดชิ้นเนื้อไขกระดูก* ● *การเจาะไขกระดูก* ● *การประเมินผลตอบสนอง*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2567;34:111-22.

Introduction

Acute myeloid leukemia (AML) is a hematologic malignancy arising from failure to control proliferation and differentiation of hematopoietic precursor cells, leading to the accumulation of blasts in the peripheral blood. This can result in symptoms of bone marrow failure, such as fatigue, weakness, infections, bleeding and bruising. AML is the most common form of acute leukemia. In Thailand, no definitive data are available concerning the incidence and prevalence of AML. A recent study in Thailand showed that de novo AML was much more common than secondary AML (90.7 vs. 9.3%)[1]. Associated risk factors for AML include older age, with 54% of patients being diagnosed at the age of 65 years or older[2].

The current standard treatment for AML involves combining chemotherapy and stem cell transplantation if indicated, depending on factors such as the subtype of AML, patient age, overall health status and other considerations. Chemotherapy is typically administered in two steps, starting with an induction phase to rapidly achieve complete remission, followed by postremission therapy to maintain the patient in remission[3].

The standard induction regimen for AML is known as the "7+3 regimen", involving administering an anthracycline for three days along with cytarabine for seven days. This regimen has been shown to achieve complete remission in 60 to 80% of patients younger than 60 years and 40 to 60% of patients older than 60[4].

The current method to evaluate treatment response in AML involves a bone marrow study including both bone marrow aspiration and bone marrow biopsy. Although many guidelines recommend evaluating treatment response with only bone marrow aspiration[4], it has been a routine practice at Siriraj Hospital to perform both procedures.

Bone marrow biopsy could definitely provide more information than bone marrow aspiration in the case of dry-tap aspiration. However, bone marrow biopsy is known to take more time and require greater technical expertise compared with bone marrow aspiration. Additionally, it can cause more discomfort and pain to the patient, potentially leading to increased anxiety when undergoing the procedure again.

Several studies have reported on the sensitivity and specificity of bone marrow biopsy compared with bone marrow aspiration to evaluate bone marrow among patients with hematologic diseases. Bone marrow aspiration alone has been shown to exhibit a sensitivity of approximately 85% and a specificity of around 100% when compared with bone marrow biopsy. Notably, bone marrow biopsy adds limited additional information in cases of acute leukemia, while bone marrow aspiration provides the most relevant information regarding cell morphology[5]. After induction chemotherapy, the percentage of blasts in bone marrow is usually lower than that before chemotherapy and is usually observed in a scattered pattern not a diffuse, cluster or sheet-like pattern. Therefore, to accurately count the residual blasts after chemotherapy, identifying the individual blast was needed. Generally, the individual blast cell is more clearly identified on an aspirate smear than as a biopsy specimen which may require additional immunohistochemical staining to increase the sensitivity on detecting individual blast cells. However, identifying blast cells on a bone marrow aspirate smear depends on experience of interpreters leading to potential inter-observer variation.

Related studies have reported a concordance rate of 92.8% between bone marrow aspiration and bone marrow biopsy to evaluate treatment response among patients with AML. Bone marrow aspiration alone has shown a sensitivity of 86.8% in assessing treatment response[6]. Based on these findings, researchers are interested in further investigating the concordance between these two methods to evaluate response after induction therapy among patients with AML. Concerning the homogeneity of the included population, only patients receiving standard induction 7+3 regimen were included. Such research could potentially reduce the need for bone marrow biopsy; thereby, decreasing patient discomfort, procedure time and cost.

Objectives

The objectives included (1) to investigate the concordance between bone marrow aspiration and bone marrow biopsy to evaluate treatment response in patients with AML receiving the "7+3 regimen" and (2) to evaluate the agreement between bone marrow aspiration and bone marrow biopsy in assessing treatment response among patients with AML after receiving induction therapy.

Materials and Methods

We conducted a retrospective chart review of 725 adult (> 18 years old) patients with AML in an inpatient department setting at Siriraj Hospital in Bangkok, Thailand, between January 1, 2012 and December 31, 2021. Out of these, a total of 233 patients with AML undergoing both bone marrow aspiration and bone marrow biopsy simultaneously were included in the study. Patients with AML M3 or APL, as well as those receiving chemotherapy other than the "7+3 regimen", were excluded from the study. This study was approved by the Siriraj Institutional Review Board, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand (COA no. Si 380/2022).

The sample size to be studied was calculated for sensitivity and specificity using the formula[7]:

$$n_{sen} = \frac{Z^2_{\alpha/2}P(1-P)}{e^2}$$

where the n is sample size; P is the hypothesized sensitivity of bone marrow aspirate to evaluate the response at the end of induction considered as 82.5% from the related study[6]. Z_{α} was considered the normal deviation, the significance level was set to a = 0.05, the $Z_{\alpha/2}$ = 1.96; e constituted the permissible error and set to 0.05. The calculated sample size was then 221. To adjust for prevalence of residual leukemia in bone marrow study from the related study[6] (average of 32.6%), the estimated adjusted sample size was (221/0.326) = 678. Based on the specificity, we used formula:

$$n_{spec} = \frac{Z^2_{\alpha/2}P(1-P)}{e^2}$$

where the n is sample size; P is the hypothesized specificity of bone marrow aspirate for evaluation of response at the end of induction which was taken as 95.8% from the related study[6]. Z_{α} was considered the normal deviation, the significance level was set to a = 0.05, the $Z_{\alpha/2}$ = 1.96; e constituted the permissible error and was set to 0.03. The calculated sample size was then 172, while the adjusted sample size was (172/[1-0.326]) = 255. Therefore, the adjusted sample size was set to 678. The targeted power of the study was 80%.

Response assessment

In this study, simultaneous bone marrow aspiration and bone marrow biopsy was used as the gold standard to evaluate response to treatment, as they are commonly practiced at Siriraj Hospital. All bone marrow aspirate smears were evaluated by a hematologist who served as the attending staff during that period (ten adult hematologists in hospital). As per IWG-AML criteria, > 200 cells were counted to determine blast percentage. A good particle was defined by the presence of spicules/particles without clotted appearance. All bone marrow biopsy samples with routine CD34 immunostaining were evaluated by the responsible hematopathologist during that period (three hematopathologists in hospital). Generally, hematologists and hematopathologists did not know the result of bone marrow evaluation of each other during examining the sample from same patient. Afterwards, hematologists who took care of patients would make the final conclusion from both results to determine the response. The response criteria are defined below.[4]

Complete remission (CR): bone marrow blasts < 5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count (ANC) ≥ 1.0 x10^9/L (1,000/μL); platelet count ≥ 100 x10^9/L (100,000/μL).

CR with incomplete hematologic recovery (CRi): all CR criteria except for residual neutropenia [< 1.0×10^9/L (1,000/μL)] or thrombocytopenia [< 100 ×10^9/L (100,000/μL)].

Partial remission (PR): decrease in bone marrow blast percentage to 5 to 25%; and decrease in pretreatment bone marrow blast percentage by at least 50%.

Final diagnosis: the conclusive diagnosis based on the interpretation of both bone marrow study methods. If these methods did not provide a definitive diagnosis, flow cytometry or expert decision-making based on chart review was used. In this study, we categorized the final result of the bone marrow study in three groups: complete remission, residual disease and nondiagnostic. "Complete remission" included CR and CRi; "residual disease" included PR and no response; and "non-diagnostic" included the rest not in "CR" and "residual disease".

Concordance: both bone marrow aspiration and bone marrow biopsy showing the same result, either complete remission, residual disease or non-diagnostic.

Discordance: bone marrow biopsy and bone marrow aspiration showing different results.

Statistical analysis

The statistical analysis in this study involved the use of descriptive and inferential statistics. Descriptive statistics were used to describe categorical variables such as sex and comorbidity in terms of frequencies and percentages. Numerical variables such as age, weight, height and lab parameters were presented as means ± standard deviation (SD), or medians ± interquartile range (IQR), along with maximum and minimum values.

Inferential statistics were performed using appropriate tests, such as the Chi-square test or Fisher's exact test for categorical data, unpaired t-test for normally distributed continuous variables, Mann-Whitney U test for non-normally distributed continuous variables and kappa statistic for agreement analysis. These tests were selected based on their suitability for analyzing the type of data collected in this study.

Univariate analysis was conducted to determine the relationship between each independent variable and the dependent variable. Variables with a p-value < 0.05 were included in a multivariate logistic regression analysis using forward stepwise method with a significance level of $p < 0.05$. The Hosmer-Lemeshow test was used to assess the goodness of fit of the final model.

All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp, Armonk, NY, USA).

Results

Baseline patient characteristics

The baseline patient characteristics are shown in Table 1. A total of 233 patients received induction chemotherapy and had bone marrow study to evaluate posttreatment. The majority of patients were female (54.5%), while 45.5% were male. The mean age at diagnosis was 45.1 years (±12.6 years). The average weight of patients was 63.1 kg (±14.0 kg), and the mean height was 163.1 cm (±9.0 cm). Mean BMI was 23.6 kg/m^2 (±4.3 kg/m^2).

In terms of comorbidities, the majority of patients had none (42.1%), while other common comorbidities included diabetes mellitus (6.9%), essential hypertension (16.3%) and dyslipidemia (11.6%). Other comorbidities such as gout, cardiovascular disease, myelodysplastic syndromes, other hematologic diseases, solid malignancy and others, were also observed in varying frequencies.

The interval between induction and bone marrow study was on average 33 days (±12 days). Complete blood count parameters showed that the mean hemoglobin level was 9.3 g/dL (±1.3 g/dL). The median white blood cell count was 4,000/mm^3 (±5,791/mm^3). The median ANC was 2,264/mm^3 (±3,635/mm^3), while the median platelet count was 225,000/mm^3 (±226,331/mm^3).

Bone marrow aspiration and bone marrow biopsy characteristics

The bone marrow aspiration specimens from patients with AML nonM3 evaluated for specimen quality, cellularity, percentage of blasts and interpretation are shown in Table 2. Most specimens had good particle quality (85.0%), while clotted (2.6%) and fluid marrow (6.9%) specimens were less common. Dry taps and bone marrow imprint specimens accounted for 1.3 and

Table 1 Baseline characteristics of patients with AML (nonM3) (n = 233)

Patient characteristic	Number (%)
Sex	
Male	106 (45.5)
Female	127 (54.5)
Age at diagnosis, years	
Mean ± SD	45.1 (±12.6)
Range	18.0-68.0
Weight, kg	
Mean ± SD	63.1 (±14.0)
Range	35.0-111.0
Height, cm	
Mean ± SD	163.1 (±9.0)
Range	142.0-186.0
BMI, kg/m^2	
Mean ± SD	23.6 (±4.3)
Range	15.0-42.7
Comorbidities	
None	98 (42.1)
Diabetes mellitus	16 (6.9)
Essential hypertension	38 (16.3)
Dyslipidemia	27 (11.6)
Gout	3 (1.3)
Cardiovascular disease	9 (3.0)
Myelodysplastic syndromes	13 (5.6)
Other hematologic disease	19 (8.2)
Solid malignancy	8 (3.4)
Others	19 (8.2)
Interval between induction and BM study, days	
Mean ± SD	33.4 (±12.6)
Range	17.0-146.0
Complete blood count	
Hemoglobin (g/dl)	
Mean ± SD	9.3 (±1.3)
Range	6.6-14.5
White blood cell count (/μL)	
Median ± IQR	4,000.0 (±5,791.1)
Range	90.0-49,000.0
Absolute neutrophil count (/μL)	
Median ± IQR	2,264.0 (±3,635.0)
Range	0.0-22,678.0
Platelet (/μL)	
Median ± IQR	225,000.0 (±226,331.0)
Range	2,000.0-1,070,000.0

SD, standard deviation; BMI, body mass index; IQR, interquartile range

Table 2 Bone marrow aspiration and bone marrow biopsy characteristics, N (%)

	Bone marrow aspiration specimen
Specimen quality	
Good particle	198 (85.0)
Clotted	6 (2.6)
Fluid marrow	16 (6.9)
Dry tap	3 (1.3)
Bone marrow imprint	10 (4.3)
Cellularity (n = 233)	
Hypercellularity	76 (32.6)
Normocellularity	57 (24.5)
Hypocellularity	69 (29.6)
Other[#]	31 (13.3)
%Blast (n = 230)	
< 5%	177 (76.0)
5-25%	33 (14.2)
> 25%	20 (8.6)
Interpretation	
Complete remission	163 (70.0)
Residual disease	53 (22.7)
Nondiagnostic	17 (7.3)
Bone marrow biopsy specimen	
Median length, cm	1.0
Range	0.2-5.7
Assessability	
Adequate	208 (89.3)
Inadequate	25 (10.7)
Cellularity (n = 226)	
Hypercellularity	84 (36.1)
Normocellularity	94 (40.3)
Hypocellularity	48 (20.6)
Interpretation	
Complete remission	196 (84.1)
Residual disease	32 (13.7)
Nondiagnostic	5 (2.1)
Final diagnosis	
Complete remission	167 (71.7)
Residual disease	65 (27.9)
Nondiagnostic	1 (0.4)
Result	
Concordance between biopsy results and final diagnosis	181 (77.7)
Discordance between biopsy results and final diagnosis	52 (22.3)

SD, standard deviation; [#]Other: inability to interpreted cellularity

4.3%, respectively. Cellularity showed hypercellularity in 32.6% of specimens, normocellularity in 24.5%, and hypocellularity in 29.6%. The majority of specimens exhibited less than 5% blasts (76.0%), while 5 to 25% blasts were present in 14.2%, and > 25% blasts in 8.6%. Interpretation revealed 70.0% complete remission, 22.7% residual disease and 7.3% nondiagnostic due to insufficient information for interpretation.

The bone marrow biopsy specimens were evaluated for median length, assessability and cellularity, as well as interpretation of results and final diagnosis. Median length was 1.0 cm (range: 0.2-5.7). Assessability was adequate in 89.3% of specimens and inadequate in 10.7%. Cellularity showed hyper-cellularity in 36.1% of specimens, normocellularity in 40.3% and hypocellularity in 20.6%. The interpretation of the results revealed that 84.1% of patients achieved complete remission, 13.7% had residual disease and 2.1% were nondiagnostic. The final diagnosis showed that 71.7% were in complete remission, 27.9% had residual disease and 0.4% were nondiagnostic. The concordance between biopsy results and final diagnosis was 77.7% with 22.3% discordance. However, the exact percentage of blasts from bone marrow biopsy was not routinely reported.

Factors associated with concordance or discordance

The factors associated with concordance or discordance in bone marrow aspiration and biopsy were analysed in this study (Table 3). No statistically significant differences were observed in concordance rates between the two sexes (p = 0.459). Similarly, no significant differences were found in concordance rates based on age (p = 0.857). Patient characteristics such as weight, height, and BMI also did not show significant differences in concordance rates (p > 0.05). Furthermore, comorbidities including the presence or absence of other health conditions, did not significantly impact concordance rates (p = 0.360).

The interval (days) between induction chemotherapy and bone marrow study differed significantly between concordance and discordance (p = 0.030). Concordance was associated with a longer mean interval (34.36±13.67 days) compared with discordance (30.08±6.92 days). CBC parameters (Hb, WBC, ANC and platelet count) also showed significant differences between concordance and discordance (p < 0.001 for all parameters) with higher values associated with concordance.

Bone marrow aspiration characteristics (specimen quality and cellularity) showed significant differences between concordance and discordance (p < 0.001 for both). Concordance was associated with good particle quality of the specimen, normocellularity and lower blast percentage (< 5%). Bone marrow biopsy characteristics (length and assessability) also showed significant differences (p = 0.050 and p < 0.001, respectively), with concordance associated with adequate assessability and normocellularity. Interpretation of bone marrow aspiration and biopsy, specifically complete remission, residual disease or nondiagnostic, also showed significant differences (p < 0.001 and p = 0.019, respectively), with complete remission being associated with concordance.

Factors associated with discordance in this study were inadequate bone marrow aspiration and biopsy specimens, as well as lower levels of WBC, ANC and platelet counts (p < 0.001).

Multivariate analysis of the factors associated with discordant result

Factors associated with discordant results between bone marrow aspiration and biopsy were assessed using both univariate and multivariate analyses. The univariate analysis showed that several factors including the interval of study, Hb level, WBC count, ANC, platelet count, cellularity, %blast and bone marrow biopsy accessibility were significantly associated with discordant results. Further multivariate analysis using the forward stepwise method revealed that ANC, cellularity of bone marrow aspiration, both hypo/hypercellularity, %blast (5-25% and > 25%) and bone marrow biopsy assessability remained significantly associated with discordant results (p < 0.05). The odds ratios (OR) and 95% confidence intervals (CI) for these variables are shown in Table 4. Among 152

Table 3 Factors associated with concordant or discordant results

Characteristic	Overall No. (%)	Concordance No. (%)	Discordance No. (%)	*p*-value
Number of patients	233 (100)	181 (77.7)	52 (22.3)	
Sex				0.459
- Male	106 (45.5)	80 (75.5)	26 (24.5)	
- Female	127 (54.5)	101 (79.5)	26 (20.5)	
Age, years (mean±SD)	45.09±12.62	45.17±12.67	44.81±12.55	0.857
Weight, kg (mean±SD)	63.09±14.02	62.76±14.14	64.27±13.63	0.494
Height, cm (mean±SD)	163.06±9.00	162.65±9.01	164.48±8.91	0.197
BMI, kg/m^2 (mean±SD)	23.62±4.32	23.62±4.41	23.61±4.05	0.996
Comorbidities				0.360
- Present	135 (57.9)	102 (75.6)	33 (24.4)	
- Absent	98 (42.1)	79 (80.6)	19 (19.4)	
Interval*, days (mean±SD)	33.41±12.59	34.36±13.67	30.08±6.92	0.030
CBC				
- Hb, g/dL (mean±SD)	9.32±1.30	9.43±1.27	8.93±1.33	0.015
- WBC/μL, median (IQR)	4,000 (1,320-7,100)	5,190 (2,300-8,000)	1,610 (810-3,400)	< 0.001
- ANC/μL, median (IQR)	2,264 (360-4,576)	2950 (860-5,068)	607 (165-1,753)	< 0.001
- Platelet x10^3/μL, median (IQR)	225 (55-396)	289 (90-426)	67 (26-204)	< 0.001
Bone marrow aspiration				
Specimen quality				< 0.001
- Good particle	198 (85.0)	166 (91.7)	32 (61.5)	
- Clotted	6 (2.6)	5 (2.8)	1 (1.9)	
- Fluid marrow	16 (6.9)	6 (3.3)	10 (19.2)	
- Dry tap	3 (1.3)	0 (0.0)	3 (5.8)	
- Bone marrow imprint	10 (4.3)	4 (2.2)	6 (11.5)	
Cellularity				< 0.001
- Normocellularity	76 (32.6)	68 (37.6)	8 (15.4)	
- Hypercellularity	57 (24.5)	46 (25.4)	11 (21.2)	
- Hypocellularity	69 (29.6)	56 (30.9)	13 (25.0)	
- Other#	31 (13.3)	11 (6.1)	20 (38.5)	
%Blast				< 0.001
< 5%	177 (77.0)	161 (89.0)	16 (32.7)	
5-25%	33 (14.3)	7 (3.9)	26 (53.1)	
> 25%	20 (8.7)	13 (7.2)	7 (14.3)	
Interpretation				< 0.001
- Complete remission	163 (70.0)	158 (87.3)	5 (9.6)	
- Residual disease	53 (22.7)	20 (11.0)	33 (63.5)	
- Nondiagnostic	17 (7.3)	3 (1.7)	14 (26.9)	
Bone marrow biopsy				
Median length, cm (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-1.5)	0.050
Assessability				< 0.001
- Adequate	208 (89.3)	169 (93.4)	39 (75.0)	
- Inadequate	25 (10.7)	12 (6.6)	13 (25.0)	

Table 3 Factors associated with concordant or discordant results (continue)

Characteristic	Overall No. (%)	Concordance No. (%)	Discordance No. (%)	*p*-value
Cellularity				0.003
- Normocellularity	84 (36.1)	69 (38.1)	15 (28.8)	
- Hypercellularity	94 (40.3)	77 (42.5)	17 (32.7)	
- Hypocellularity	48 (20.6)	33 (18.2)	15 (28.8)	
Interpretation				0.019
- Complete remission	196 (84.1)	158 (87.3)	38 (73.1)	
- Residual disease	32 (13.7)	21 (11.6)	11 (21.2)	
- Non-diagnostic	5 (2.1)	2 (1.1)	3 (5.8)	

SD, standard deviation; IQR, interquartile range; ANC, absolute neutrophil count; BMI, body mass index

*interval between induction chemotherapy and bone marrow assessment

#Other: inability to interpret cellularity

Table 4 Univariate and multivariate analysis of factors associated with discordant result between bone marrow aspiration and bone marrow biopsy

Factor	Univariate		Multivariate	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Interval of study, days	1.75 (1.18-2.61)	0.006		
Complete blood count				
- Hb	0.72 (0.55-0.94)	0.014		
- WBC	0.9997 (0.9996-0.9998)	< 0.001		
- ANC	0.9996 (0.9994-0.9998)	< 0.001	0.9998 (0.9996-0.9999)	0.035
- Platelet	0.9999 (0.9999-0.9999)	< 0.001		
Bone marrow aspiration				
Cellularity				
- Hypercellularity[a]	0.08 (0.03-0.21)	< 0.001	0.032 (0.007-0.142)	<0.001
- Hypocellularity[a]	0.14 (0.05-0.37)	< 0.001	0.050 (0.012-0.205)	<0.001
%Blast				
5-25%[b]	31.67 (12.12-82.75)	< 0.001	81.69 (22.22-300.33)	<0.001
> 25%[b]	4.59 (1.63-12.92)	< 0.001	5.65 (1.38-23.17)	<0.016
Bone marrow biopsy				
Assessability	4.72 (2.00-11.14)	< 0.001	3.89 (1.01-15.02)	0.049
Cellularity				
Hypercellularity[c]	0.09 (0.02-0.48)	0.005		
Hypocellularity[c]	0.09 (0.02-0.49)	0.006		

CI, confidence interval; Hb, hemoglobin; WBC, white blood cell; ANC, absolute neutrophil count

[a]compared with normocellularity of bone marrow aspiration group; [b]compared with %blast < 5% group

[c]compared with normocellularity of bone marrow biopsy group

Table 5 Agreement between bone marrow aspiration and bone marrow biopsy

		Bone marrow biopsy			Total
		Complete remission	Nondiagnostic	Residual disease	
Bone marrow aspiration	Complete remission	157	1	5	163
	Nondiagnostic	9	3	5	17
	Residual disease	30	2	21	53
Total		196	6	31	233

patients with ANC > 1,000/μL, the concordance rate was 85.5% (95%CI: 78.9-90.7). For a further specific subgroup among 134 patients having both ANC >1,000/μL and adequate bone marrow aspirate sample (good particle), the concordance rate was 91.0% (95%CI: 84.9-95.3).

Agreement between bone marrow aspiration and bone marrow biopsy

Cohen's κ was calculated to assess the agreement between two bone marrow study methods to evaluate the response after inducing chemotherapy in 233 patients with AML at Siriraj Hospital, categorizing outcomes into complete remission, partial response and non-diagnostic. The results showed fair agreement between the two methods, with a calculated κ of 0.379 (95%CI: 0.264 to 0.488), and a *p*-value < 0.001. (Table 5)

Discussion

The results of our study showed the concordance between two bone marrow study method was 77.7%, and with 22.3% discordance. The results of this study are consistent with a related review article; 2017 ELN recommendations for diagnosis and management of AML among adults that recommend bone marrow biopsy only when dry tap, or as our study may refer to inadequate specimens[4]. However, our study revealed lower concordance rate than a related study (77.5 vs. 92.8%)[6]. From the author's opinion, explanations include a higher rate of inadequate assessability of bone marrow biopsy in our study (10.7 vs. 4.9%). No specific research has investigated the factors influencing concordance between bone marrow aspiration and bone marrow biopsy in evaluating treatment response among patients with AML having received induction chemotherapy. Findings from this study identified factors such as the interval between induction chemotherapy and bone marrow study, complete blood count (CBC) parameters including hemoglobin level, white blood cell count, ANC and platelet count, specimen quality (particle quality and cellularity) and bone marrow biopsy characteristics (length and assessability of specimen) as significant factors associated with concordance or discordance between the two procedures. Among patients with ANC > 1,000/μL with good particle of bone marrow aspiration, the concordance rate was higher than the rest (91.0 vs. 32.5%).

To our knowledge, no specific research has investigated the factors influencing concordance between bone marrow aspiration and bone marrow biopsy to evaluate treatment response among patients with AML who have undergone induction chemotherapy. Our study identified several significant factors associated with concordance or discordance between the two procedures including the interval between induction chemotherapy and bone marrow study, complete blood count (CBC) parameters (such as hemoglobin level, white blood cell count, ANC and platelet count), specimen quality (particle quality and cellularity) and bone marrow biopsy characteristics (length and assessability of the specimen).

Based on our findings, we suggest that patients with ANC > 1,000/μL with adequate bone marrow aspirate smear may not need further bone marrow biopsy due to high concordance rate (91%) between bone marrow aspiration and bone marrow biopsy.

Strengths and Limitations

The strength of this study lies in its potential practical applications and implications for clinical practice or policy-making in our hospital. However, several limitations were encountered in this study. Firstly, the small sample size may limit the generalizability of the findings or reduce the statistical power of the study. Additionally, some data such as complications from the procedure or information related to the performer and its potential impact on specimen quality, were not recorded, which could have been important factors to consider. To clearly identify the patients not requiring bone marrow biopsy in addition to bone marrow aspiration in routine clinical practice, a prospective study with a well-controlled design on all steps of bone marrow study and evaluation including collecting data of bone marrow aspirate smear quality assessed immediately at bedside by grossly inspection is warranted.

Conclusion

Several factors were found to be associated with concordance or discordance in bone marrow aspiration and biopsy. These included interval of study days, CBC parameters, specimen quality, cellularity, accessibility and interpretation. These findings suggest that attention to these factors may be important in achieving concordance in bone marrow evaluation, and further studies may be needed to better understand the impact of these factors on clinical decision-making and patient outcomes.

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Conflicts of interest

The authors declare they have no conflict of interest.

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