



Original Article

Analysis of Cancer Patient Decision-Making and Health Service Utilization after Enforcement of the Life-Sustaining Treatment Decision-Making Act in Korea

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Purpose This study aimed to confirm the decision-making patterns for life-sustaining treatment (LST) and analyze medical service utilization changes after enforcement of the Life-Sustaining Treatment Decision-Making Act.

Materials and Methods Of 1,237 patients who completed legal forms for life-sustaining treatment (hereafter called the LST form) at three academic hospitals and died at the same institutions, 1,018 cancer patients were included. Medical service utilization and costs were analyzed using claims data.

Results The median time to death from completion of the LST form was three days (range, 0 to 248 days). Of these, 517 people died within two days of completing the document, and 36.1% of all patients prepared the LST form themselves. The frequency of use of the intensive care unit, continuous renal replacement therapy, and mechanical ventilation was significantly higher when the families filled out the form without knowing the patient's intention. In the top 10% of the medical expense groups, the decision-makers for LST were family members rather than patients (28% patients vs. 32% family members who knew and 40% family members who did not know the patient's intention).

Conclusion The cancer patient's own decision-making rather than the family's decision was associated with earlier decision-making, less use of some critical treatments (except chemotherapy) and expensive evaluations, and a trend toward lower medical costs.

Key words Terminally ill, Life support care, Neoplasms

Introduction

End of life (EOL) care must ensure the patients' best interests, respect self-determination, and protect human dignity and value. Along with the marked development of medical services, EOL care has become aggressive and raised the issue of medically futile treatment of terminally ill patients [1-3]. Unfortunately, such aggressiveness has not reduced mortality rates [4] and might sometimes oppose a terminally ill patient's preference [5,6].

In 2018, the act on life-sustaining treatment (LST) determination was enforced after some incidents that sparked debate over life-prolonging treatment in Korea. This act aimed to assure the patient's best interest and respect their autonomy in self-determination rights [7]. According to this

law, a patient's right to self-determination is supposed to be communicated and protected [8].

According to recent studies, around one-third of the patients in Korea made decisions for LST on their own and had a short median time of two days from confirmation of the EOL process to death [9,10]. These results appear to reflect the increased awareness of Korean patient autonomy by taking charge of their own decisions compared to previous findings, which showed that all do-not-resuscitate consents were made between the physician and family without involving the patient before the enforcement of this law [11,12]. These results need to be compared to the data of Western nations to promote and develop more protection and respect of patient autonomy from the early phase and ultimately improve EOL care outcomes. In the United States, the Patient Self-Deter-

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mination Act has been enforced since December 1991 [13]. Along with this law, the physician orders for life-sustaining treatment (POLST) program was developed in Oregon and is now actively applied in 43 states [14]. Studies reported that the majority of the patients are involved in POLST discussions in settings ranging from hospitals and hospice to communities in the United States [14,15]. These findings seem to be affected by the relatively long periods of POLST program operation and cultural differences giving more weight to patient autonomy in Western countries. In the case of Taiwan, one of the first Asian countries to create a law on foregoing LST and with a similar cultural background involving the family's role in EOL decision-making, the Hospice Palliative Care Act, which permits the withdrawal of treatment from terminally ill patients at their request, was enacted in 2000, and the Patient Right to Autonomy Act was enforced in early 2019 [16]. Taiwan's national policies increased hospice utilization by terminal cancer patients, demonstrated less invasive treatments during the EOL period, and reduced medical costs [17].

Given these findings with evolving medical-ethics-legal changes, we speculated that Korea's LST law indeed provides patient autonomy and contributes to the appropriate level of care based on doctor-patient shared decisions for EOL care in real clinical practice as the goal of the law intended. Thus, studies on the quality of EOL decisions and clinical outcomes such as healthcare utilization affected by decision-making would be valuable.

This study aimed to examine the characteristics of LST from the self-determination act, analyze the differences in the utilization of several health services and costs expended depending upon who was the LST decision-maker, and changes in health service utilization after enactment of the act in Korea. We targeted cancer patients because cancer is a leading cause of death in Korea [18] and included the data of two tertiary-level academic hospitals, which are leaders in the Institutional Ethics Committees of several hospitals taking responsibility under this law in Korea.

Materials and Methods

1. Study population

This study was a retrospective analysis of the claims data of patients who completed legal forms for life-sustaining treatment (hereafter called LST forms) at three academic hospitals and died at the same institution from February 2018 to February 2019 after enforcement of the law. The three academic hospitals were Seoul National University Hospital (SNUH), Asan Medical Center, and Dongguk University Ilsan Hospital, which operate an institutional ethics commit-

tee as required by LST law in Korea. Seoul National University Hospital and Asan Medical Centers are tertiary referral hospitals with more than 1,700 beds each and do not operate inpatient hospice-palliative care units. Dongguk University Ilsan Hospital is a 642-bed medical center that has had working inpatient hospice-palliative care units since June 2019. Based on the law, patients with other diseases such as liver cirrhosis, chronic obstructive pulmonary disease, and acquired immunodeficiency syndrome may also receive an LST form. However, only data from cancer patients were analyzed because most of the data were from cancer patients (84.9%, 1,024/1,206), and we wanted to investigate the trends in the changes in health service utilization for a homogeneous disease group. Patients who wrote advance statements (AS) on life-sustaining treatment similar to the US's advance directives were excluded because the period from the time of writing the AS to the time of death was unknown, and the accurate calculation of medical expenses was complicated using claims data. Patients discharged after creating the LST form from these three hospitals and those who died in other hospitals were not included for the same reason. Lastly, if the patient died within two days of LST form preparation, the case was judged not suitable for medical cost analysis and was excluded.

2. Classification of decision-maker based on LST forms

Before deliberating our findings, it is important to understand the LST law's regulatory framework and legal documents in Korea. First, this act defined the two concepts of "end of life" (the patient's death is considered imminent due to rapid deterioration of the patient's condition) and "terminal stage" (the patient is expected to die in several months) [19]. These decisions should be made by the judgment of two doctors, of which one is a physician who assumes the main responsibility for the patient. At the EOL or terminal stage, legal form No. 1 can be completed by the patient's own will, whereas completion of the other two forms (forms No. 11 and 12) should be considered by the patient's family. The difference between these forms is whether the patient's family can presume the patient's will. These three forms are supposed to be reflected in clinical situations through a legal form (form No. 13), resembling the POLST used in the United States. The important notable fact is that all these documents can be used only in hospitals equipped with an institutional ethics committee.

3. Data collection

To analyze the differences in variables related to LST, we collected patient data on demographics, health service utilization, and total hospitalization costs from the date of completion of the LST forms to death.

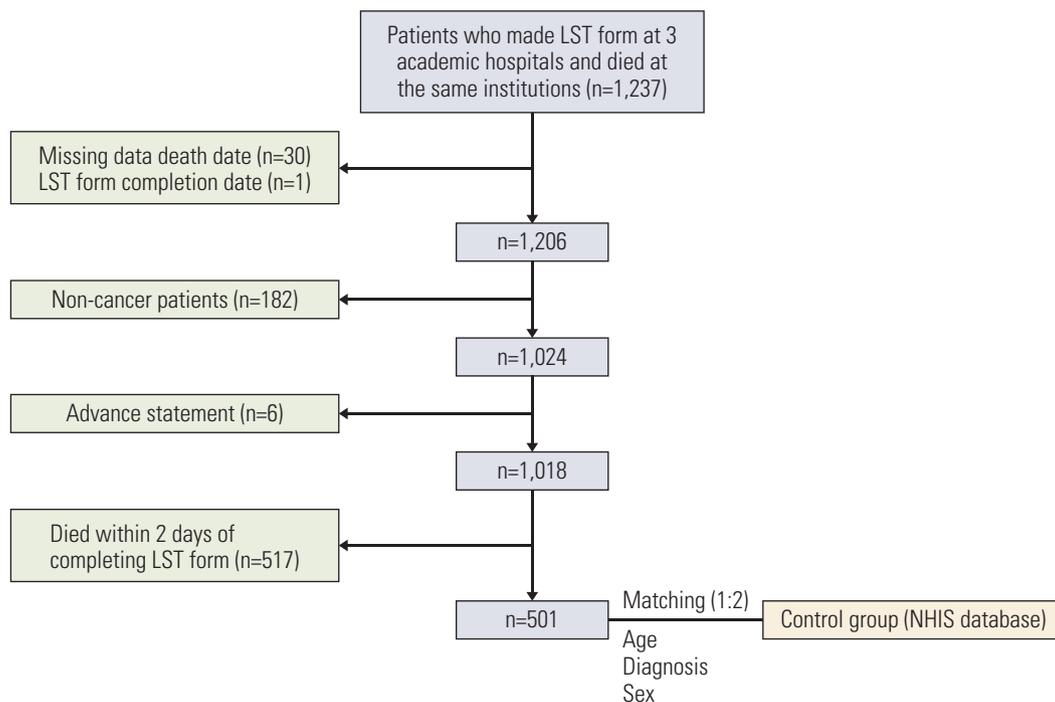


Fig. 1. Consort diagram. LST form, legal forms for life-sustaining treatment; NHIS, National Health Insurance Service.

The health service utilization data extracted from claims data included the use of anticancer drugs; intensive care units (ICU); expensive imaging tests such as computed tomography (CT) scans, magnetic resonance imaging, and positron emission tomography/CT; mechanical ventilation; dialysis, and cardiopulmonary resuscitation (CPR). The use of dialysis was defined as dialysis that was performed only after completion of the LST forms, not dialysis performed before.

To compare the difference in health service utilization data before and after the enactment of the law, the data from the Korean National Health Insurance Service (NHIS) database were used as controls. The control group was designated as patients who had claims for treatment with cancer diagnostic codes since 2014 and died in 2015 and 2016 using the NHIS database. We matched the age, sex, and cancer diagnostic codes of the control and study groups in a 2:1 ratio.

The daily medical expenses of the patients were defined as the total hospitalization medical expenses from the date of completing the LST form to the date of death divided by the date. The medical expense data were divided according to the three individual types of LST forms.

4. Statistical analysis

Descriptive statistics were performed to analyze the parameters of the LST forms after enforcement of the law. The chi-square test was conducted for the frequency analysis of

health service utilization and demographic characteristics. To ascertain the differences in medical costs according to the LST form decision-maker, Wilcoxon's rank-sum test or the Kruskal-Wallis test was performed. Statistical analysis was performed using SAS ver. 9.4 (SAS Institute Inc., Cary, NC).

Results

1. Baseline characteristics

Of the 1,237 patients who completed the LST form at the three academic hospitals and died at the same institutions, 1,018 cancer patients were included in the survey (Fig. 1). The median patient age was 65 years (range, 18 to 119 years), and 61.7% (628/1,018) were male. The median time to death from completion of the LST form was 3 days (range, 0 to 248 days). In detail, the period from form creation to death was 5 days (range, 0 to 248 days) for the group in which the patient completed the LST form (LST form No. 1, patient group), 2 days (range, 0 to 104 days) for the group where the decision-makers were caregivers who knew the patient's intents (LST form No. 11, family-patient group), and 1 day (range, 0 to 170 days) for the group that made LST decision based on unanimous consensus of the family (LST form No. 12, family group).

Of the 1,018 cancer patients who completed the LST form, 517 people died within two days of completing the document

Table 1. Characteristics based on time to death from LST form completion

	Time to death from LST form completion (day)		p-value
	0-2 (n=517)	> 2 (n=501)	
Decision-maker			
By patients (Form No. 1)	120 (23.2)	248 (49.5)	< 0.001
By family who know patient's intention (Form No. 11)	183 (35.4)	130 (25.9)	
By all family members in situations where the patient's intention is unknown (Form No. 12)	214 (41.4)	123 (24.6)	
Age (yr)			
< 35	12 (2.3)	11 (2.2)	0.708
35-44	42 (8.1)	25 (5.0)	
45-54	59 (11.4)	58 (11.6)	
55-54	144 (27.9)	144 (28.7)	
65-74	141 (27.3)	143 (28.5)	
75-84	93 (18.0)	98 (19.6)	
≥ 85	25 (4.8)	21 (4.2)	
Sex			
Female	202 (39.1)	188 (37.5)	0.612
Male	315 (60.9)	313 (62.5)	

Values are presented as number (%). p-value obtained from chi-square test. LST form, legal forms for life-sustaining treatment.

(Table 1). In the case of death within two days of document preparation, the patient's intention for LST was reflected in 58.6%. Otherwise, it was reflected in 75.4% of the cases, given the sum of the frequencies of LST form No. 1 and LST form No.11. In the group that died two days after filling out the LST form, there were more patient decisions than those of family members who created the form.

2. Health service utilization divided by decision-maker

According to the classification by type of LST form, there was no difference in sex or age between the groups (Table 2). However, the frequency of ICU, continuous renal replacement therapy (CRRT), and mechanical ventilation use was significantly higher when the family filled out the form without knowing the patient's intention. There was no difference between the groups in the performance of imaging tests and CPR. The rate of chemotherapy use was 11.2% in the group where the patient filled out the form, which was higher than that in the other groups ($p=0.027$).

3. Health service utilization before and after act enforcement

The number of patients who died more than two days after completing LST forms was 501. The control group using claims data was generated by matching with hospital data based on age group, sex, diagnosis at a 2:1 ratio (Table 3). Due to the low prevalence of some types of cancer, it was impossible to match 2:1 in five cases (Hodgkin lymphoma, acute erythroid leukemia, tongue cancer, small bowel cancer,

and malignant neoplasm of the mediastinum, part unspecified).

Table 4 shows the data after matching several variables. CPR performance and the use of anticancer drugs were significantly reduced after the act was enforced ($p < 0.001$). Imaging tests such as CT scans and positron emission tomography (PET) scans were performed significantly less than before law enforcement ($p < 0.001$ and $p=0.042$, respectively). The rate of ICU use in hospitalizations in which death occurred was 9.93% before the law was enforced and 13.97% thereafter. The CRRT utilization rate was higher after law enforcement than before (3.99% vs. 1.2%). There was no difference in the rate of mechanical ventilator use and dialysis before and after enforcement of the law.

4. Differences in medical expenses divided by decision-maker and subgroup analysis

The median medical costs were as low as 528,586 Korean won (\$440.5) when the patient was the decision-maker for LST ($p < 0.001$). By analyzing the subpopulation of patients who prepared the LST form, we confirmed the conditions in which the medical expenses were high (Table 5). The top 10% of the medical expenses were incurred by a higher proportion of male patients than the other 90% ($p=0.035$). The medical costs were higher when the LST decision-maker was a family member (28% for patient group vs. 32% for family-patient group and 40% for family group) and when the LST decision was delayed (median time to death from completion of LST form, 5 days in the top 10% group vs. 8 days in

Table 2. Health service utilizations divided by LST form

	Type of LST form			p-value
	No. 1	No. 11	No. 12	
Sex				
Female	95 (38.2)	53 (41.1)	41 (33.3)	0.438
Male	154 (61.8)	76 (58.9)	82 (66.7)	
Age	63 (20-90)	68 (22-95)	70 (22-116)	< 0.001
ICU				
No	232 (93.2)	111 (86.0)	88 (71.5)	< 0.001
Yes	17 (6.8)	18 (14.0)	35 (28.5)	
Chemotherapy				
No	221 (88.8)	125 (96.9)	112 (91.1)	0.027
Yes	28 (11.2)	4 (3.1)	11 (8.9)	
Hemodialysis				
No	245 (98.4)	123 (95.3)	117 (95.1)	0.132
Yes	4 (1.6)	6 (4.7)	6 (4.9)	
CRRT				
No	246 (98.8)	124 (96.1)	111 (90.2)	< 0.001
Yes	3 (1.2)	5 (3.9)	12 (9.8)	
Ventilator care				
No	242 (97.2)	114 (88.4)	94 (76.4)	< 0.001
Yes	7 (2.8)	15 (11.6)	29 (23.6)	
CT scan				
No	198 (79.5)	113 (87.6)	96 (78.0)	0.094
Yes	51 (20.5)	16 (12.4)	27 (22.0)	
MRI scan				
No	241 (96.8)	124 (96.1)	117 (95.1)	0.730
Yes	8 (3.2)	5 (3.9)	6 (4.9)	
PET scan				
No	248 (99.6)	129 (100)	122 (99.2)	0.593
Yes	1 (0.4)	0	1 (0.8)	
CPR				
No	249 (100)	128 (99.2)	123 (100)	0.236
Yes	0	1 (0.8)	0	

Values are presented as number (%). p-value obtained from chi-squared test. CPR, cardiopulmonary resuscitation; CRRT, Continuous renal replacement therapy; CT, computed tomography; ICU, intensive care unit; LST form, legal forms for life-sustaining treatment; LST form No. 1, LST plan by patient; LST form No. 11, LST plan based on verification of intention of the patient by two or more family members; LST form No. 12, LST plan based on unanimous consensus of the family; MRI, magnetic resonance imaging, PET, positron emission tomography.

the lower 90%, $p=0.001$). The subgroup that utilized health services such as the ICU, CRRT, ventilator care, and CPR with statistical significance was the top 10% of the medical cost group.

Discussion

We demonstrated that one-third of the LST decisions in cancer patients was made by the patient, and the time from

completion of the legal LST form to death was a median of only three days. Health service utilization and costs were dependent upon the decision-maker and higher if the decision-makers were family members. The health service utilization during the last admission had a trend toward the lower usage of CPR, imaging tests such as CT and PET, and anticancer drugs compared to before enforcement of the law.

The short time, a median of three days from completion of any of the three legal forms to death in our study, was similar to the previous findings from SNUH [9], while the very

Table 3. Demographic characteristics of national insurance database^{a)} and institutional data^{b)}

Variable	Before law enforcement (n=997)	After law enforcement (n=501)	p-value
Sex			
Female	372 (37.3)	189 (37.7)	0.884
Male	625 (62.7)	312 (62.3)	
Age (yr)			
< 35	21 (2.1)	11 (2.2)	> 0.99
35-44	54 (5.4)	26 (5.2)	
45-54	112 (11.2)	58 (11.6)	
55-54	288 (28.9)	145 (28.9)	
65-74	286 (28.7)	143 (28.5)	
75-84	194 (19.5)	97 (19.4)	
≥ 85	42 (4.2)	21 (4.2)	
Disease			
Solid tumor	869 (87.2)	436 (87.0)	0.935
Hematologic malignancy	128 (12.8)	65 (13.0)	

Values are presented as number (%). p-value obtained from chi-squared test. ^{a)}Patient information before law enforcement, ^{b)}Patient information after law enforcement.

wide distribution of days from LST decision-making to death reflects the difficulty in estimating terminal or end-stage disease, as is well known. Also, the fact that patients made LST decisions in around one-third of the cases was not different from a previous study [9]. Even though the decision time for LST was significantly longer in cases where the decision-maker was the patient in our study and previous findings in Korea, it was different from the US data of the Oregon POLST Registry decedents with cancer where the median was 5.1 weeks [20]. This may be caused by several factors such as the lack of time to acclimate to this law, cultural differences regarding patient autonomy in Korea, and other reasons. From two papers written at 10-year intervals, we can assume that the trend is for Korean cancer patients to decide their will regarding EOL decisions. One was data from 2009, before the enforcement of the LST Act, from a study on whether Korean terminal cancer patients really wanted to make decisions by themselves. The authors revealed that even though 78.5% of the patients were aware of their terminal status, only 21.7% made decisions on their own [21]. Therefore, the author doubted the real possibility of the universal application of patient autonomy for cancer patients in Korea. After 10 years, another study investigated a similar issue under the current LST law [22]. Here, 71.3% of the advanced cancer patients were willing to have a conversation related to LST with their physicians. Based on this study, it appears that we could make decisions with patients involving up to about 70% of the advanced cancer patients under this law. More research is needed to determine to what extent this law still has room to expand in the real world because the remaining 30% or more of advanced cancer patients in Korea would

want to leave their decision to their family or physicians. In this case, we can promote the intervention of improving communication between patients and their family members as surrogate decision-makers with an awareness of the limitations on the autonomy of patients in LST decision-making.

By including the treatments listed on form No. 13, we tried to compare the health service utilization according to decision-makers and before enacting the law. Our results showing the significant decrease in CPR procedures after the enforcement of the law are consistent with the findings from a study comparing the performance of CPR after the documentation of terminal or EOL process to death [9]. However, the ICU use and CRRT rates were relatively high under this law in the present study. Initially, we hypothesized the decreased use of all of these medical services. As death approaches, orders setting more limits were usually made despite the listed POLST orders, which could change in both directions to be more or less aggressive [20]. However, when we considered that the sample of analyzed patients was acquired mainly from tertiary academic medical hospitals, critical care would be utilized more due to institutional factors. This finding suggests the necessity to further study comparisons between similar institutional settings or emphasize the physician's duty for more active engagement in the EOL process earlier to avoid potentially futile treatment. Sincere engagement is performed through a shared discussion between the physician and patient. Presently, the legal transactional mode of advance planning is shifting toward a communication model that accurately translates the patient's wishes [23]. A recent study found that many doctors in SNUH had serious difficulties communicating with

Table 4. Health service utilizations comparison between before and after law enforcement

	Before law enforcement (n=997)	After law enforcement (n=501)	p-value
Use of ICU			
No	898 (90.0)	431 (86.0)	0.016
Yes	99 (10.0)	70 (14.0)	
Chemotherapy			
No	791 (79.3)	458 (91.4)	< 0.001
Yes	206 (20.7)	43 (8.6)	
Hemodialysis			
No	979 (98.2)	485 (96.8)	0.092
Yes	18 (1.8)	16 (3.2)	
CRRT			
No	985 (98.8)	481 (96.0)	0.001
Yes	12 (1.2)	20 (4.0)	
Ventilator care			
No	890 (89.3)	450 (89.8)	0.805
Yes	107 (10.7)	51 (10.2)	
CT scan			
No	709 (71.1)	407 (81.2)	< 0.001
Yes	288 (28.9)	94 (18.8)	
MRI scan			
No	959 (96.2)	482 (96.2)	0.968
Yes	38 (3.8)	19 (3.8)	
PET scan			
No	981 (98.4)	499 (99.6)	0.042
Yes	16 (1.6)	2 (0.4)	
CPR			
No	961 (96.4)	500 (99.8)	< 0.001
Yes	36 (3.6)	1 (0.2)	

Values are presented as number (%). p-value obtained from chi-square test. CPR, cardiopulmonary resuscitation; CRRT, continuous renal replacement therapy; CT, computed tomography; ICU, intensive care unit; MRI, magnetic resonance imaging, PET, positron emission tomography.

patients and family members during LST discussions [24]. Unfortunately, little research has addressed the communication model of LST discussion in Korea until now. We proposed a shared decision model, Seek-Engage-Explore-Decide-Support (SEED), through a study of in-depth interviews of terminal cancer patients and family members who completed LST forms, and the model should be tested to meet the multiple dimensions of good communication in Korea [25].

The difference in medical services utilization according to decision-makers in this study is interesting. Chemotherapy use was higher in cases where decisions were made by the patient. This finding was similar to the preference analysis of cancer patients toward the selection of LST on legal form No. 13 [22]. Among the patients who signed the form, only 31.9% wanted to stop chemotherapy, whereas all 72 participants refused CPR and mechanical ventilation. The high rates of

chemotherapy seemed to be associated with earlier findings demonstrating the patient's own will when they were still undergoing palliative chemotherapy. The will of advanced cancer patients to continue chemotherapy even when completing the Korean POLST was also confirmed in our study. We suggest reconsidering the scope of LST by the extent of the treatments that could be withdrawn or withheld in a real clinical setting or using a two-step approach to decide LST, as suggested by Kim et al. [22], especially for cancer patients. These will help to ensure that cancer patients near the EOL receive beneficial, not futile, treatment.

This study had some limitations. First, it is an analysis of only patient data from some institutions, not national data. It does not reflect the situation of EOL care in hospice centers or nursing facilities. However, two of the three hospitals included in the study were Korea's representative tertiary referral hospitals and have data on a large number of patients. These

Table 5. Differences of medical expenses divided by subgroup

	Medical costs group		p-value
	Lower 90%	Top 10%	
Sex			
Female	177 (39.2)	12 (24.0)	0.035
Male	274 (60.8)	38 (76.0)	
LST form			
No. 1	235 (52.1)	14 (28.0)	0.003
No. 11	113 (25.1)	16 (32.0)	
No. 12	103 (22.8)	20 (40.0)	
Time to death (day)	8 (3-248)	5 (3-43)	0.001
Type of health service utilization			
ICU			
No	414 (91.8)	17 (34.0)	< 0.001
Yes	37 (8.2)	33 (66.0)	
Chemotherapy			
No	416 (92.2)	42 (84.0)	0.048
Yes	35 (7.8)	8 (16.0)	
Hemodialysis			
No	438 (97.1)	47 (94.0)	0.234
Yes	13 (2.9)	3 (6.0)	
CRRT			
No	447 (99.1)	34 (68.0)	< 0.001
Yes	4 (0.9)	16 (32.0)	
Ventilator care			
No	428 (94.9)	22 (44.0)	< 0.001
Yes	23 (5.1)	28 (56.0)	
CT scan			
No	371 (82.3)	36 (72.0)	0.078
Yes	80 (17.7)	14 (28.0)	
MRI scan			
No	436 (96.7)	46 (92.0)	0.101
Yes	15 (3.3)	4 (8.0)	
PET scan			
No	450 (99.8)	49 (98.0)	0.058
Yes	1 (0.2)	1 (2.0)	
CPR			
No	451 (100)	49 (98.0)	0.003
Yes	0	1 (2.0)	

p-value obtained from chi-square test. CPR, cardiopulmonary resuscitation; CRRT, continuous renal replacement therapy; CT, computed tomography; ICU, intensive care unit; LST form, legal forms for life-sustaining treatment; LST form No. 1, LST plan by patient; LST form No. 11, LST plan based on verification of intention of the patient by two or more family members; LST form No. 12, LST plan based on unanimous consensus of the family; MRI, magnetic resonance imaging, PET, positron emission tomography.

institutional factors caused the relatively higher use of medical services after the enactment of the LST law. Second, the condition of the last hospitalization in which the death event occurred was the same, but the time to death was not uniformly controlled between the two groups before and after the enforcement of the law. Due to this, the control group's observation period was longer, and it is possible that more

medical services were observed. Third, since the research was based on retrospective analysis and claims data, it had the disadvantage that it was difficult to grasp the exact medical situations. Also, the data may be biased because patients with less than two days from LST form creation to death were removed from the medical cost analysis.

In summary, we demonstrated the landscape of decision-

making and health care utilization after one year of enacting the LST law in Korea. This study founded that the cancer patient's decision-making was associated with earlier decision-making, less use of some critical treatments (except chemotherapy) and expensive evaluations, and a trend toward lower medical costs than family decisions. Based on these results, further studies are expected to shape better enrichment of EOL care according to patient preferences under the current legislative framework.

Ethical Statement

The Institutional Review Board of the three hospitals approved the study. Due to the study's retrospective nature, informed consent was not required. The IRB approval numbers were E-1811-047-984 for Seoul National University Hospital, 2018-1533 for Asan Medical Center, and 2018-08-005 for Dongguk University Ilsan Hospital.

Author Contributions

Conceived and designed the analysis: Kim D, Kim MS, Shin SJ, Kim DY, Heo DS, Lim CM.

Collected the data: Yoo SH, Seo S, Lee HJ, Kim MS, Shin SJ, Heo DS, Lim CM.

Contributed data or analysis tools: Kim D, Yoo SH, Seo S, Lee HJ, Lim CY.

Performed the analysis: Kim D, Lim CY.

Wrote the paper: Kim D, Kim DY.

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

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