# Differences in the diagnosis and treatment of hematologic malignancies attributable to health insurance coverage

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# Abstract

Medical care should be equally provided to the public regardless of their financial capability. In the real world, expenditures directly out from the patient sector decide the medical journey, even in a country with national health insurance. The aim of this study was to investigate whether there are differences in the diagnostic and treatment processes in hematologic malignancies based on patient characteristics, such as health insurance status.

Through the review of 5614 "CBCs with differential count" results with abnormal cells from 358 patients from January 2010 to June 2017, 238 patients without past medical histories of hematologic malignancies were enrolled. Excluding reactive cases, 206 patients with hematologic malignancy were classified into 8 disease categories: acute leukemia, myelodysplastic syndrome, myeloproliferative neoplasm (MPN), myelodysplastic syndrome/MPN, lymphoid neoplasm, plasma cell neoplasm, r/o hematologic malignancy, and cancer.

The patients' age, sex, disease categories and follow-up durations showed associations with the clinical course. The "refusal of treatment" group was the oldest and had a relatively higher percentage of females, whereas those who decided to transfer to a tertiary hospital were younger. The age, clinical course, and follow-up durations were different across health insurance statuses. The medical aid group was the oldest, and the group whose status changed from a medical insurance subscriber to a medical aid beneficiary during treatment was the youngest. The majority of patients who refused treatment or wished to be transferred to a tertiary hospital were medical insurance subscribers. The percentage of patients who were treated in this secondary municipal hospital was higher in the medical-aid beneficiaries group than in the medical insurance group. Follow-up durations were longest in the status change group and shortest in the medical insurance group.

Almost all medical aid beneficiaries with hematologic malignancies opted to continue treatment at this secondary/municipal hospitals, indicating that this category of medical institutions provides adequate levels and qualified healthcare services to those patients. The secondary municipal hospital provides qualified healthcare services for medical aid beneficiaries with hematologic malignancies.

**Abbreviations:** BM = bone marrow, CBC w/diff = complete blood count with differential, HSCT = hematopoietic stem cell transplantation, MDS = myelodysplastic syndrome, MPN = myeloproliferative neoplasm, NHI = national health insurance, PBS = peripheral blood smear, SES = socioeconomic status.

Keywords: hematologic malignancy, Korea, medical process, municipal hospital, national health insurance system

# 1. Introduction

The national health insurance (NHI) system applies to residents of Korea; the government also provides medical aid programs as a part of the public assistance system for those who are unable to pay for their own healthcare coverage. Therefore, there are differences in the medical expenses paid by the person depending on socioeconomic status (SES). Medical centers in Korea are classified as 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> grades according to the number of

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The data that support the findings of this study are not publicly available due to [their containing information that could compromise the privacy of research participants] but are available from the corresponding author [EYR].

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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wards, and there is a difference in the total cost that patients must pay based on grade.

The complete blood count (CBC) with differential (w/diff) is an inexpensive, convenient and valuable test and useful as a routine test for hematologic diagnosis.<sup>[1,2]</sup> If abnormal cells are found in CBC w/diff, the next step is usually a physician-requested peripheral blood smear (PBS) examination. PBS examination has direct diagnostic utility for certain groups of hematologic diseases while providing adjunctive information to CBC results. Bone marrow (BM) examinations are usually requested in response to abnormalities in the CBC and/or PBS results.

This medical center is a general hospital (a secondary referral center) with the characteristics of a public hospital (municipal medical center). Compared with tertiary referral centers, secondary medical centers result in lower patient expenditures for medical treatment and thus can provide quality care to low-income patients. However, in the case of severe diseases, there is a marked trend toward seeking treatment in tertiary, specialized hospitals. In the case of hematologic malignancy, especially when aggressive treatment (hematopoietic stem cell transplantation, HSCT) is desired, young patients in particular tend to be treated in tertiary hospitals, which have greater cumulative experience in treating the disease.

The aim of this study was to investigate whether there are differences in the diagnostic and treatment processes in hematologic malignancies based on patient characteristics, such as health insurance status.

# 2. Materials and methods

# 2.1. Study population

We reviewed the CBC w/diff results obtained at Seoul National University Boramae Medical Center from January 2010 to June 2017. A total of 5614 CBC w/diff results from 385 patients showed more than 1% blasts, immature (metamyelocytes or less mature) granulocytes or abnormal/atypical lymphocytes. Among these patients, 147 patients who had already been diagnosed and treated for hematologic disorders or malignancies were excluded, and the remaining 238 patients were enrolled in this study.

# 2.2. Demographic and clinical characteristic data collection

Information about age, sex, diagnosis, past medical history (whether the patient had already been diagnosed and treated for a hematologic disorder or malignancy), health insurance status, eligibility for medical aid, and the duration from the date of first appearance of abnormal cells to the most recent follow-up date before July 2019 was obtained from the review of the electronic medical records. The CBCs w/diff in Ethylenediaminetetraacetic acid-anticoagulated whole blood samples were obtained using an XE-2100 (Sysmex Corporation, Kobe, Japan) and an XN-9000 hematology analyzer (Sysmex Corporation, Kobe, Japan). Prior to reporting, a morphological review was performed on patients who showed abnormal cells without accumulated findings.<sup>[3]</sup> PBSs, BM aspirations, and BM trephine biopsy sections were reviewed by hematopathologists. In cases where a BM examination was difficult to perform, leukemia could be diagnosed through flow cytometric immunophenotyping of PB blasts. In general, a diagnosis of hematologic malignancy was made according to the "World Health Organization classification of tumors of hematopoietic and lymphoid tissues" from a review of the BM and PBSs, immunophenotyping, chromosomal analysis, and molecular analysis.<sup>[4]</sup>

### 2.3. Statistical analysis

Continuous variables with a normal distribution are presented as the mean (standard deviation); nonnormal variables are reported as the median (interquartile range), and categorical variables are expressed as frequencies or percentages. Analysis of variance or the independent t test was performed for continuous variables, and Pearson chi-square test or Fisher exact test was used for categorical variables to assess differences among groups. A Pvalue less than .05 indicated a significant result. Statistical analysis was performed using Statistical Package for the Social Sciences 22.0 for Windows (SPSS, Chicago, IL).

# 2.4. Ethical approval

This study adhered to the tenets of the Declaration of Helsinki, and the study protocol was approved by the institutional review board of Seoul National University Boramae Medical Center (Institutional Review Board approval number: 30-2018-59), which waived the requirement for informed consent because the study had a retrospective design.

### 3. Results

#### 3.1. Characteristics of the study population

A total of 238 patients with abnormal cells in the CBC w/diff and without a history of hematologic disorder/malignancy were enrolled. The demographic data, health insurance status, and clinical characteristics are shown in Table 1. The 206 patients with hematologic malignancies were classified into 8 disease categories, and the diagnosis with the highest frequency was acute leukemia (55.3%). More than half of patients continued treatment at this institution after diagnosis, 18.5% of patients decided to transfer to another medical center, and 9.7% refused treatment. Medical insurance subscribers constituted 84.9% of the patients, medical aid beneficiaries constituted 10.1%, and 5.0% of subjects changed from being eligible for medical insurance to medical aid beneficiaries. The follow-up period ranged from 0 to 3512 days. Compared with the patients with reactive disease, patients with confirmed or strongly suspected hematologic or malignant disorders were older and had a longer follow-up period.

# 3.2. Association between clinical course and the characteristics of the 206 subjects with hematologic/ malignant disorders

There were significant differences in patient characteristics, including age, sex, diagnostic workup and follow-up duration, for different clinical courses and decisions, such as treatment or transfer to other hospitals (Table 2 and Fig. 1). Patient age was associated with the clinical course: patients who refused treatment and died before treatment were relatively older, whereas those who wanted to transfer to tertiary hospitals were relatively younger ( $P = 1.05 \times 10^{-12}$ ). The male/female ratio was inversed only in the refused treatment group, with a significantly higher frequency of females (P = .015). PBSs were performed for almost every patient, but the BM examination rate was different

# Table 1

### Characteristics of the 238 study subjects.

|   | Total        | Reactive <sup>*</sup> | Hematologic/malignant <sup>†</sup> | ${\it P}$ value $^{\ddagger}$ |
|---|--------------|-----------------------|------------------------------------|-------------------------------|
| Characteristics                         | N=238        | N=32                  | N=206                              |                               |
| Age (yr)                                | 62.7 (24.2)  | 48.8 (61.0)           | 64.7 (22.5)                        | $5.40 \times 10^{-5}$         |
| Sex (male)                              | 149 (62.6%)  | 18 (56.3%)            | 131 (63.6%)                        | NS                            |
| Blast (+)                               | 190 (79.8%)  | 8 (25.0%)             | 182 (88.3%)                        | $9.66 \times 10^{-17}$        |
| Immature granulocyte (+)                | 44 (18.5%)   | 7 (21.9%)             | 37 (18.0%)                         | NS                            |
| Abnormal/atypical lymphocyte (+)        | 43 (18.1%)   | 20 (62.5%)            | 23 (11.2%)                         | $2.19 \times 10^{-12}$        |
| PBS (+)                                 | 224 (94.1%)  | 19 (59.4%)            | 205 (99.5%)                        | $4.96 \times 10^{-12}$        |
| BM exam (+)                             | 168 (70.6%)  | 1 (3.1%)              | 167 (81.1%)                        | $2.20 \times 10^{-19}$        |
| Disease category                        |              |                       |                                    | NA                            |
| Acute leukemia                          | 114 (47.9%)  |                       | 114 (55.3%)                        |                               |
| MDS                                     | 9 (3.8%)     |                       | 9 (4.4%)                           |                               |
| MPN                                     | 28 (11.8%)   |                       | 28 (13.6%)                         |                               |
| MDS/MPN                                 | 4 (1.7%)     |                       | 4 (1.9%)                           |                               |
| Lymphoid neoplasm                       | 17 (7.1%)    |                       | 17 (8.3%)                          |                               |
| Plasma cell neoplasm                    | 4 (1.7%)     |                       | 4 (1.9%)                           |                               |
| r/o hematologic malignancy <sup>§</sup> | 29 (12.2%)   |                       | 29 (14.1%)                         |                               |
| Cancer (solid tumor)                    | 1 (0.4%)     |                       | 1 (0.5%)                           |                               |
| Reactive <sup>*</sup>                   | 32 (13.4%)   | 32 (100.0%)           |                                    |                               |
| Clinical course                         |              |                       |                                    | NA                            |
| Treatment                               | 122 (51.3%)  |                       | 122 (59.2%)                        |                               |
| Transfer to tertiary medical institute  | 44 (18.5%)   |                       | 44 (21.4%)                         |                               |
| Refusal of treatment <sup>  </sup>      | 23 (9.7%)    |                       | 23 (11.2%)                         |                               |
| Death prior to treatment                | 17 (7.1%)    |                       | 17 (8.3%)                          |                               |
| Reactive <sup>*</sup>                   | 32 (13.4%)   | 32 (100.0%)           |                                    |                               |
| Insurance status                        |              |                       |                                    | NS                            |
| Medical-insurance                       | 202 (84.9%)  | 28 (87.5%)            | 174 (84.5%)                        |                               |
| Medical-aid                             | 24 (10.1%)   | 4 (12.5%)             | 20 (9.7%)                          |                               |
| Change in status                        | 12 (5.0%)    | 0 (0.0%)              | 12 (5.8%)                          |                               |
| Follow-up duration (day)                | 38.0 (285.0) | 0.0 (3.0)             | 60.5 (370.0)                       | $2.15 \times 10^{-13}$        |

Data are presented as frequencies (%) and medians (interquartile range).

BM = bone marrow, MDS = myelodysplastic syndrome, MPN = myeloproliferative neoplasm, NA = not available, NS = not significant, PBS = peripheral blood smear.

\* No hematologic disorder or malignant disorder.

<sup>†</sup> Diagnosed or highly suspected of hematologic or malignant disorder.

\* Comparison between reactive and hematologic/malignant disorder groups by means of chi-square or Fisher exact test and Mann–Whitney U test.

<sup>§</sup> No confirmatory diagnosis by means of BM exam.

|| Except supportive care.

between groups. The majority of the treatment or transfer group underwent BM examinations; however, more than 50% of the refused treatment or died before treatment group did not (P = 2.68 $\times$  10<sup>-10</sup>). The clinical course was significantly associated with disease category ( $P = 5.06 \times 10^{-8}$ ). In the treatment, transfer and refusal groups, acute leukemia was the most common (63.9%, 47.7%, and 39.1%, respectively), and "suspected of hematologic malignancy" was the most common category in the death before treatment group, with more than 50%. "Suspected of hematologic malignancy" was also observed frequently in the transfer and refusal groups (20.5% and 47.8%), ranking second. In the treatment group, MPN was the second-most common disease category (16.4%), followed by lymphoid malignancy (10.7%). The longest follow-up duration was observed in the treatment group and was significantly longer than that of the remaining groups (275.0 vs 5.0, 23.0, and 10.0 days; P value =  $2.34 \times 10^{-26}$ ).

# 3.3. Association between health insurance status and characteristics among patients with hematologic/ malignant disorder

Sex, abnormal cell type, workup, and diagnosis were not different for insurance statuses. There were differences in age, clinical course, and follow-up duration among the different insurance

statuses (Table 3 and Fig. 1). The medical-aid beneficiary group was the oldest (70.4 years), and the group whose status changed from insurance subscriber to medical-aid beneficiary was the youngest (52.1 years); this difference was statistically significant (P=.044). The clinical course showed a significant association with patient insurance status (P=.008). Patients who sought treatment in this hospital were more common in the medical aid beneficiary group (17/20) and status change group (12/12) than in the medical insurance subscriber group (93/174). All those who wanted to transfer to tertiary hospitals (44/44, 100%) and the majority who refused treatment (22/23, 95.7%) were medical insurance subscribers. Patients who sought treatment in this hospital were more common in the medical-aid beneficiaries group (17/20, 85.0%) and status change groups (12/12, 100%) than in the medical insurance subscribers group (93/174, 53.4%). The follow-up durations of each group were significantly different: 38.5 days for the medical insurance subscriber group, 235.5 days for the medical aid beneficiary group, and 1470.0 days for the status change group (P=.001).

# 4. Discussion

If abnormal findings are observed in CBC and a hematologic/ malignant disorder is suspected, typically, PBS and BM are Table 2

| Characteristics                         | Clinical course   |   |  |                                   |                              |
|---|-------------------|---|--|-----------------------------------|------------------------------|
|   | Treatment N = 122 | Transfer to tertiary medical institute $N = 44$ | Refusal of treatment <sup>*</sup> $N = 23$ | Death prior to treatment $N = 17$ | $\pmb{P}$ value <sup>†</sup> |
| Age (yr)                                | 64.7 (16.8)       | 40.4 (28.1)                                     | 82.8 (19.9)                                | 72.5 (14.9)                       | $1.05 \times 10^{-12}$       |
| Sex (male)                              | 79 (64.8%)        | 31 (70.5%)                                      | 8 (34.8%)                                  | 13 (76.5%)                        | .015                         |
| Blast (+)                               | 104 (85.2%)       | 43 (97.7%)                                      | 20 (87.0%)                                 | 15 (88.2%)                        | NS                           |
| Immature granulocyte (+)                | 22 (18.0%)        | 11 (25.0%)                                      | 3 (13.0%)                                  | 1 (5.9%)                          | NS                           |
| Abnormal/atypical lymphocyte (+)        | 14 (11.5%)        | 2 (4.5%)  | 5 (21.7%)                                  | 2 (11.8%)                         | NS                           |
| PBS (+)                                 | 122 (100.0%)      | 44 (100.0%)                                     | 22 (95.7%)                                 | 17 (100.0%)                       | NS                           |
| BM exam (+)                             | 116 (95.1%)       | 34 (77.3%)                                      | 9 (39.1%)                                  | 8 (47.1%)                         | $2.68 \times 10^{-10}$       |
| Disease category                        |                   |   |  |                                   | $5.06 \times 10^{-8}$        |
| Acute leukemia                          | 78 (63.9%)        | 21 (47.7%)                                      | 9 (39.1%)                                  | 6 (35.3%)                         |                              |
| MDS                                     | 6 (4.9%)          | 2 (4.5%)  | 1 (4.3%)                                   | 0 (0.0%)                          |                              |
| MPN                                     | 20 (16.4%)        | 8 (18.2%)                                       | 0 (0.0%)                                   | 0 (0.0%)                          |                              |
| MDS/MPN                                 | 2 (1.6%)          | 2 (4.5%)  | 0 (0.0%)                                   | 0 (0.0%)                          |                              |
| Lymphoid neoplasm                       | 13 (10.7%)        | 1 (2.3%)  | 2 (11.8%)                                  | 1 (5.9%)                          |                              |
| Plasma cell neoplasm                    | 2 (1.6%)          | 1 (2.3%)  | 0 (0.0%)                                   | 1 (5.9%)                          |                              |
| r/o hematologic malignancy <sup>‡</sup> | 0 (0.0%)          | 9 (20.5%)                                       | 11 (47.8%)                                 | 9 (52.9%)                         |                              |
| Cancer (solid tumor)                    | 1 (0.8%)          | 0 (0.0%)  | 0 (0.0%)                                   | 0 (0.0%)                          |                              |
| Follow-up duration (day)                | 270.5 (1309.0)    | 5.0 (10.0)                                      | 23.0 (17.0)                                | 10.0 (20.0)                       | $2.34 \times 10^{-26}$       |

among the 206 nationte with hemotologie/molign

Data are presented as frequencies (%) and medians (interquartile ranges).

BM = bone marrow, MDS = myelodysplastic disorder, MPN = myeloproliferative disorder, NS = not significant, PBS = peripheral blood smear.

Except supportive care.

<sup>†</sup> Comparison by means of chi-square or Fisher exact test and Mann–Whitney U test.

\* No confirmatory diagnosis by means of BM exam.

subsequently examined to confirm the diagnosis. However, if the patient's general condition is bad, the patient is very old or the patient and family strongly refuse treatment, only supportive care is provided until death without a final diagnosis. In addition, when a hematologic malignancy is strongly suspected (eg, PB blasts > 5%), it is not uncommon for a patient to request immediate transfer to a tertiary hospital without undergoing confirmation. The results of this study show that age is an important factor in determining the diagnostic workup or the treatment after diagnosis. Children and young adults often chose to transfer to tertiary hospitals for aggressive treatment, including HSCT, when diagnosed or suspected of hematologic malignancy, so the median age was the lowest in this group, whereas very elderly patients were more likely to refuse treatment or even diagnostic workups, including BM examination. Very old patients may actually have physical conditions that make certain treatments, such as chemotherapy, difficult to tolerate, or their "old age" may act as an impetus for family members or the patient to pass on treatment in advance and accept the natural course of the disease. It is difficult to accurately distinguish the patient's situation, and sometimes the causes are complex. There were more elderly patients in the died before treatment group than in the treatment group or the transfer group, and they had already come to the hospital with a serious condition or had a sudden deterioration in the condition, representing patients for whom the BM diagnosis could not be obtained.

Interestingly, there was a difference in the clinical course according to sex. The proportion of female patients was significantly higher in the refused treatment group, but other characteristics, such as age, follow-up duration, BM examination rate, abnormal cell type and insurance status, were not different between male and female patients (data not shown). The life expectancy of Koreans is longer among females (85.7 years) than among males (79.7 years),<sup>[5]</sup> but there was no difference in age among the subjects of the present study (median age 62.6 vs 63.1

years, data not shown). The proportion of those over 80 years old was higher among female patients (19.1%) than among male patients (12.1%), but the difference was not significant (data not shown). It is difficult to explain the reasons for the sex differences based on the results of this study alone, but it is estimated that some sociocultural or psychological factors may be at play. Elderly Koreans, especially elderly women, tend to be very reluctant to put an economic burden on their families, and this is considered one of the reasons for refusal of treatment. In addition, since husbands are usually older than their wives and women have a longer life expectancy, older male patients are more likely than female patients to have a surviving spouse to support treatment, which may also be related to the higher proportion of women in the refused treatment group. There are no data to evaluate the actual income level other than the insurance status; therefore, it is hard to verify whether the economic factor is due to this difference.

In Korea, patients with severe diseases tend to prefer tertiary hospitals; this is also common among patients with hematologic malignancies. Considerable numbers of patients who expected to receive treatment for any of these diseases in the secondary hospital in this study preferred to be transferred to a tertiary hospital. If they wished to be transferred to other hospitals, most preferred one of several tertiary hospitals that specialize in the treatment of hematologic disorders and actively perform HSCT. Approximately three-quarters of the patients who transferred to tertiary hospitals made the decision to transfer after receiving a hematologic diagnosis through BM examination, and the rest were transferred under suspicion of hematologic malignancy. Since a large number (>5%) of blasts in the PB strongly suggest a hematologic malignancy such as leukemia, even before the BM examination, this information alone could help patients make decisions.

Health insurance type represents the individual or household SES in the Republic of Korea. As compulsory social insurance,



Figure 1. Association between (A, C) age and (B, D) follow-up duration and the clinical course and health insurance status of hematologic disorder patients. Age and follow-up duration showed significant differences across clinical courses ( $P = 1.05 \times 10^{-12}$  and  $2.34 \times 10^{-26}$ ) and health insurance statuses (P = .044 and .001), respectively.

Korean health insurance covers the whole population living in the country (97.1%), except for medical-aid beneficiaries (2.9%).<sup>[6]</sup> The government's medical aid program is a form of public assistance scheme that ensures a minimum livelihood for low-income households and assists with self-help by providing medical services. Medical-aid beneficiaries are individuals or members of families with an income below the minimum cost of living according to the Korean National Basic Living Security Act.<sup>[7]</sup> The Korean healthcare delivery system, managed by the NHI, secures the continuation of primary, secondary, and tertiary care, ensures proper healthcare services, and eases overcrowding in large-scale medical centers.<sup>[8]</sup>

Medical-aid beneficiaries rarely refused treatment (only 1 patient), and none of the medical-aid beneficiaries transferred to a tertiary hospital, since patients supported by the medical-aid program in Korea recoup almost all medical costs for treatment. Although there was no difference in the frequency of disease categories among health insurance statuses, the age of medical-aid beneficiaries was the oldest, none of them refused treatment, and none of them transferred to another hospital. Socioeconomic

disparities in the probability of transfer have been described for other disorders; Korean patients with a higher SES were more likely to be transferred to hospitals with a greater capacity for postresuscitation care in cardiac arrest studies.<sup>[9]</sup> The patients in the medical-aid beneficiary group are thought to be treated at a municipal secondary hospital due to the minimal benefits from transferring to a tertiary institution and to continue treatment due to the lack of a medical expense burden. Although medical-aid beneficiaries receive compensation for the treatment costs at tertiary hospitals, the total payments for nonreimbursed items at tertiary institutions are greater than those at secondary hospitals. It is presumed that municipal hospitals are preferred by medical aid beneficiaries because of the lower cost of nonreimbursed items. From January 1, 2018, the "extra fees for care by the selected physician of choice" were abolished, but it was still effective at the time of the study, and accordingly, the treatment costs at tertiary hospitals were higher than those at secondary medical institutions. Among secondary hospitals, municipal hospitals in particular exempt medical aid patients from "extra fees for care by the selected physician of choice". In addition to the lower medical costs, another reason for selecting a municipal

Table 3

#### Association between health insurance and clinical characteristics among the 206 patients with hematologic/malignant disorder.

|   | Health Insurance status |                       |                          |                             |
|---|-------------------------|-----------------------|--------------------------|-----------------------------|
| Characteristics                         | Medical-insurance       | Medical-aid<br>N = 20 | Change in status<br>N=12 | <b>P</b> value <sup>*</sup> |
|   | N=174                   |                       |                          |                             |
| Age (yr)                                | 66.0 (22.8)             | 70.4 (17.5)           | 52.1 (27.2)              | .044                        |
| Sex (male)                              | 109/174 (61.4%)         | 17/20 (70.8%)         | 8/12 (66.7%)             | NS                          |
| Blast (+)                               | 155/174 (89.1%)         | 16/20 (80.0%)         | 11/12 (91.7%)            | NS                          |
| Immature granulocyte (+)                | 31/174 (17.8%)          | 3/20 (15.0%)          | 3/12 (25.0%)             | NS                          |
| Abnormal/atypical lymphocyte (+)        | 19/174 (10.9%)          | 3/20 (15.0%)          | 1/12 (8.3%)              | NS                          |
| PBS (+)                                 | 173/174 (99.4%)         | 20/20 (100.0%)        | 12/12 (100.0%)           | NS                          |
| BM exam (+)                             | 139/174 (79.9%)         | 16/20 (80.0%)         | 12/12 (100.0%)           | NS                          |
| Disease category                        |                         |                       |                          | NS                          |
| Acute leukemia                          | 96/174 (55.2%)          | 10/20 (50.0%)         | 8/12 (66.7%)             |                             |
| MDS                                     | 8/174 (4.6%)            | 1/20 (5.0%)           | 0/12 (0.0%)              |                             |
| MPN                                     | 21/174 (12.1%)          | 4/20 (20.0%)          | 3/12 (25.0%)             |                             |
| MDS/MPN                                 | 4/174 (2.3%)            | 0/20 (0.0%)           | 0/12 (0.0%)              |                             |
| Lymphoid neoplasm                       | 14/174 (8.0%)           | 2/20 (10.0%)          | 1/12 (8.3%)              |                             |
| Plasma cell neoplasm                    | 4/174 (2.3%)            | 0/20 (0.0%)           | 0/12 (0.0%)              |                             |
| r/o hematologic malignancy <sup>†</sup> | 27/174 (15.5%)          | 2/20 (10.0%)          | 0/12 (0.0%)              |                             |
| Cancer (solid tumor)                    | 0/174 (0.0%)            | 1/20 (5.0%)           | 0/12 (0.0%)              |                             |
| Clinical course                         |                         |                       |                          | .008                        |
| Treatment                               | 93/174 (53.4%)          | 17/20 (85.0%)         | 12/12 (100.0%)           |                             |
| Transfer to tertiary medical institute  | 44/174 (25.3%)          | 0/20 (0.0%)           | 0/12 (0.0%)              |                             |
| Refusal of treatment <sup>‡</sup>       | 22/174 (12.6%)          | 1/20 (5.0%)           | 0/12 (0.0%)              |                             |
| Death prior to treatment                | 15/174 (8.6%)           | 2/20 (10.0%)          | 0/12 (0.0%)              |                             |
| Follow-up duration (day)                | 38.5 (266.0)            | 235.5 (1568.0)        | 1470.0 (1694.0)          | .001                        |

Data are presented as frequency (%) and median (interquartile range).

BM = bone marrow, MDS = myelodysplastic syndrome, MPN = myeloproliferative neoplasm, NS = not significant, PBS = peripheral blood smear.

\* Comparison by means of chi-square or Fisher exact test and Mann-Whitney test

<sup>†</sup> No confirmatory diagnosis by means of BM exam.

\* Except supportive care.

(public) hospital is that there is less psychological resistance to remaining in one due to its perceived image, as they are well known to have benefits for medical-aid beneficiaries and secondtier patients.

In contrast, all patients who were transferred to the tertiary hospital and most who refused treatment were medical insurance subscribers had a higher SES than those who received medical assistance and paid much higher costs for the same treatment. Medical utilization by poorer patients not enrolled in medical aid programs and by nearly poor patients is significantly lower than that of medical aid enrollees, and low-income groups excluded from medical aid could have an unmet need for medical care and could experience poverty due to medical costs.<sup>[7]</sup> Patients who do not meet the requirements for medical aid beneficiaries but are experiencing economic difficulties have to pay part of the medical expenses themselves, so continuing treatment can consume a greater proportion of the household income for these patients than for medical aid beneficiaries. Therefore, the proportion of patients who refused treatment or who transferred to a tertiary hospital for active treatment, such as HSCT, was significantly higher in the group of patients with insurance than in the group of medical aid beneficiaries.

Among younger medical insurance subscribers, treatment refusal or pretreatment death was not common, but eligibility changes were observed over the long course of treatment. Elderly medical insurance subscribers refused treatment more frequently than medical aid beneficiaries. The period from the time when abnormal cells were first identified to the most recent follow-up before July 2019 was different across the insurance status groups. In the case of those with the longest morbidity period, there was a change in insurance eligibility, which was thought to be due to the length of treatment. Insured patients were considered to have the shortest follow-up period because the frequency of patients transferring or refusing treatment was higher than that of patients with medical aid benefits. Patients with longer follow-up periods were youngest and more often demonstrated changes in insurance eligibility. It should not be overlooked that insurance eligibility changes over time in relatively young treatment groups. This is presumed to be because income changes and medical expenses increase due to illness among middle-aged individuals, who have the greatest household spending. Therefore, we should consider providing adequate health care services to these niche groups with low income who are unable to access necessary health care.

There were several limitations in this study. Although we were able to check the patient's insurance status, we were not able to distinguish the type of medical benefits despite the possibility that there might have been differences in the clinical course and characteristics between medical aid type 1 (for those incapable of working) and type 2 (capable of working). Additionally, no information other than insurance type regarding the decisionmaking process for tertiary hospital transfer or refusal of treatment was available.

This study has limitations, as it was a retrospective study conducted in a single institution targeting hematologic malignancy, a less common disease category. However, to the best of our knowledge, this is the first report comparing the clinical course and treatment decision patterns between medical aid beneficiaries and NHI subscribers among hematologic malignancy patients. In the future, through a multicenter prospective study that expands target diseases to serious diseases other than hematologic malignancy, we might elucidate these trends further and obtain more reliable results to guide a better understanding of characteristic-specific differences.

Although this study showed that medical beneficiaries continued to receive medical services such as chemotherapy in public health institutes, outcomes including survival were not evaluated. Medical beneficiaries may have extreme patterns of medical service use (excessive use of medical services without outof-pocket expenses or alienation from certain medical services). In future subsequent studies, we would like to analyze health care outcomes, including survival rate, and the reason why patients make certain decisions.

Comparing and analyzing differences in medical processes and related decision-making according to patient socioeconomic characteristics, disease groups, and medical institutions (whether it is a public medical institution) is expected to help allocate medical resources and government finances and implement policies to provide more appropriate medical services to medically vulnerable individuals.

# 5. Conclusions

Patients with hematologic diseases showed different clinical courses and medical processes depending on age, diagnosis and insurance status. However, medical aid beneficiaries rarely chose to transfer or refuse treatment, and the rate of continuing treatment at this institution was overwhelmingly high, indicating that secondary and municipal hospitals provide proper healthcare services to vulnerable individuals and serve as public medical institutions.

# **Author contributions**

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