ORIGINAL ARTICLE

BONE MARROW BIOPSIES IN OLDER ADULTS: ASSESSING DIAGNOSTIC ACCURACY AND PRE-DIAGNOSIS CONCORDANCE

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Abstract

Introduction: Bone marrow biopsy is widely used for the diagnosis of hematological diseases and malignancies that increase with age. We aimed to show the contribution of bone marrow biopsies to the diagnostic process by comparing pathological diagnoses and clinical preliminary diagnoses in the patient group aged 65 and over.

Materials and Method: The study included 1,821 patients aged 65 and over who underwent bone marrow biopsy between 2019 and 2024. Clinical preliminary diagnoses, patient demographic information, and pathology reports of the departments requesting bone marrow biopsy were accessed through the patient information system. Pathological definitive diagnoses and clinical diagnoses were categorized and statistical analysis was performed.

Results: 30.8%(n=563) of the clinical pre-diagnoses were Multiple Myeloma, 18.5%(n=338) were Myelodysplastic Syndrome and 14.2%(n=258) were Chronic Myeloproliferative Disorders. Pathological examination was sufficient for diagnosis in 6.8%(n=124). Of these, 45.5%(n=772) were diagnosed with malignancy. Of the pathological diagnoses, 14.5%(n=265) were Multiple Myeloma, 7.4%(n=135) were Chronic Myeloproliferative Disorders and 2.9%(n=53) were diagnosed with Myelodysplastic Syndrome. When the diagnoses were compared, it was seen that there was a discrepancy rate of 38.1% (n=616). The highest discrepancy was in the Hematology department at a rate of 59.4% (n=366) and was statistically significant (p=0.024). The second highest discrepancy was in the Oncology department at a rate of 20.5% (n=126).

Conclusion: The high diagnostic discordance in clinics suggests that current diagnostic algorithms may not be sensitive enough. Our study showed that bone marrow biopsy should be performed in patients aged 65 years and older based on accurate clinical indications and that new diagnostic protocols should be focused on development.

Keywords: Bone Marrow Examinations; Aged; Pathology.

INTRODUCTION

Bone marrow biopsy (BMB) is a critical diagnostic procedure widely used in the evaluation of haematological diseases and certain non-haematological conditions (1). In addition to cytomorphological analysis, BMB facilitates advanced diagnostic assessments, such as immunophenotyping, flow cytometry, cytogenetic testing and molecular genetic tests (2). BMB plays a critical role in both the diagnosis and staging of leukemias and lymphomas, and it may need to be performed multiple times when clinically indicated (1). Furthermore, in chronic myeloproliferative diseases (CMPDs), essential findings such as bone marrow fibrosis, which can only be identified through BMB, hold significant diagnostic value (1). In the context of solid tumors, the detection of bone marrow metastases is crucial for staging and prognostic assessment, as these findings remain indispensable in guiding treatment strategies (1). The increased prevalence of haematological disorders and malignancies in older patients underscores the importance of BMB in this age group (3). The geriatric population, defined as individuals aged 65 years and older, represents a highly heterogeneous group. Notably, the physiological age of patients, rather than their chronological age, is a critical factor in determining the appropriateness of invasive procedures such as BMB. In frail or severely debilitated patients, particularly those aged 85 years and older, the risks associated with BMB, and other diagnostic interventions may outweigh the potential benefits. However, the diagnostic efficacy of BMB and its alignment with clinical predictions in the older population have not yet been thoroughly investigated (4).

The incidence of haematological disorders increases with age, often complicating the diagnostic process due to non-specific symptoms and multiple comorbidities (3). In cases of anaemia, thrombocytopenia and unexplained cytopenia, BMB stands out as a crucial tool for identifying underlying causes, particularly when traditional diagnostic methods fall short (5). For instance, Riley et al. demonstrated that BMB had high specificity in diagnosing haematological malignancies, such as acute leukaemia and lymphoma (6). A review by Bain revealed that BMB provided over 90% diagnostic accuracy for haematological malignancies (7), which is particularly significant given the increased incidence of malignancies in older patients (3).

Incorrect or insufficient clinical assessments may lead to unnecessary BMBs, exposing patients to the additional risks of invasive procedures (7). Unnecessary biopsies increase patients' anxiety, pain and complication risks, and they prolong the diagnostic process, imposing additional costs on the healthcare system (7-9). In older patients, these unnecessary interventions can lead to significant issues in terms of safety and efficient resource use (10). When appropriate, advanced diagnostic tests, such as immunophenotyping and molecular genetic analyses, can be used to supplement or even replace BMB when adequate peripheral samples are available. However, particularly in hematology and oncology, BMB remains an indispensable source of diagnostic material, especially for cytopenia evaluations. Therefore, it is crucial to ensure that BMBs are conducted based on accurate clinical indications and are aligned with clinical pre-diagnoses.

A retrospective study by Manion et al. analysed 119 bone marrow aspirates and biopsies from patients aged 85 or older. The study found that 43% of the procedures yielded specific diagnoses, particularly in cases involving haematological malignancies. However, the diagnostic yield was lower for non-specific symptoms, such as unexplained cytopenia (11). These findings emphasise the importance of conducting BMB with the correct indications and algorithms in the older population to avoid additional invasive procedures. Stratifying older patients based on physiological rather than chronological age can improve the accuracy and safety of invasive diagnostic interventions.

This study aimed to retrospectively evaluate the pathological results of BMBs performed in patients aged 65 or above and compare these results with the patients' clinical pre-diagnoses. We hope that our findings will provide guidance in establishing biopsy algorithms for older patients.

METHODS

In this retrospective study, BMBs evaluated in the pathology laboratory of a tertiary healthcare centre between 2019 and 2024 were analysed. The study included patients aged 65 or older who underwent BMB. The exclusion criteria were being a patient younger than 65 years and having incomplete data for a case. All the data for the included participants were retrospectively retrieved from the hospital's electronic medical records. Ethical approval for this study was obtained. Patient consent was not required.

Data Recording

Patient data were retrospectively accessed through the hospital's electronic database. Demographic data, including patient age and sex, were recorded. The departments that requested BMBs were categorised as follows:

- Medical departments (haematology, oncology, internal medicine, nephrology, geriatrics and rheumatology)
- Surgical departments (orthopaedics, surgical oncology, general surgery and urology)
- Intensive care units
- Other departments (pulmonology, cardiology, infectious diseases, physical therapy and rehabilitation)

The preliminary clinical diagnoses were categorised as follows:

- No preliminary diagnosis provided
- Multiple myeloma
- Myelodysplastic syndrome (MDS)
- Chronic myeloproliferative hematopathies (CMPHs)
- Chronic lymphocytic leukaemia (CLL)
- Lymphoma (Hodgkin and non-Hodgkin)
- Acute myeloid leukaemia (AML)
- Amyloidosis
- Anaemia
- Metastasis

The pathological diagnoses were recorded as follows:

- Insufficient sample
- Multiple myeloma
- MDS
- CMPHs
- CLL
- Lymphoma (diffuse large B-cell lymphoma, follicular lymphoma, Hodgkin lymphoma, hairy cell leukaemia and mantle cell lymphoma)
- AML
- Acute lymphoblastic leukaemia (ALL)
- Hypercellular marrow
- Hypocellular marrow
- Non-specific findings

Definition of Concordance and Discordance

Concordance was defined as the alignment between preliminary clinical diagnoses provided by the requesting departments and the definitive pathological diagnoses obtained through BMB. Discordance, on the other hand, referred to cases where the pathological findings did not match the clinical pre-diagnoses. This discordance may highlight diagnostic challenges, the complexity of non-specific symptoms in elderly patients,

or insufficient clinical data provided during the diagnostic process. For the purposes of this study, discordance did not include insufficient samples, which were categorised separately.

Bone Marrow Processing Technique

BMB material was admitted to the pathology department, and routine tissue processing was performed. The samples were embedded in paraffin blocks, and 3 µm thick sections were taken for microscopic examination. These sections were stained with haematoxylin–eosin to prepare slides. If necessary, additional histochemical and immunohistochemical tests were performed to aid the diagnosis. The microscopic evaluation, conducted by expert pathologists, involved documenting the morphological findings and test results electronically. These findings were used to reach definitive diagnoses.

Statistical Analysis

All the data were analysed using the software SPSS Statistics. In this article, demographic data are expressed as means±standard deviations, while categorical variables are expressed as percentages. After excluding cases with no preliminary diagnosis and insufficient samples, the departments with the highest rates of malignancy diagnoses and the most common malignancy diagnoses were identified and expressed as percentages. The preliminary and pathological diagnoses for each department were categorised as either concordant or discordant, and interdepartmental comparisons were performed using chi-square and Fisher's exact tests. A p-value of <0.05 was considered statistically significant.

RESULTS

In this study, a total of 1,821 patients were evaluated. The mean age of the participants was 74.8 years, with an age range of 65 to 95 years. The patient group comprised 44% (n=801) females and 56% (n=1,020) males. The majority of pathology requests originated from internal medicine departments, with haematology accounting for the highest proportion (57.3%, n=1,043), followed by medical oncology (21.8%, n=398) and general internal medicine (7.2%, n=132). Requests from nephrology, geriatrics and rheumatology each constituted less than 5% of the total (Table 1).

Regarding the initial clinical diagnoses, the most common was multiple myeloma, which accounted for 30.8% (n=563) of cases. This was followed by MDS (18.5%, n=338) and chronic myeloproliferative disorders (CMPDs) (14.2%, n=258). Less common diagnoses included CLL (3.1%, n=56), lymphoma (13.8%, n=251) and AML (6.9%, n=117).

The pathological evaluations yielded various diagnoses. A total of 6.8% (n=124) of the samples were deemed insufficient for a definitive diagnosis. Among the confirmed pathological findings, multiple myeloma was diagnosed in 14.5% (n=265) of cases, CMPDs in 7.4% (n=135) of cases and MDS in 2.9% (n=53). Lymphomas were further classified into subtypes, with diffuse large B-cell lymphoma identified in 7.1% (n=130) of cases. Other less common subtypes included follicular lymphoma, Hodgkin lymphoma, hairy cell leukaemia and mantle cell lymphoma. Among the types of acute leukaemia, AML and ALL were diagnosed at rates of 6% (n=110) and 0.5% (n=9), respectively (Table 1).

Non-specific bone marrow changes were categorised as hypercellular (21.8%, n=398) and hypocellular (2.4%, n=43), making these some of the most frequently observed findings. Additionally, non-specific pathologies were diagnosed in 25.7% (n=469) of cases.

A total of 1,624 samples from various departments were analysed in this study. Of these, 852 were diagnosed with non-specific findings, while malignancy was identified in 772 samples. When the malignancy rates were analysed by department, haematology had the highest rate at 59.6% (n=459),

Table 1. Characteristics of the study cohort (n=1821)

Age, mean (min-max)	74.8 (65-95)
Sex, n (%)	
Women	801 (44)
Men	1020 (56)
Medical department requesting biopsy, n (%)	
Internal Medicine	
Hematology	1043 (57.3)
Medical Oncology	398 (21.8)
General Internal Medicine	132 (7.2)
Nephrology	65 (3.6)
Geriatrics	18 (1.0)
Rheumatology	7 (0.4)
Intensive Care Unit	79 (4.3)
Surgical Departments	22 (1.2)
Others	57 (3.2)
Preliminary diagnoses	
Unspecified	82 (4.5)
Multiple Myeloma	563 (30.8)
Myelodysplastic Syndrome (MDS)	338 (18.5)
Chronic Myeloproliferative Hematopathies (CMPH)	258 (14.2)
Chronic Lymphocytic Leukemia (CLL)	56 (3.1)
Lymphoma	251 (13.8)
Acute Myeloid Leukemia (AML)	117 (6.9)
Amyloidosis	21 (1.2)
Anemia	71 (3.8)
Metastasis	64 (3.5)
Pathological diagnoses	
Insufficient sample	124 (6.8)
Multiple Myeloma	265 (14.5)
MDS	53 (2.9)
CMPH	135 (7.4)
CLL	32 (1.8)
Lymphoma	
Diffuse large B-cell lymphoma (DBBH) Lymphoma	130 (7.1)
Follicular lymphoma	6 (0.3)
Hodgkin Lymphoma	3 (0.2)
Hairy cell Leukemia	5 (0.3)
Mantle cell Lymphoma	7 (0.4)
AML	110 (6)
ALL	9 (0.5)
Hypercellularity	398 (21.8)
Hypocellularity	43 (2.4)
Nonspecific	469 (25.7)

which was statistically significant (p=0.026). This was followed by the oncology department, with a malignancy rate of 19.6% (n=151) (Table 2).

The malignancy rate in the samples from the general internal medicine department was 7.3% (n=56), while it was 4.0% (n=31) in the nephrology department. In the samples from the geriatrics and rheumatology departments, the malignancy rates were 0.8% (n=6) and 0.0% (n=0), respectively. The samples from the intensive care unit had a malignancy rate of 2.7% (n=43), while the rate was 1.0% (n=8) in the surgical departments.

When comparing the initial clinical diagnosis with the final pathological diagnosis, 61.9% (n=1,001) of diagnoses were found to be concordant, while 38.1% (n=616) were discordant. The highest discordance rate was observed in the haematology department (59.4%, n=366), which was statistically significant (p=0.024). The oncology department had a discordance rate of 20.5% (n=126), making it the second highest one (Table 3).

The discordance rates in the general internal medicine and nephrology departments were 5.8% (n=36) and 4.9% (n=30), respectively. The geriatrics department had a notably low discordance rate (0.5%, n=3), while no discordance was observed in the rheumatology department. The samples from the intensive care unit had a discordance rate of

Table 2. Malignancy diagnosis according to departments

Department, n (%)	Non-specific (n=852)	Malignity (n=772)	p
Hematology	482 (57.3)	459 (59.6)	
Oncology	211 (25.1)	151 (19.6)	
General Internal Medicine	52 (6.2)	56 (7.3)	
Nephrology	30 (3.6)	31 (4.0)	
Geriatrics	9 (1.1)	6 (0.8)	p=0.026
Rheumatology	4 (0.5)	0 (0.0)	
Intensive Care Unit	25 (3.0)	43 (2.7)	
Surgical departments	11 (1.3)	8 (1.0)	
Others	17 (2.0)	16 (2.1)	

Table 3. Concordance rates among the departments ordering the biopsies

Department, n, (%)	Concordant (n=1001)	Discordant (n=616)	p
Hematology	578 (57.8)	366 (59.4)	
Oncology	238 (23.8)	126 (20.5)	
General Internal Medicine	73 (7.3)	36 (5.8)	
Nephrology	31 (3.1)	30 (4.9)	
Geriatrics	12 (1.2)	3 (0.5)	0.024
Rheumatology	4 (0.4)	0 (0.0)	
Intensive Care Unit	32 (3.2)	36 (5.8)	
Surgical departments	13 (1.3)	6 (1.0)	
Others	20 (2.0)	13 (2.1)	

5.8% (n=36), whereas the rate was 1.0% (n=6) in the surgical departments. The other departments exhibited a discordance rate of 2.1% (n=13).

DISCUSSION

In our study, we retrospectively examined the concordance between clinical pre-diagnoses and pathological BMB findings in patients aged 65 years or older. Data from a total of 1,821 patients were analysed, and 1,624 biopsy samples from various clinics were evaluated. The findings indicate that BMB is a critical tool in diagnosing haematological disorders in the elderly population. Notably, biopsy requests from departments such as internal medicine, haematology and oncology were frequently associated with a high rate of malignancy diagnoses, underscoring the high diagnostic sensitivity of these departments (3, 4).

The high rate of malignancy detection (59.6%, p=0.026) in biopsies requested by the haematology department supports the accuracy of biopsies performed under suspicion of haematological diseases. As reported in the literature, the incidence of haematological malignancies increases with age, which prompts haematology clinics to request biopsies with greater caution (6). However, the high discordance rate (59.4%) between pre-diagnoses and pathological diagnoses in haematology suggests the need for significant improvements in the diagnostic process. This discordance not only leads to unnecessary biopsies but also poses a risk to patient safety due to the invasive nature of the procedures; it also generates unnecessary costs for the healthcare system (10).

Although the biopsy requests from the oncology department were largely based on a suspicion of malignancy, the discordance rate between clinical pre-diagnoses and pathological findings was relatively high (20.5%). This suggests that the diagnostic algorithms used in this department may need a thorough review. While the malignancy detection rate was 19.6% among oncology patients, which reflects the fact that biopsy requests are often based on malignancy pre-diagnoses, clinical evaluations should be conducted with greater precision (12, 13). These results emphasise the need for more effective use of advanced diagnostic tests (e.g., flow cytometry and molecular genetic tests) and a multidisciplinary approach (14).

The lower malignancy rates observed in departments such as general internal medicine, nephrology and intensive care (7.3%, 4.0% and 2.7%, respectively), coupled with the high proportion of non-specific findings, indicate that these clinics faced a broader spectrum of diagnostic uncertainties. In elderly patients, the prevalence of non-specific symptoms may lead to unnecessary BMB procedures It is essential to consider the heterogeneity of the geriatric population in these cases. While chronological age is often used as a benchmark, physiological age plays a more critical role in decision-making for invasive procedures. In frail or severely debilitated patients, particularly those aged 85 years and older, the risks associated with BMB and other diagnostic interventions may outweigh the potential benefits. However, it is important to note that in certain conditions such as chronic myeloproliferative diseases, critical findings like bone marrow fibrosis, which is detectable only via BMB, play a significant diagnostic role. Similarly, in solid tumours, while bone marrow biopsies are less frequently diagnostic compared to metastasis screening purposes, the absence of metastases in such cases cannot be interpreted as discordance, as this information is still highly relevant for oncological decision-making.

The low discordance rates between pre-diagnoses and pathological findings in the geriatrics and rheumatology clinics (0.5% and 0.0%, respectively) suggest that biopsy requests in these departments were made with greater caution and based on more specific criteria. Avoiding unnecessary invasive procedures in older patients

is crucial for patient safety and quality of life (11, 15). Our findings highlight that the discordance observed in certain cases originates from the misalignment between clinical pre-diagnoses and pathological outcomes. This discordance is not merely a diagnostic challenge but also increases the likelihood older individuals undergoing additional invasive tests or procedures, further complicating their clinical management. Efforts should be directed at minimizing such discrepancies through improved diagnostic algorithms and better communication of clinical indications on pathology request forms.

In our study, the high rates of non-specific bone marrow changes (21.8% hypercellular, 2.4% hypocellular) demonstrate that BMB in the elderly population is essential not only for malignancy diagnosis but also for evaluating various haematological disorders (2, 16). In particular, peripheral blood cytopenia warrant careful evaluation to ensure that appropriate diagnostic samples are obtained, and unnecessary invasive procedures are avoided. Non-specific findings such as hypo- and hypercellular bone marrow, while categorized as non-specific in this study, may still provide critical diagnostic insights when correlated with specific clinical scenarios, such as suspected multiple myeloma. However, the inadequacy of 6.8% of the samples highlights the need for improvements in biopsy techniques and the quality of specimens (17). Stratifying older patients based on physiological rather than chronological age can improve the accuracy and safety of invasive diagnostic interventions. Moreover, advanced diagnostic methods, such as immunophenotyping and molecular genetic analyses, may supplement or even replace BMB in certain cases when adequate peripheral samples are available, reducing the need for unnecessary biopsies. Future studies should consider stratifying elderly patients into more specific age groups to better evaluate the appropriateness of invasive procedures. For instance, distinguishing between patients aged 65-79, 80-85, and above 85 years could provide clearer insights into the risks and benefits of BMB in these subgroups.

The development of new diagnostic algorithms is critically needed to prevent unnecessary invasive procedures in the older population (18). Incorporating a multidisciplinary approach that includes geriatric assessments can aid in tailoring diagnostic and therapeutic interventions based on the patient's physiological capacity and expected benefit, particularly in advanced age groups. The high discordance rate (38.1%) identified in our study suggests that current clinical protocols may not be sensitive enough for elderly patients. More advanced non-invasive tests (e.g., imaging techniques and genetic analyses) should be used before performing BMB, particularly in haematology and oncology departments. This approach could better determine the need for biopsies, thus reducing unnecessary invasive procedures and enhancing patient safety (14, 19).

One of the key strengths of this study is its comprehensive retrospective analysis, which highlighted the importance of BMB in diagnosing haematological diseases in the elderly population. By evaluating samples from various clinical departments, the study effectively assessed both diagnostic processes and the concordance between clinical pre-diagnoses and pathological findings. Furthermore, the comparison of malignancy detection rates and interdepartmental diagnostic discrepancies provided valuable insights into the sensitivity of diagnostic algorithms, especially for older patients. This kind of analysis is crucial to optimise diagnostic procedures in this demographic. However, the study also has certain limitations. The retrospective design may have introduced bias in the data collection. Furthermore, the fact that 6.8% of biopsy samples were deemed insufficient indicates that biopsy techniques and sample quality should be improved. Another limitation is the potential impact

of incomplete or poorly documented pathology request forms. These inconsistencies may have contributed to the observed discordance between clinical pre-diagnoses and pathological findings, particularly in cases involving non-specific bone marrow changes. Ensuring better communication and comprehensive clinical details on pathology request forms is essential to improving diagnostic accuracy. Additionally, the classification of hypo- and hypercellular bone marrow findings as non-specific in this study may have underestimated their diagnostic significance. Future studies should aim to correlate such findings more closely with clinical indications to better evaluate their role in specific conditions, such as multiple myeloma. The high rates of discordance, particularly in the haematology and oncology departments, suggest that existing diagnostic algorithms may not be sufficiently sensitive for older patients. This highlights the need for the expanded use of advanced diagnostic tests (e.g., molecular genetic analyses and advanced imaging techniques) before resorting to invasive procedures in order to improve diagnostic accuracy and patient safety.

In conclusion, our study underscores the importance of performing BMB in the older population based on accurate clinical indications. In older patients, BMB should be performed with careful consideration of the benefit-to-risk ratio, especially in those aged 80 years and older. Optimising multidisciplinary assessments and diagnostic processes not only enhances patient safety but also contributes to the cost-effectiveness of the healthcare system. Future studies should focus on developing new protocols to optimise diagnostic processes in older patients. Age-specific stratification could further improve the safety and efficacy of BMB in this population. These measures may reduce the discordance between clinical pre-diagnoses and pathological findings, thereby streamlining the diagnostic process. Additionally, integrating a multidisciplinary approach that includes geriatric assessments into diagnostic algorithms could enhance decision-making and improve patient outcomes, particularly in frail and vulnerable older individuals.

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