# The Impact of Integrating the Palliative Prognostic Index into Palliative Consultation on Patients with Haematologic Malignancies: A Case control study

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## Abstract

# Background

The study aims to investigate the influence of integrating the Palliative Prognostic Index (PPI) into the consultation system for patients with haematologic malignancies.

# Methods

We retrospectively enrolled 53 patients with haematologic malignancies. The PPI was evaluated at the first palliative consultation. Patients were divided into two groups: before the use of the PPI (23 patients) and after the use of the PPI (30 patients).

# Results

We first confirmed that the life expectancy for patients with haematologic malignancies was correlated with the PPI score ranking ($p < 0.01$). For patients with a PPI score > 6, agreement to attend hospice care was significantly higher ($p = 0.01$). After the use of the PPI, the mean survival time from the first consultation to death was 131.4 ± 55.9 days, which was significantly longer than before the use of the PPI ($p < 0.01$). Meanwhile, more leukaemia patients received palliative consultation and fewer antibiotics in their end of life care. Although there was no difference in agreement for hospice care after the first consultation, we believed that the concept of palliative care had been delivered to patients and their families.

# Conclusions

The PPI score is a good prognostic index for patients with haematologic malignancies. The use of the PPI score in the first consultation enables patients, families and haematologists to become aware of the necessity of palliative care.

## Background

Palliative care for haematologic malignancies is unique and challenging; however, it presents several problems.(1–4) First, for patients suffering from haematologic malignancies, more observation of their life expectancy is required, because their mortality depends on the type of cancer involved; the life expectancy of leukaemia patients, for example, would not be same as that of patients with a different malignancy.(3, 5) Furthermore, although many palliative prognostic tools are available for terminal-stage care, such as the Palliative Prognostic Index (PPI) (6), no tool suitable for haematologic malignancies has been identified.(6, 7)

In palliative care for haematologic malignancies, the timing of the intervention remains an unsolved issue.(3, 5) Multiple common factors have been used to determine the timing for hospice care, including cancer type, age, the intensity of therapy and performance status.(8) In addition, the rapid advancement of treatment modalities has improved the overall life expectancy of a patient, which in turn has changed the life trajectory. Therefore, there is a need to continually adjust the optimal timing for intervention for different types of haematologic malignancies.

At the same time, it remains challenging for patients in the terminal stages of haematologic malignancies to maintain quality at the end of life.(9, 10) In clinical practice, it is difficult to define ‘curative intent’ or ‘symptomatic relief’ for some management methods, such as blood transfusion and antibiotic use. Therefore, further investigation is needed into how a reliable predictor influences the intensity of clinical management.

Research conducted by Chou et al indicated that the PPI is a reliable indicator of life expectancy for patients with terminal haematologic malignancies.(6) The PPI has been validated and adapted for use in palliative care for patients with solid cancer.(11, 12) However, Chou et al did not mention the quality of hospice care in their studies. Therefore, to gain insight into the clinical impact of PPI, this study analyses the outcome at Chang Gung Memorial Hospital from the first consultation.

## Methods

# Study design

Data were collected from two cohorts of patients receiving treatment at Keelung Chang Gung Memorial Hospital. The first group of patients attended the palliative consultations at our hospital from January 2012 to August 2013. During this period, many patients expired within 24 hours, so we hoped to find a reliable indicator for patients and their families to understand their life expectancy. Consequently, our palliative care team decided to create a PPI recording system at the initiation of the palliative consultation, and the patients involved formed the second group. These patients received consultation from January 2016 to August 2017. To gain a better understanding of the clinical impact of the PPI recording system in our practice, the period of data collection was the same as for the first set of data. A prior study reported that the PPI index could be helpful for clinical nurse specialists to improve prognostic accuracy,(11) so we hoped to establish a useful consultation system to improve the quality of our hospice care.

In this study, the haematologic tumour board at Keelung Chang Gung Memorial Hospital confirmed the diagnoses of haematologic diseases. Studies have indicated that haematologic oncologists limit hospice referrals because they are concerned about the adequacy of the services provided.(13) Because all of the haematologists in our hospital received training in hospice care and are licensed specialists, we were able to reduce inconsistencies in providing care for these patients.

Finally, a total of 53 patients were enrolled in this study. Because this study is retrospective, the results did not interfere with the decision-making process following treatment. The PPI was determined by a clinical physician at a patient's first consultation at the hospital. The data collected throughout the study included not only information about the patient's clinical condition and the intervention but also the reasons for discontinuing the consultations. The institutional review board of Chang Gung Memorial Hospital approved this study. (IRB No. 201507911B0D001, 202101470B0).

# Statistical analysis

We used descriptive statistics to describe the participants' demographic characteristics. Basic demographic data were summarised as n (%) for categorical variables and median with the interquartile range (Q1–Q3) for continuous variables, respectively. We used Pearson $\chi^2$ or Fisher's exact test to examine the statistical significance between the variances. An independent-sample *t* test was performed to compare the mean PPI score before and after the PPI was used in the consultation system. Overall survival was calculated using the Kaplan–Meier method. Eight potential prognostic factors were included in the univariate and multivariate analysis. All factors used in the univariate analysis were examined in the multivariate analysis, but only those factors with statistical significance were displayed. All factors that were at least marginally associated with overall survival ($p \leq 0.2$) were entered into the multivariate analysis. To understand the impact of independent factors on overall survival, we used multivariate Cox proportional hazard model using forward logistic regression analysis. All analyses described above were performed using the Statistical Package for the Social Sciences for Windows, version 21.0, and results were considered significant when $p < 0.05$.

# Results

Table 1 shows the demographic characteristics of the 53 patients with haematologic malignancies (men, 40; women, 13; mean age, 76.7 years; age range 69–83 years) who received hospice care. Lymphoma was predominant among these patients, followed by leukaemia, multiple myeloma and myeloproliferative disorder/myelodysplastic syndrome. Of the 53 patients, 32 (60.4%) died within 24 hours after their first palliative consultation.

Table 2 shows the characteristics of 23 patients in the first group (men, 17; women, 6; mean age, 76.7 years; age range 57–93 years) who received hospice care before the integration of the PPI score. During this period, 564 patients with terminal solid tumours received hospice care at our hospital. Lymphoma was predominant among these patients, followed by leukaemia (including acute myeloid leukaemia and acute lymphoblastic lymphoma), multiple myeloma and myeloproliferative disorder/myelodysplastic syndrome. Of the 23 patients, 10 (43.7%) died within 24 hours after their first consultation. After applying the PPI score, 30 patients with haematologic malignancies (23 male) received hospice care. During the same period, there was an increase in the number of patients with terminal solid tumours who received hospice care consultation (771 patients). The mean age of these patients was 74 years (range, 25–95 years), and the main type of cancer in this group was leukaemia. The number of deaths within 24 hours

declined (8 of 30 patients, 26.67%). After the PPI was implemented, we observed several interesting results. Although there was no apparent difference between the two groups in terms of the distribution of the PPI score, the type of cancer diagnosed did change significantly ($p = 0.03$), with leukaemia becoming the predominant type of cancer. The number of patients who expired within 24 hours also notably decreased ($p = 0.04$). With regard to treatment modality, only the frequency of antibiotic use showed a significant decrease (86.96–56.67%, $p = 0.03$). Compared with the first period, the proportion of patients receiving hospice care at the first palliative consultation did not increase in the second group.

After 2 years of follow-up, we assessed whether the life expectancy of patients with haematologic malignancies after the first palliative consultation was associated with the PPI score. Figure 1a shows that the median overall survival in patients with a PPI score > 6 and ≤6 was 23.1 ± 7.6 days and 269.3 ± 118.2 days, respectively. The clinical impact of the PPI intervention on survival is shown in Fig. 1b. Before the PPI score was used, the median overall survival was only 12.0 ± 12.3 days. After we started our programme, the median survival time was 131.4 ± 55.9 days, which was significantly longer ($p < 0.01$).

Table 3 shows the impact of the PPI score on patient care. Although more leukaemia patients were included after the PPI intervention, the distribution of PPI score (> 6 or ≤ 6) also showed no difference. Patients with a PPI score greater than 6 required more support, especially in terms of blood transfusion (54.72%, $p = 0.05$), antibiotic use (58.49%, $p = 0.02$), and oxygen supplementation (73.58%, $p < 0.01$). The number of deaths within 24 hours after the first consultation and the patient or family's agreement to hospice care were also significantly associated with a PPI score > 6 ($p < 0.01$ and 0.02, respectively).

Next, we enrolled disease type, age > 65 years, gender, PPI score > 6 and aggressive interventions, including blood transfusion, antibiotic use, oxygen supplementation and pain control, as prognostic factors in the univariate and multivariate analyses. Both antibiotic use and PPI score > 6 were independent factors of overall survival. The group with a PPI score > 6 showed an increased risk of death (hazard ratio [HR] [95% confidence interval {CI}] 2.82 [1.32–6.03], $p = 0.01$). Antibiotic use did not improve the patient's outcome instead of increasing the risk of death (HR [95% CI)] 3.68 [1.64–8.29], $p < 0.01$).

# Discussion

According to previous studies, the PPI is considered a predictor of life expectancy.(12, 14) In our study, we demonstrated the clinical impact after the integration of PPI into the consultation system for haematologic malignancy, which has not been previously reported. At first, the baseline data indicated that the total number of cancer patients receiving hospice care increased. Chiang et al also demonstrated that the quality of end of life improved in Taiwan from 2002 to 2011.(15) Unlike cases of solid tumours, the number of patients receiving hospice care for haematologic malignancy in our hospital did not increase dramatically. However, the type of disease obviously changed, and more patients with acute leukaemia could receive palliative consultation. At the same time, after we started our consultation earlier, the number of patients who expired within 24 hours declined significantly.

Second, the mean PPI score at the first consultation was > 6, which suggested that the life expectancy for those patients was less than 3 weeks.(14) In cases of haematologic malignancies, it is crucial that the concept of hospice care is promoted at an earlier stage.(7) Based on the overall survival of patients after the first consultation, our programme reached the goal of starting hospice care earlier.

Third, this study investigated the outcomes before and after the integration of the PPI score. Our results showed that patients with a PPI score > 6 required more interventions to alleviate their symptoms. Although all caregivers involved in this study were well trained in hospice care, the frequency of aggressive intervention was still high. Previous studies showed that one-third of patients undergo blood transfusions, and 90% receive antibiotic treatment during the last week of their lives.(16) Aggressive interventions such as blood transfusions, antibiotic use and oxygen supplementation were therefore still commonly used during the patients' last weeks or days in our hospital. It has, for example, been reported that blood transfusions could relieve symptoms with minimal harm.(17) For patients with myelodysplastic syndromes and leukaemia, adequate blood transfusion could maximise the benefit of hospice care and help with the hospice referral.(18, 19) For these reasons, blood transfusions and oxygen supplementation are used frequently in our clinical practice. According to the results of our multivariate analysis, the use of antibiotics did not improve the clinical outcome, which is a reminder to physicians to avoid ineffective medical treatment. The number of participants who received hospice care was significantly higher in patients with a PPI score > 6. The data emphasise the role of the PPI score in explaining the terminal stages of cancer to patients and their families.

Previous studies reported that a sequential change in PPI score within 1 week is a good predictor of the life expectancy of patients with haematologic malignancies.(8, 12) During the COVID-19 pandemic, the use of hospice inpatient care reduced dramatically.(20) A good predictor of mortality can help physicians provide adequate palliative care, including the decision for home hospice care. Nowadays, only the palliative performance scale has been mentioned Fiorentino et al.(21) in terms of its use for predicting the mortality of patients with COVID-19. Consequently, we hope to determine whether the number of patients receiving hospice care at home increases with the use of the PPI.

This study has at least two limitations. First, only 53 patients were enrolled. Thus, some bias will be present when using the statistical methods. The second limitation is the lack of other palliative care services in our hospital, such as home hospice care. Focusing only on symptomatic relief is not so attractive for patients with terminal-stage haematologic malignancy. It is necessary to expand our work in palliative care to provide a better quality of end of life.

We discovered that patients with a PPI score > 6 are good candidates for initiation of hospice care. However, more effort is needed to improve the quality of end of life for patients with haematologic malignancies.

# Conclusion

The implementation of the PPI score for predicting the life expectancy of terminally patients with haematologic malignancies could help promote hospice care among physicians, patients and their families. Through the early initiation of palliative consultation, appropriate care can be provided, including reducing ineffective treatment.

# Declarations

### Ethics approval and consent to participate

The study was approved by institutional review board approval (IRB number: 201507911B0D001, 202101470B0)

### Consent for publication

The authors declare no conflicts of interest.

### Availability of data and materials

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

### Competing interests

The authors declare that they have no competing interests


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### Authors' contributions

Mrs. Hui-Chen, Lee is a specialist nurse, facilitating the clinical practice and collecting data. Dr Yen-Min Huang and Dr. Yueh-Shih Chang are hematologists with hospice training in Taiwan and in charge in patient cares. Dr. Yueh-Shih Chang complete the writing. Dr. Chien-Hong Lai and Dr. Cheng-Hsu Wang are the leaders of hospice term and help for study design. Dr. Chien-Hong Lai takes the responsibility of this article.


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# Tables

**Table 1:** The baseline characteristics for patients with haematologic cancer

| Patient characteristics (n=53) | Number (% or range) |
|---|---|
| Age (IQR) | 79 (69, 83) |
| Gender | |
| Male | 40(75.5%) |
| Female | 13(24.5%) |
| Median PPI score | 9 (6.25, 12.5) |
| Disease type | |
| Lymphoma | 23 (43.4%) |
| Leukemia [a] | 19 (25.8%) |
| Multiple myeloma | 8 (15.1%) |
| MPN/MDS | 3 (6.7%) |
| Expired within 24 hours after 1$^{st}$ consultation | 32 (60.4%) |

[a] : *include acute myeloid leukemia and acute lymphoid leukemia*

PPI= *Palliative Prognostic Index,* MPN = *Myeloproliferative disorder,* MDS = *Myelodysplastic syndrome*

**Table 2:** The difference for patients with haematologic cancer before and after using palliative prognostic index at 1st time palliative consultation

| | Before PPI use | After PPI use | |
|---|---|---|---|
| Patients receiving palliative consultation(n) | | | |
| Hematologic malignancy | 23 | 30 | |
| Solid tumor | 563 | 771 | |
| Age (IQR) | 76.7 (57, 93) | 74 (25, 95) | |
| Gender(M/F) | 17/6 | 23/7 | |
| PPI score ≤ 6, > 6 | 5/18 | 8/22 | *P* = 0.15 |
| Expired within 24 hours after 1st consultation | 10/13 | 8/22 | *P* = 0.04* |
| Disease type | | | *P* = 0.03* |
| Lymphoma | 10 | 13 | |
| Leukemia [a] | 5 | 14 | |
| Multiple myeloma | 7 | 1 | |
| MPN/MDS | 1 | 2 | |
| Intervention modalities | | | |
| With/without blood transfusion | 13/10 | 22/8 | *P* = 0.25 |
| With/without the use of antibiotic | 20/3 | 17/13 | *P* = 0.03* |
| With/without the supplement of O2 | 20/3 | 27/3 | *P* = 0.76 |
| With/without morphine use | 5/18 | 8/22 | *P* = 1.00 |
| Receiving hospice care or not (Do not resuscitation order) | 7/16 | 8/22 | *P* = 0.77 |

**= significan*t

[a] : *includes acute myeloid leukemia and acute lymphoid leukemia*

PPI= *Palliative Prognostic Index,* MPN = *Myeloproliferative disorder,* MDS = *Myelodysplastic syndrome*

**Table legend:** This table demonstrates several important changes during this period. Although the total number receiving hospice care increased, the total case number for haematologic malignancies did not

change significantly. By using the PPI score evaluated, more leukemia patients and family agreed to receive palliative care. Meanwhile, physicians also reduced the use of antibiotics obviously to avoid unnecessary treatment.

**Table 3:** The factors associate with patients with palliative prognostic index above 6 (n=53)

| | The PPI > 6 (n=40) | The PPI ≤ 6 (n=13) | |
|---|---|---|---|
| Disease type | | | $_P$ = 0.40 |
| Lymphoma | 17 | 6 | |
| Leukemia [a] | 13 | 6 | |
| Multiple myeloma | 7 | 1 | |
| MPN/MDS | 3 | 0 | |
| Intervention modalities | | | |
| With/without blood transfusion | 29/11 | 6/7 | $_P$ = 0.05* |
| With/without the use of antibiotic | 32/8 | 5/8 | $_P$ = 0.01* |
| With/without the supplement of O2 | 40/0 | 7/6 | $_P$ = <0.01* |
| With/without morphine use | 11/29 | 2/11 | $_P$ = 0.47 |
| Expired within 24 hours after 1st consultation | 20/20 | 1/13 | $_P$ = <0.01* |
| Receiving hospice care or not (Do not resuscitation order) | 15/25 | 0/13 | $_P$ = 0.01* |

**= significan*t

[a] : *includes acute myeloid leukemia and acute lymphoid leukemia*

PPI= *Palliative Prognostic Index,* MPN = *Myeloproliferative disorder,* MDS = *Myelodysplastic syndrome*

**Table legend:** For better understanding the real influence of PPI score, the basic characteristics of PPI above 6 were shown in this table. Despite of disease type, patients with PPI above 6 suffered from more severe symptoms and needed more interventions. At the same time, patients with PPI above 6 agreed to receive hospice care significantly. It is no wonder patients and their family more time to understand and agree receiving hospice care at the first-time consultation even the using of PPI

**Table 4:** Univariate and multivariate analysis about overall survival for patients with HMs

| | OS | | | |
|---|---|---|---|---|
| | Univariate | | Multivariate | |
| | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| Disease type | 1.00(0.50-1.96) | 0.97 | | |
| Age above 65 | 0.74(0.33-1.66) | 0.46 | | |
| Gender | 1.14(0.54-2.42) | 0.73 | | |
| PPI score above 6 | 2.26(0.94-5.44) | 0.07* | 2.82(1.32-6.03) | 0.01* |
| Blood transfusion | 0.99(0.50-1.96) | 0.97 | | |
| Antibiotic use | 3.05(1.30-7.17) | 0.01* | 3.68(1.64-8.29) | <0.01* |
| O2 supplement | 2.32(1.30-11.42) | 0.30 | | |
| Pain control (morphine use) | 0.83(0.40-1.72) | 0.61 | | |

**= significan*t

PPI= *Palliative Prognostic Index*

# Figures

**Figure 1a:**

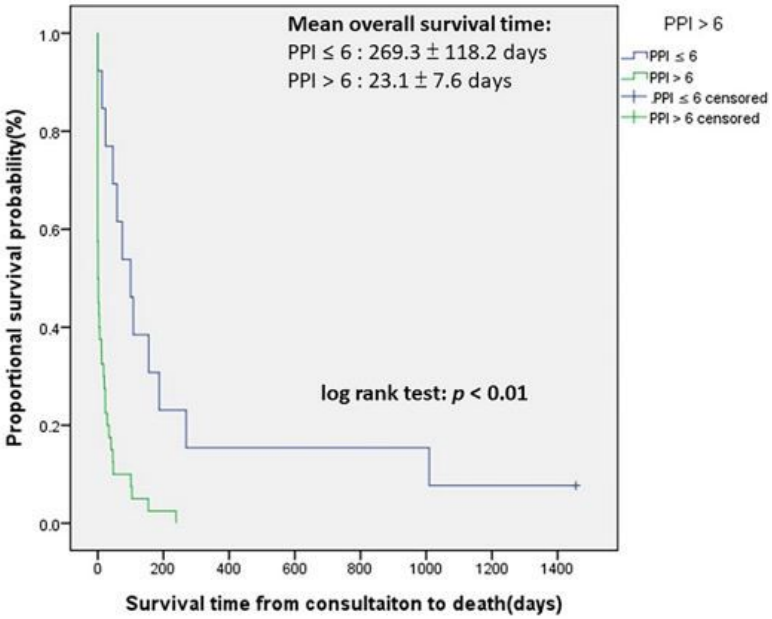
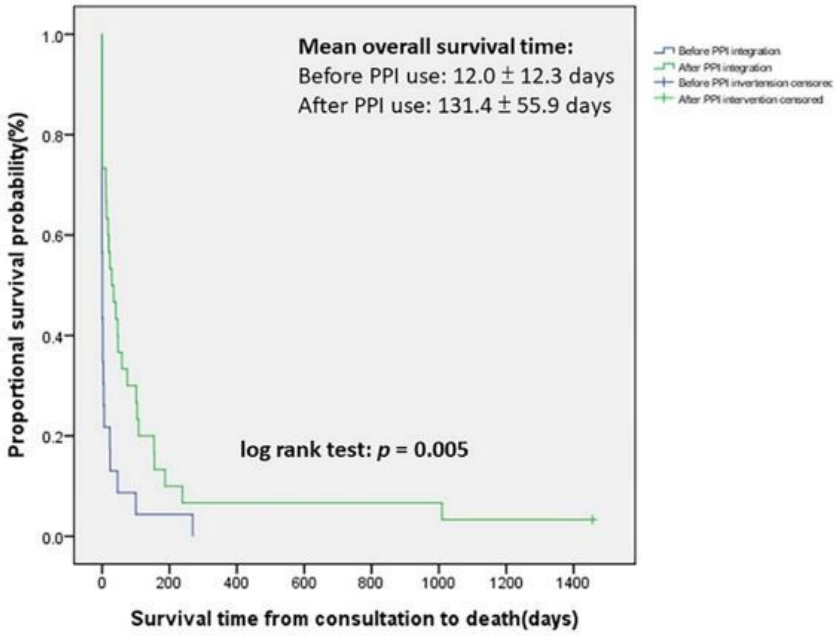



**Figure 1b**




## Figure 1

The clinical impact of palliative prognostic index on survival. 1a. Palliative prognostic index above 6 could successfully predicts patient's life expectancy in terminal haematologic malignancy patients. 1b. After PPI integrated into the palliative consultation system, the timing for starting hospice care was significantly earlier than before.