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Lactate dehydrogenase as a prognostic factor for survival time of terminally ill cancer patients: A preliminary study

Sang-Yeon Suh[a,*], *Hong-Yup Ahn*[b]

[a]*Department of Family Medicine, Dongguk University International Hospital, 814 Siksa-dong, Ilsan-dong-gu, Koyang-si, Gyeonggi-do, South Korea*

[b]*Department of Statistics, Dongguk University, Seoul, South Korea*

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ABSTRACT

This study evaluated lactate dehydrogenase (LDH) as a prognostic factor for survival time in terminal cancer patients. We prospectively followed 93 consecutive inpatients with terminal cancer in one general hospital. Cox's proportional hazard model was used to adjust the influence of some clinical and laboratory variables on survival time. For 25 patients, LDH levels at 2 weeks and 1 week before death were compared by paired *t* test. In multivariate analysis, elevated LDH level (⩾313 IU/L) was confirmed as an unfavourable indicator for survival time (hazard ratio = 2.087, $p = 0.002$). Serum LDH levels were significantly increased as the patients approached death. A combined index comprising LDH levels, C reactive protein levels, uric acid levels, presence of moderate to severe pain, fatigue, hypotension and performance status demonstrated a good stratification value for predicting survival time. Our results showed that serum LDH level can be a useful predictor of survival time of terminally ill cancer patients.

1. Introduction

Estimation of remaining life expectancy is one of the greatest concerns of terminal cancer patients and is an essential consideration in the planning of palliative care. Objective parameters for predicting life expectancy will enhance the accuracy of prognosis. Although an experienced doctor's prediction of survival time has unique discriminability,[1] it is not applicable for less experienced and young professionals. Furthermore, experienced palliative medical doctors tend to overestimate the life expectancy of their patients.[2–4] Therefore, objective indicators will assist both experienced and less experienced doctors in the planning of palliative care.

The well-known laboratory parameters for survival time prediction in advanced cancer patients are leucocytosis,[5,6] lymphocytopenia,[5,6] and C reactive protein.[7,8] The prognostic role of lactate dehydrogenase (LDH) has been widely investigated in special cancer groups. Elevated LDH is consistently reported as a prognostic factor for poor survival in lung cancer,[9,10] pancreatic cancer,[11] colorectal cancer,[12] prostate cancer,[13] and haematologic malignancies.[14,15]

The median survival time of terminal cancer patients in hospice institutes has been reported to be as short as one month.[5] Terminally ill cancer patients show similar clinical manifestations, regardless of primary cancer type, which are termed 'terminal cancer syndrome'.[16] As the histologic type of cancer is not an important prognostic factor in the terminal phase of cancer, the study on prognostication of terminally ill cancer patients needs to include various cancer types. Two studies have investigated LDH as a predictor of mortality in general cancer populations. Bozcuk et al. reported that LDH was an important indicator of in-hospital mortality for hospitalised cancer patients not in the

* *Corresponding author:* Tel.: +82 31 961 7495; fax: +82 31 961 7695.
E-mail address: lisasuhmd@hotmail.com (S.-Y. Suh).
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terminal stage.[17] Although they investigated retrospectively advanced cancer patients with good performance status, the patients' symptoms or signs were not considered. Therefore, more research is needed to determine the prognostic role of LDH for terminal cancer patients. Although one recent study showed that LDH was a useful predictor of survival time in patients with terminal cancer, the sample size was only 25 patients which might not be large enough to support the role of LDH in predicting survival time.[18]

We conducted a prospective study, including various cancer types, symptoms, signs and other serological variables, to evaluate LDH's value as a predictor of survival time in terminal cancer patients.

2. Patients and methods

2.1. Patients

This study enrolled 93 consecutive patients who had been admitted to the palliative care unit at the NHIC Ilsan Hospital between July 2004 and April 2005. All patients had incurable cancer in terminal stage and had been referred from other hospitals, home, or other wards of the same hospital for hospice care. Patients who refused blood tests were excluded from the study. Informed consent for the use of personal information for analysis was given by all patients. The study protocol was approved by the Institutional Review Board of Dongguk University International Hospital.

2.2. Data collection

Data were collected from the patients and the caregivers regarding demographic and disease-related factors, clinical symptoms, and the physical examination findings at the time of hospitalisation. Routine laboratory tests were performed weekly. A designated doctor, a resident of family medicine, entered the data on structured data sheets. The demographic and disease-related factors included age, gender, body mass index, type of cancer, site of metastasis, cancer treatment, and dosage of analgesics. The clinical symptoms included pain, weight loss, dyspnea, anorexia, nausea, vomiting, oliguria, and sleep disturbance. Pain severity was estimated using a numeric rating scale (NRS; range, 0–10). The physical examination findings included blood pressure, performance status and changes in consciousness, fever, ascites, and edema. Low blood pressure was defined as a systolic blood pressure (SBP) of 90 mmHg or lower. The performance status was measured using Eastern Cooperative Oncology Group (ECOG; range, 0–4) performance status.

Blood was sampled on admission for LDH, haemoglobin, leukocytes, neutrophil fraction, lymphocyte fraction, thrombocytes, random blood sugar, creatinine, albumin, liver enzymes, bilirubin, prothrombin time, sodium, potassium, triglyceride, cholesterol, uric acid, c-reactive protein, calcium, and phosphorous. Serum LDH was then measured serially every week. Survival time was defined as the period from the day of admission to the day of death. The research was finished on May 20, 2005.

2.3. Statistical analysis

The 50 percentile of the data for the LDH concentration at the time of hospitalisation was used to divide the subjects into two groups: the low LDH group with LDH less than 313 IU/L, and the elevated LDH group with 313 IU/L or higher. We analysed the differences in the demographic and disease-related variables between the two LDH groups with Chi-square test or Fisher's exact test. The median survival time of the subjects was determined by Kaplan–Meier method. The log-rank test was performed to compare the survival time according to independent variables. Multivariate analysis of the relationships between LDH concentration and survival time was performed using Cox's proportional hazard model. We examined the plot of $\ln\{-\ln[S(t)]\}$, where $S(t)$ is the Kaplan–Meier estimate of the survival curves, against the logarithm of the time for each level of the variables in the study. The result suggested that the Cox regression model was the most appropriate for parametric modelling of the data. Hence, the final model was built using the Cox regression model fitted with a stepwise variable selection procedure. All the variables were dichotomised to assess the hazard ratio (HR) in multivariate analysis.

To establish a new scoring system that accounted for prognosis in terminally ill cancer patients, HRs of significant prognostic factors in multivariate analysis were used. Pain was categorised as moderate to severe (NRS 5–10), and mild (NRS 0–4, reference category). Fatigue and hypotension (SBP $\leqslant$90 mmHg) were dichotomised as 0 (absence) and 1 (presence). ECOG performance status was categorized as 1–3, and 4. Serum C reactive protein level was categorised as $\geqslant$9.5 mg/dL, and <9.5 mg/dL. Serum uric acid level was categorised as $\geqslant$7.2 mg/dL, and <7.2 mg/dL.

To assign the partial score value, we took the nearest integer of each HR, and then we divided the integers by 2. The prognostic score was calculated for each case by summing the partial scores, which ranged from 0 to 11. To explore the association between prognostic score and survival time, the survival curves were compared among the assessments according to the different prognostic scores of the study subjects. The survival curves were calculated by Kaplan–Meier method, and comparisons were based on the log-rank test. Cut-off points for survival time prediction of shorter than 3 weeks were determined based on the median value of the prognostic score.

Twenty-five patients underwent consecutive serological tests at both 2 weeks and 1 week before death. Paired *t*-test was performed to assess the change of serum LDH concentration before death.

All statistical analyses were performed with the SPSS statistical package for Windows version 12.0 (Chicago, IL, USA). The significance level was 0.05 for all statistical tests.

3. Results

The study subjects comprised 93 patients hospitalised during the research period. At the time of analysis (20 May 2005), 89 patients (95.7%) had died and the remaining four survivors were censored on this day for the purpose of analysis. The fol-

low-up times of these censored patients ranged from 34 to 106 days. The median survival time was 19 days (95% confidence interval (CI); 14–24).

3.1. Demographic characteristics

The median age was 65 years (range 30–87), with the largest age decade being sixties (33.3%), followed by seventies (25.8%) and eighties or older (14.0%). The number of males was 48 (51.6%). The primary site of cancer in descending order of incidence was the lung, stomach, colon, and liver. One patient had both lung and liver cancer (1.1%), and the primary site of origin was unknown in another (1.1%). There was a significant difference between the two LDH groups in the primary site of cancer ($P = 0.041$) (Table 1).

3.2. Univariate analysis related to survival time

There were no significant differences in survival time according to age, gender, and type of cancer. Significantly shorter survival times were observed in the following conditions: having fatigue ($P < 0.001$), medium or higher level of pain ($P = 0.025$), oliguria (<400 ml/day; $P = 0.025$), low blood pressure (SBP < 90 mmHg; $P < 0.001$), low performance status (ECOG = 4; $P < 0.001$), high LDH concentration (⩾313 IU/L; $P < 0.001$), increasing leukocytes (>11,000 /mm^3; $P = 0.020$),

Table 1 – Demographic characteristics of subjects (n = 93) and two groups categorised by serum lactate dehydrogenase (LDH) levels

Characteristics	Total *n* (%)	LDH Groups (*n* (%))		*P* Value*
		Low	Elevated	
Sex				
Male	48 (51.6)	23 (50.0)	25 (53.2)	0.837
Female	45 (48.4)	23 (50.0)	22 (46.8)	
Age (yrs)				
<40	6 (6.5)	3 (6.5)	3 (6.4)	0.779[a]
40–49	7 (7.5)	3 (6.5)	4 (8.5)	
50–59	12 (12.9)	4 (8.7)	8 (17.0)	
60–69	31 (33.3)	18 (39.1)	13 (27.7)	
70–79	24 (25.8)	11 (23.9)	13 (27.7)	
⩾80	13 (14.0)	7 (15.2)	6 (12.8)	
BMI[b] (kg/m^2)				
<18.5	11 (25.6)	9 (37.5)	2 (10.5)	0.164[a]
18.5–22.9	18 (41.9)	7 (29.2)	11 (57.9)	
23.0–24.9	9 (20.9)	5 (20.8)	4 (21.1)	
⩾25.0	5 (11.6)	3 (12.5)	2 (10.5)	
Primary cancer site				
Lung	19 (20.4)	7 (15.2)	12 (25.5)	0.041[a]
Stomach	17 (18.3)	8 (17.4)	9 (19.1)	
Colon	13 (14.0)	3 (6.5)	10 (21.3)	
Liver	7 (7.5)	3 (6.5)	4 (8.5)	
Others	37 (39.8)	25 (54.3)	12 (25.5)	
Metastatic site				
Liver	39 (41.9)	19 (41.3)	20 (42.6)	0.903
Lung	31 (33.3)	15 (32.6)	16 (34.0)	0.883
Bone	23 (24.7)	9 (19.6)	14 (29.8)	0.253
Brain	8 (8.6)	4 (8.7)	4 (8.5)	0.975
Others	26 (28.0)	15 (32.6)	11 (23.4)	0.323
Previous treatment				
Surgery	27 (29.0)	12 (26.1)	15 (31.9)	0.536
Chemotherapy	43 (46.2)	17 (37.0)	26 (55.3)	0.076
Radiotherapy	24 (25.8)	10 (21.7)	14 (29.8)	0.375
None	35 (37.6)	21 (45.7)	14 (29.8)	0.114
Opioids (OME/d[c], mg)				
0	37 (39.8)	19 (41.3)	18 (38.3)	0.945[a]
1–99	50 (53.8)	24 (52.2)	26 (55.3)	
⩾100	6 (6.5)	3 (6.5)	3 (6.4)	

LDH groups categorised according to serum LDH levels: low group (<313 IU/L, *n* = 46) and elevated group (⩾313 IU/L, *n* = 47).
a By Fisher's exact test.
b Body mass index.
c Oral morphine equivalent a day.
* *P* values by Pearson's Chi-square test except values marked by 'a'.

increasing neutrophil fraction (>75%; $P = 0.030$), decreasing thrombocytes ($P = 0.030$), elevated serum C reactive protein (⩾9.5 mg/dL; $P = 0.015$), high uric acid concentration of serum (⩾7.2 mg/dL; $P < 0.001$), low albumin concentration of serum (<3.0 g/dL; $P = 0.019$), hyperbilirubinemia (>1.0 mg/dL; $P = 0.003$), prolonged prothrombin time (INR >1.12; $P = 0.001$), and hypocholesterolemia (<130 mg/dL; $P < 0.001$) (Tables 2 and 3).

The median survival time of 27 days (95% CI; 19–35) in the low LDH group was significantly longer than that of 14 days (95% CI; 10–18) in the elevated LDH group (HR = 2.235, $P < 0.001$) (Table 4 and Fig. 1).

3.3. Multivariate analysis related to survival time

The results of multivariate analysis are shown in Table 4. Medium or higher level of pain (HR = 1.761, $P = 0.014$), fatigue (HR = 3.026, $P < 0.001$), low performance status (HR = 1.815, $P = 0.025$), hypotension (HR = 7.554, $P < 0.001$), elevated serum LDH level (HR = 2.087, $P = 0.002$), elevated serum CRP level (HR = 1.984, $P = 0.002$) and elevated serum uric acid level (HR = 2.853, $P < 0.001$) were selected as independent and significant prognostic factors of poor survival time.

3.4. Scoring system based on hazard ratios

Based on these results, we established a new scoring system to estimate the survival time of terminally ill cancer patients. In calculating the prognostic score, we used the seven variables that were identified as significant indicators for survival time in the multivariate analysis. Table 5 shows the partial score value for each variable, which was obtained by dividing the nearest integer of each HR by 2. The results in Table 5 revealed the relationship between the magnitude of the effect on survival time and the prognostic variables. The distribution of the prognostic scores was zero in 7.5%, 1.0–2.0 in 35.5%, 2.5 in 9.7%, 3.0–4.0 in 17.2%, 4.5–6.0 in 23.7%, 6.5–8.0 in 2.2%, and 8.5 or more in 4.3%.

Table 2 – Median survival time by demographic and clinical characteristics of study subjects

Characteristics	*n* (%)	Death (%)	Median (Days)	95% CI	*P* Value*
Sex					
Male	48 (51.6)	45 (93.7)	14	10–18	0.113
Female	45 (48.4)	44 (87.8)	22	16–28	
Age(yrs)					
<65	40 (43.0)	39 (97.5)	18	8–28	0.151
⩾65	53 (56.9)	50 (94.3)	22	14–26	
Primary cancer site					
Lung	19 (20.4)	19 (100.0)	13	9–17	0.051
Stomach	17 (18.3)	17 (89.5)	15	11–19	
Colon	13 (14.0)	11 (84.6)	24	11–37	
Liver	7 (7.5)	7 (100.0)	4	1–7	
Others	37 (39.8)	37 (100.0)	27	19–35	
Fatigue					
Yes	52 (55.9)	50 (96.2)	11	8–14	<0.001
No	41 (44.1)	39 (95.1)	34	29–39	
Pain[a]					
Mild	47 (50.5)	43 (91.5)	24	19–29	0.025
Moderate	15 (16.1)	15 (100.0)	22	9–35	
Severe	31 (33.3)	31 (100.0)	12	8–16	
Hypotension					
Yes	5 (0.5)	5 (100.0)	3	1–5	<0.001
No	88 (95.5)	84 (95.5)	20	15–24	
Oliguria					
Yes	16 (17.2)	16 (100.0)	14	6–22	0.025
No	77 (82.8)	73 (94.8)	18	0–39	
Weight loss					
Yes	66 (70.1)	65 (98.5)	17	13–22	0.082
No	27 (29.0)	24 (88.9)	25	15–35	
ECOG					
0–1[b]	4 (4.3)	2 (50.0)	43	37–60	<0.001
2	16 (17.2)	14 (87.5)	45	30–59	
3	32 (34.4)	32 (100.0)	22	19–25	
4	41 (44.1)	41 (100.0)	10	6–14	

a Severity of pain: mild (NRS 0–4), moderate (NRS 5–6) and severe (NRS 7–10).
b No subject scored 0 on ECOG.
* *P* values by log-rank test of Kaplan–Meier method.

Table 3 – Median survival time by serologic and radiologic characteristics of study subjects

Characteristics	*n* (%)	Death (%)	Median (Days)	95% CI	*P* Value*
LDH[a] (IU/L)					
<313	46 (49.5)	43 (93.5)	27	19–35	<0.001
⩾313	47 (50.5)	46 (97.9)	14	10–18	
White blood cell counts ($\times 10^3/mm^3$)					
⩽11.0	57 (61.3)	54 (94.7)	23	17–29	0.020
>11.0	36 (38.7)	35 (97.2)	14	7–21	
Neutrophil fraction (%)					
⩽75	29 (31.2)	26 (89.7)	30	18–42	0.030
>75	64 (68.8)	63 (98.4)	17	12–21	
Haemoglobin (g/dL)					
<10.0	32 (34.4)	31 (96.9)	18	9–27	0.089
⩾10.0	61 (65.6)	58 (95.1)	19	13–25	
Platelet ($\times 10^3/mm^3$)					
<150	29 (31.2)	29 (100.0)	15	11–19	0.030
⩾150	64 (68.8)	60 (95.7)	20	15–25	
CRP[b] (mg/dL)					
<9.5	70 (75.3)	66 (94.3)	10	5–15	0.015
⩾9.5	23 (24.7)	23 (100.0)	20	15–25	
Uric acid (mg/dL)					
<7.2	71 (76.3)	67 (94.4)	24	19–28	<0.001
⩾7.2	22 (23.7)	22 (100.0)	7	2–12	
Albumin (g/dL)					
<3.0	56 (60.2)	55 (98.2)	14	10–18	0.019
⩾3.0	37 (39.8)	34 (91.9)	24	14–34	
Bilirubin (mg/dL)					
⩽1.0	63 (67.7)	60 (67.4)	23	17–29	0.003
>1.0	30 (32.3)	29 (96.7)	13	10–16	
PT[c] (INR)					
⩽1.12	43 (46.2)	40 (93.0)	25	17–33	0.001
>1.12	50 (53.8)	49 (98.0)	13	8–18	
Cholesterol (mg/dL)					
<130	28 (30.4)	26 (92.9)	11	8–14	<0.001
⩾130	64 (69.6)	62 (96.9)	23	17–29	
Pleural effusion					
Yes	38 (40.9)	38 (100.0)	15	10–20	0.635
No	55 (59.1)	51 (92.7)	22	16–28	
Pneumonia					
Yes	33 (35.5)	33 (100.0)	14	9–18	0.747
No	60 (64.5)	56 (93.3)	22	17–27	

a Lactate dehydrogenase.
b C reactive protein.
c Prothrombin time.
* *P* values by log-rank test of Kaplan–Meier method.

Fig. 2 shows the survival curves of two groups with different prognostic scores: the high (prognostic score ⩾2.5, $n = 53$, 57%) and low (prognostic score <2.5, $n = 40$, 43%) prognostic score groups. The former survived for a significantly shorter time than the latter ($P < 0.001$) with mean survival times ± standard error (95% CI) of 15 ± 1.6 (11.8–18.1) and 33 ± 3.2 (30.7–43.1) days, respectively.

On all 93 assessments of the study subjects, a cut-off point to predict whether patients would live longer than 3 or 4 weeks was explored. Table 6 shows the sensitivity, specificity, positive predictive value, and negative predictive value with each cut-off point. The cut-off point for the prognostic score was set at 2.5 as this was the median value of the prognostic score.

Table 4 – Univariate and multivariate analysis of survival time with Cox's proportional hazard model

Variables	Univariate			Multivariate		
	HR	95% CI	P*	HR	95% CI	P
Pain (moderate to severe)	1.574	1.025–2.417	0.038	1.761	1.124–2.760	0.014
Fatigue	2.931	1.875–4.583	<0.001	3.026	1.610–5.057	<0.001
ECOG (4)	1.926	1.258–2.947	0.003	1.815	1.079–3.054	0.025
Hypotension (SBP < 90 mmHg)	1.574	1.025–2.417	0.038	7.554	2.548–22.39	<0.001
Elevated S. CRP (⩾9.5 mg/dL)	1.805	1.104–2.951	0.019	1.984	1.154–3.441	0.002
Elevated S. uric acid (⩾7.2 mg/dL)	2.868	1.722–4.776	<0.001	2.853	1.610–5.057	<0.001
Elevated S. LDH (⩾313 IU/L)	2.235	1.418–3.520	0.001	2.087	1.306–3.336	0.002

SBP = Systolic blood pressure; S = serum.
* P values by Cox's regression analysis.

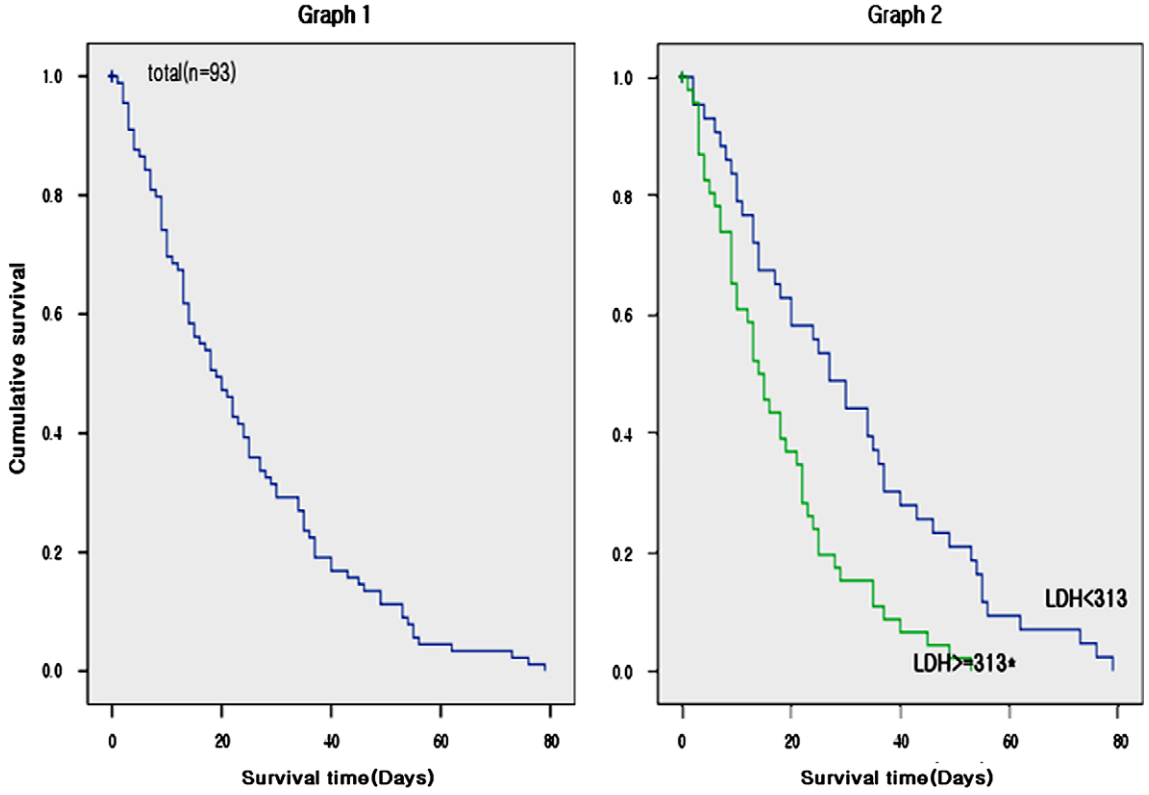

Fig. 1 – Kaplan–Meier survival curves (* indicates 'statistically significant'). Graph 1. Survival curve of 93 study subjects; Graph 2. Survival curves of two groups categorised by serum LDH level: low LDH group (<313 IU/L, *n* = 46), and elevated LDH group (⩾313 IU/L, *n* = 47). Elevated LDH group showed significantly shorter survival time than the low LDH group. *P* value <0.001 by log-rank test.

3.5. *Changes in serum LDH concentration between 2 weeks and 1 week before death*

In 25 patients, average serum LDH concentration measured consecutively at 2 weeks and 1 week before death were 504.04 ± 347.11 IU/L and 630.40 ± 417.32 IU/L, respectively. This increase in LDH concentration was significant ($P = 0.008$, data not shown).

4. Discussion

LDH has been widely investigated as a prognostic factor in specific cancer groups. Elevated serum LDH level was consistently identified as a prognostic factor for poor survival in lung cancer, renal cell carcinoma,[19] head and neck cancer,[20] prostate cancer, colorectal cancer, and haematologic malignancies. LDH was also reported as an important indicator of in-hospital mortality for general advanced cancer, not in terminal stage group.[17] The study was a retrospective analysis without consideration for clinical factors such as patient's symptoms and signs which could influence survival time. In addition, all of the study subjects had good performance status (ECOG ⩽3). In contrast, our study had the strengths that LDH was adjusted with various clinical factors and novel serological variables such as uric acid and C reactive protein, and that we examined the relationship prospectively. Our re-

Table 5 – Hazard ratios and partial scores of significant predictors for the length of survival time in the final model

	Severity	Hazard ratio	Partial score
Pain	Mild (NRS 0–4)		0
	Moderate to severe (NRS 5–10)	1.761	1.0
Fatigue	No		0
	Yes	3.026	1.5
ECOG	1–3		0
	4	1.815	1.0
Hypotension	No (SBP[a] ⩾90mmHg)		0
	Yes (SBP<90mmHg)	7.554	4.0
Elevated S[b]. CRP	<9.5 mg/dL		0
	⩾9.5 mg/dL	1.984	1.0
Elevated S. uric acid	<7.2 mg/dL		0
	⩾7.2 mg/dL	2.853	1.5
Elevated S. LDH	<313 IU/L		0
	⩾313 IU/L	2.087	1.0

Prognostic score = Pain score + fatigue score + ECOG score + hypotension score + CRP score + uric acid score + LDH score.
a Systolic blood pressure.
b Serum.

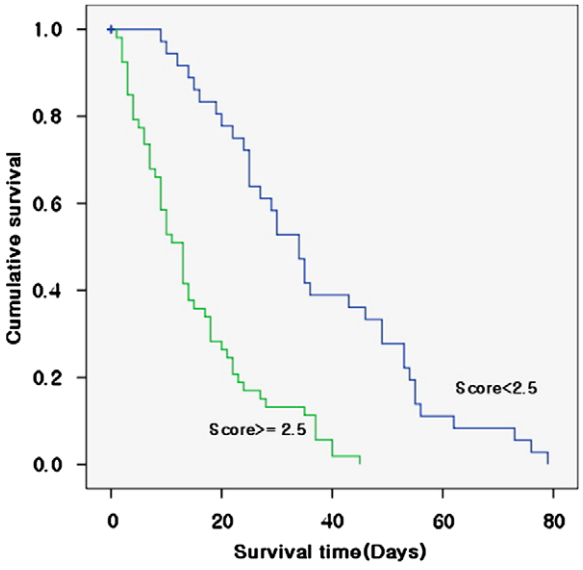

Fig. 2 – Survival curves of two groups with different prognostic scores. Kaplan–Meier survival curves of high (⩾ 2.5, *n* = 53) and low (<2.5, *n* = 40) prognostic score groups. The former showed significantly shorter survival time than the latter. *P* value <0.001 by log-rank test.

sults demonstrated that serum LDH level was significantly associated with survival time (HR = 2.087, *P* = 0.002) in patients with terminal cancer.

The reduction of pyruvate by nicotinamide adenine dinucleotide (NADH) to form lactate is catalysed by LDH. LDH and lactate are known to reflect the tumour burden and invasive potential of tumour.[21] High LDH level was associated with poor therapy response and recurrence of cancer.[22,23] Thus LDH has been suggested to be a marker of tumour aggressiveness. LDH is also related to the damage to cardiac muscles, lung, and erythrocytes and thus can be regarded as a marker of sepsis or multiple organ failure.[17] Liver cell necrosis due to hepatic failure or metastasis to the liver can elevate LDH level, as can complications of cancer and progression of underlined cancer.[24]

Serum LDH levels increased in the terminal phase and rose significantly between 2 weeks and 1 week before death in our patients. This finding supports the role of LDH as a predictor of life expectancy in terminally ill cancer patients.

Our cutoff value of LDH level, 313 IU/L, was similar to that of previous studies. Earlier researchers suggested serum LDH levels of 220 IU/L in metastatic renal cell carcinoma,[19] 240 IU/L in small cell lung cancer,[10] 320 IU/L in non-small cell lung cancer,[9] and 470 IU/L in metastatic pancreatic cancer[11] as having prognostic value. However, our high LDH level of 313 IU/L was not the highest value in studies related to survival time of cancer patients. Bozcuk et al. classified high LDH level as more than 378 IU/L in advanced cancer patients.[17] This difference may be due to ethnicity, primary cancer type, or reason for admission. The reasons for admission of Bozcuk's study included life-threatening situations such as intractable vomiting or oncological emergencies. From these data, it can

Table 6 – Accuracy of prediction for study subjects(93 patients)

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Prediction of shorter than 3 weeks	76	67	74	70
Prediction of shorter than 4 weeks	71	73	85	55

be hypothesised that the relationship between serum LDH level and survival time is not simply a negative correlation. Serum LDH level may fluctuate with the passage of time or may reflect complications of cancer. Such influences merit future research.

Although previous studies reported that pain severity has nothing to do with survival time,[25] our study identified an independent relationship between survival time and moderate to severe pain. According to an earlier report, acute aggravation of pain or development of severe pain was a prognostic factor for poor survival,[26] but it was not investigated if moderate to severe pain at the time of hospitalisation indicated acute deterioration.

Fatigue showed an independent prognostic relevance in a recent study.[27] Fatigue may reflect consequences of cancer cachexia, which is a common cause of death in terminal cancer patients.

Hypotension indicates circulatory collapse, which is related to sepsis or disseminated intravascular coagulation. It may be the result from the altered vascular permeability of cancer patients. The highest HR suggests hypotension is related to life-threatening complications.

C reactive protein also reflects tumour burden and malignant potential.[28] CRP was also associated with poor nutritional status in one previous study.[29] Malnutrition can shorten survival time through impaired immunity.

Uric acid has been shown to be a prognostic factor of cardiovascular mortality and morbidity in the general population. A recent study showed that uric acid can be useful in predicting life expectancy in terminally ill cancer patients.[30] Increasing serum uric acid level is believed to act as the body's danger signal of cellular injury and hypoxia, thereby decreasing renal function.

This study had several limitations. First, our patient sample was too small to demonstrate the effect of multiple variables on survival time. Thus this study is reported as a preliminary study. Second, our patients were restricted to one local hospital. A larger, multicentre design will be needed in further studies. Third, our patients do not represent a general population of patients with terminal cancer such as might be found in other countries. Our prognostic score might not be applicable to other populations with different malignancies. Fourth, for patients whose prognostic score was near the cut-off points, survival time prediction might not be practical.

Our study, however, was significant for its integration of diverse clinical factors and its analysis for the first time of changes in the serum LDH level of patients as they approach death. The LDH levels of patients with terminal cancer hospitalised for hospice care were significantly related to survival time, along with performance status, pain, fatigue, hypotension, serum C reactive protein level, and serum uric acid level.

Most terminal patients and their families want to know how much time is allowed, and accurate prognostication will assist terminal patients and their families prepare themselves. There is undoubtedly discrepancy among subjective assessments. The serological variable is an objective parameter which can easily be interpreted by anyone, regardless of clinical experience. Although blood sampling in terminal patients may be deemed invasive, the on-going maintenance of laboratory data is an element of routine management of inpatient care for the early detection of complications such as hypercalcemia and hyperkalemia. To avoid unnecessary laboratory examination, doctors should decide the interval of blood sampling in terminal patients with consideration for their wishes.

Our findings suggest that serum LDH level can be a useful prognostic factor of survival time in terminally ill cancer patients. However, a multicentre research with a large population is needed to generalise this result.

Conflict of interest statement

None declared.

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