Optimal Timing for Hospice-shared Care in Terminal Cancer Patients

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Abstract

The optimal timing for initiating palliative care in cancer patients varied widely. This retrospective population-based study aimed to determine the optimal initiation timing of hospice-shared care (HSC), which maximizes the beneficial effects of quality of care (QOC) and medical expenses among terminal cancer patients. We extracted cancer patients who were in their last year of lives during 1 January 2010 to 31 December 2013 from a nationwide database. After the selection and matching process, 1,714 patients (67.7±13.2 years, 62.7% male) were enrolled and categorized into the HSC group and usual care (UC) group (n=857 in each group). By suing the generalized linear mixed-effects model for comparisons between groups, we found that the HSC groups showed generally better QOC in the four indices (with emergency room visit, hospitalization, intensive care unit admission, and receiving chemotherapy) than the UC group in those who initiated HSC 8-60 days before death.

The HSC group also had significantly lower medical expenses than the UC group in those who initiated HSC 15-90 days before death. In conclusion, HSC initiation before the last eight days and 15 days of lives were found to effectively improve QOC and save medical expenses, respectively, among patients with terminal cancer.

Introduction

The patients with terminal cancer face suffering when their health situations progressively become worse. Palliative and hospice care is a method to maintain patients' quality of life and assist with a natural death [1-4]. The utilization rates of palliative and hospice care among terminal cancer patients are higher in western countries (30% - 48%) [5-7] and lower in Asian countries (9% - 12%) [8-10].

In Taiwan, the National Health Insurance (NHI) has started to reimburse hospital-based and home-based hospice care since 2000. However, hospice care utilization rates did not grow satisfied, which kept at about 20% after a 10-year effort. The limited number of hospice service institutions and the shortage of hospice beds in hospitals are two critical reasons for the stagnant use of hospice care [11,12]. As a result, terminally ill cancer patients have to keep staying in the acute medical ward receiving active and curative treatment instead of palliative and hospice care as their wish [11,13,14]. To resolve the above limitation, the Taiwan NHI developed the hospice-shared care (HSC) program in 2011. The HSC program provides specialist consultation regarding palliative and hospice care in the acute medical ward. The HSC program in Taiwan is similar to the palliative care or palliative care consultation in the western countries [11,13,15,16] and has been demonstrated to effectively improve quality of care (QOC) and significantly save medical expenditure among terminal cancer patients [17-19].

Since palliative and hospice therapy is alternative management that replaces curative therapy for patients with cancers, these managements' initiation timing is crucial. Currently, the existing knowledge supports the concept that earlier palliative and hospice therapy or consultation is associated with better QOC and fewer medical expenses [20-22]. However, the cut-off time points of "early" initiation were defined by pre-set study protocol instead of the real-world data and were widely varied from 2 weeks to 32 weeks before death in previous investigations [20-22]. These shortcomings prohibited the demonstration of the whole picture regarding the association between clinical benefits and the initiation timing of palliative and hospice care.

We hypothesized that there is a U-shaped association between HSC initiation timing and clinical benefits, and the optimal initiation timing of HSC is a range of period rather than a time point. Thus we conducted the current study to determine the optimal timing of HSC initiation, which maximizes the beneficial effects of QOC and medical expenses among terminal cancer patients.

Methods

Study design and patient selection

We conducted this retrospective population-based study using the data of Taiwan's National Health Insurance Research Database (NHIRD) in the period from 1 January 2010 to 31 December 2013. The NHIRD is an encrypted database, including much medical and healthcare-associated information of the NHI program, which provides comprehensive medical care covering more than 99% of the 23 million people in Taiwan [23].

Firstly, we extracted patients with end-of-life (EOL) status defined as the last year of lives from the database. Subsequently, we selected patients who received HSC as their de novo hospice care as one population and patients who did not receive hospice care into another population.

After a matching process of patients from the two populations, we established an "HSC group" and a "usual care (UC) group" as a control group. Then we compared the QOC and medical expenses between the patients with the same survival periods of the two groups.

Data collection and measurements

The basic demographic information included age, gender, income, and Charlson comorbidity index (CCI) calculated by the primary and secondary diagnosis codes of outpatient and inpatient services within one year before patients' deaths [24].

The hospital characteristics included region, hospital level, and numbers of hospital beds and hospice beds of the index hospital. The index hospital was defined as the hospital where the patient most frequently hospitalized or the hospital where the patient most frequently visited if the patient did not have hospitalization [11,25] in the last year before death.

Matching process

Similar to the matching process reported by a previous study [26], we conducted the matching process for the two groups according to the following four criteria: (1) The same year of death (namely, 2010, 2011, 2012, 2013). (2) The same cancer diagnoses established according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes 140-208. (3) The same propensity scores calculated using logistic regression (included age, gender, CCI, income, occupation, hospital traits, hospice bed density) and matching one-to-one using the nearest neighbor matching technique. (4) The same survival periods which were defined as the period from receiving HSC (in those received HSC) or usual management in either outpatient or inpatient setting (in those who did not experience HSC) to death. We categorized the survival period as 1−3 days, 4−7 days, 8−14 days, 15−30 days, 31−60 days, 61−90 days, 91−180 days, and 180−365 days [25].

Endpoints of the study

We defined the QOC by the six indices evaluated within the last month before patients' death. The six indices contained "with emergency room visit," "with hospitalization," "with intensive care unit (ICU) admission," "receiving chemotherapy," "with hospitalization≧14 days," and "death in the hospital" [27]. Besides the six individual indices, we also calculated a "total QOC score" using these six QOC indices to evaluate the QOC, with a lower score indicative of a better QOC.

Besides, we calculated the total medical expenses by adding all the cost of outpatient care (including in the emergency department) and hospitalizations after receiving HSC and converted the amount from New Taiwan dollar to Unites States dollar (USD) by the 30:1 ratio.

Ethical considerations

The study design conformed to the Helsinki Declaration revised in 2013 and the ethical guidelines. The Institutional Review Board of Saint Mary's Hospital Luodong approved the current study (approval # SMHIRB104004) and waived the need for informed consent since all personal data were de-identified in the database for protecting privacy. We performed the study following the study protocol and relevant guidelines.

Statistical Analysis

We used the SPSS 22.0 (PASW Statistics for Windows, Version 22.0, Chicago, IL, USA: SPSS Inc.) and R 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria, accessed https://www.r-project.org) software for statistical analyses. A two-tailed p ≤ 0.05 was considered statistically significant in all statistical analyses.

The categorical variables and the continuous variables were presented as number (percentage) and mean ± standard deviation (SD), respectively.

We evaluated the differences between groups using the generalized linear mixed-effects model (GLMM), which utilized the random clustering effect of hospitals and the year of death to control the habitual influence of each hospital's treatment in each year. For more details, we used the binomial GLMM to compare the categorical variables, the GLMM to compare the continuous variables with normal distribution, and the log-link function of the gamma GLMM to compare the continuous variables with abnormal distribution (namely, medical expenses).

The comparisons of the categorical variables were expressed using the adjusted odds ratio (AOR) with a 95% confidence interval (CI). The comparisons of the continuous variables were expressed using the adjusted relative ratio (ARR) with 95% CI, and the adjusted mean difference (AMD) between the two groups. The AMD was calculated by the least-squares mean along with the GLMM.

Results

From the nationwide database, we extracted 7,396 patients at the EOL stage who died from 1 January 2010 to 31 December 2013. Among them, 2,394 (32.4%) patients had ever experienced hospice care (including hospital-based and home-based hospice care and HSC) during the last year before death, and 1,215 patients (16.4%) received HSC as their de novo hospice care. On the other hand, 5,002 patients (67.6%) had never received any type of hospice care before death.

After the matching process, we conducted the HSC and the UC groups, each consisting of 857 patients. (Figure 1) The total 1,714 patients (67.7±13.2 years, 62.7% male) had a mean CCI of 10.5 ± 4.5 points, and a mean survival period of 43.5 ± 57.1 days (median, 21 days). Not surprisingly, the basic characteristics of the HSC group and the UC group were not significantly different because of the matching process. (Table 1)

Table 1. Comparisons of the basic characteristics between the HSC and UC groups

	HSC group (n=857)	UC group (n=857)	p-value
Gender_male	550 (64.2%)	524 (61.1%)	0.200
Age, years	67.5 ± 13.3	67.9 ± 13.2	0.578
Income_300-1,000 USD per month	237 (27.7%)	268 (31.3%)	0.724
Charlson Comorbidity Index, points	10.6 ± 4.3	10.5 ± 4.7	0.222
Hospital level_medical center	488 (56.9%)	489 (57.1%)	0.973
Hospital area_northern area	341 (39.8%)	347 (40.5%)	0.808
Hospice bed density, % *	0.3 ± 0.5	0.3 ± 0.7	0.227

Note: *defined as the percentage of hospice beds relative to each hospital's annual total cancer deaths. The categorical variables and continuous variables were presented as n (%) and mean±standard deviation, respectively. We used the binominal generalized linear mixed-effects model for comparing the categorical variables and the generalized linear mixed-effects model for comparing the continuous variables with a normal distribution. In these models, the hospital attributes and death year were placed in the random-effects model for control.

Abbreviations: HSC = hospice shared care, UC = usual care, USD = United States dollar

Comparisons of QOCbetween groups

Comparing to the entire UC group, the entire HSC group had significantly lower proportion of "with emergency room visit" (51.2% versus 60.6%, AOR (95% CI)= 0.63 (0.21 - 16.78), p<0.001), "with ICU admission" (21.1% versus 35.5%, AOR (95% CI)= 0.46 (0.36 - 0.57), p<0.001), "receiving chemotherapy" (4.1% versus 13.5%, AOR (95% CI)= 0.25 (0.17 - 0.39), p<0.001), but higher proportion of "with hospitalization≧14 days" (60.7% versus 32.3%, AOR(95% CI)= 3.28 (2.68 - 4.02), p<0.001) during the last month before death. Other QOC indices including "with hospitalization," "death in the hospital," and "total QOC scores" were not significantly different between the two groups.

In the further comparisons between the subgroups categorized by survival periods, we found that the entire HSC groups showed generally better QOC in the four indices ("with emergency room visit," "with hospitalization," "with ICU admission," and "receiving chemotherapy") but worse QOC in the index "with hospitalization≧14 days" then the entire UC group in the "G8-14d," "G15-30d," and "G30-60d" subgroups.

As to the "total QOC scores," the scores indicated that the entire HSC group had worse QOC than the entire UC group in the "G4-7d" and "G8-14d" subgroups but better QOC in the "G15-30d" and "G31-60d" subgroups. Since the QOC was evaluated within the last month before death, these results indicated that compared to the entire UC group, the entire HSC group had significantly worse QOC before receiving HSC but better QOC after receiving HSC. (Table 2 and Figure 2)

Table 2. Comparisons of the QOCbetween the HSC and UC groups

		Total patients	Subgroups stratified by survival periods							
			G1-3d	G4-7d	G8-14d	G15-30d	G31-60d	G61-90d	G91-180d	G181-365d
	n (HSC/UC)	857/857	18/18	62/62	269/269	171/171	159/159	73/73	69/69	36/36
Total QOC scores	HSC	2.8 ± 1.2	2.9 ± 0.8	3.1 ± 0.9	2.9±1.24	2.8 ± 1.2	2.7 ± 1.2	2.6 ± 1.3	2.5 ± 1.4	2.5 ± 1.3
	UC	2.8 ± 1.4	2.4 ± 1.6	2.6 ± 1.3	2.64±1.34	3.1 ± 1.5	3.1 ± 1.2	2.8 ± 1.4	2.8 ± 1.4	2.9 ± 1.3
	ARR (95% CI)	1.74 (0.87-3.47)	1.74 (0.87-3.47)	1.55 (1.04-2.31)*	1.25 (1-1.55*)	0.75 (0.57-1.00)*	0.66 (0.50-0.86)**	0.81 (0.52-1.25)	0.73 (0.46-1.16)	0.71 (0.39-1.27)
With emergency room visit	HSC	439 (51.2%)	12 (66.7%)	36 (58.1%)	139 (51.7%)	91 (53.5%)	77 (48.4%)	35 (47.9%)	33 (47.8%)	16 (43.2%)
	UC	519 (60.6%)	14 (77.8%)	39 (62.9%)	179 (66.5%)	110 (64.3%)	92 (57.9%)	33 (45.2%)	35 (50.7%)	17 (47.2%)
	AOR (95% CI)	0.63 (0.21-16.78)***	0.55 (0.11-2.80)	0.87 (0.37-2.08)	0.47 (0.31-0.7)***	0.58 (0.36-0.94)*	0.57 (0.34-0.94) *	1.12 (0.53-2.36)	0.98 (0.37-2.08)	0.8 (0.28-2.29)
With hospitalization	HSC	710 (82.8%)	18 (100.0%)	61 (98.4%)	201 (74.7%)	148 (87.1%)	133 (83.6%)	61 (83.6%)	57 (82.6%)	31 (83.8%)
	UC	720 (84.0%)	11 (61.1%)	51 (82.3%)	218 (81.0%)	147 (86.0%)	145 (91.2%)	62 (84.9%)	55 (79.7%)	31 (86.1%)
	AOR (95% CI)	0.89 (0.68-1.16)	1.62 (0.89-1.19)	1.17 (1.07-1.37)*	0.64 (0.41-0.99)*	1.13 (0.59-2.15)	0.49 (0.25-0.99)*	0.94 (0.37-2.41)	1.71 (1.64-105.37)	0.83 (0.23-3.02)
With ICU admission	HSC	181 (21.1%)	4 (22.2%)	19 (30.6%)	55 (20.4%)	29 (17.1%)	38 (23.9%)	13 (17.8%)	16 (23.2%)	7 (18.9%)
	UC	304 (35.5%)	8 (44.4%)	15 (24.2%)	90 (33.5%)	63 (36.8%)	65 (40.9%)	23 (31.5%)	25 (36.2%)	15 (41.7%)
	AOR (95% CI)	0.46 (0.36-0.57)***	0.30 (0.02-3.77)	1.42 (0.62-3.27)	0.48 (0.32-0.73)***	0.33 (0.2-0.57)***	0.44 (0.27-0.73)**	0.47 (0.22-1.02)	0.52 (0.62-3.27)	0.28 (0.08-1.01)
Receiving chemotherapy	HSC	35 (4.1%)	1 (5.6%)	6 (9.7%)	11 (4.1%)	5 (2.9%)	3 (1.9%)	5 (6.8%)	4 (5.8%)	0 (0.0%)
	UC	116 (13.5%)	3 (16.7%)	9 (14.5%)	29 (10.8%)	32 (18.7%)	25 (15.7%)	8 (11%)	6 (8.7%)	4 (11.1%)
	AOR (95% CI)	0.25 (0.17-0.39)***	0.29 (0.03-3.14)	0.57 (0.17-1.85)	0.34 (0.17-0.71)**	0.13 (0.05-0.35)***	0.1 (0.03-0.34)***	0.53 (0.14-1.92)	0.69 (0.17-1.85)*	—
With hospitalization≧14 days	HSC	520 (60.7%)	3 (16.7%)	23 (37.1%)	206 (76.6%)	110 (64.7%)	91 (57.2%)	33 (45.2%)	31 (44.9%)	23 (62.2%)
	UC	277 (32.3%)	2 (11.1%)	12 (19.4%)	36 (13.4%)	69 (40.4%)	70 (44.0%)	38 (52.1%)	34 (49.3%)	16 (44.4%)
	AOR (95% CI)	3.28 (2.68-4.02) ***	2.24 (0-7071.07)	2.54 (1.09-5.95)*	6.24 (4.84-8.02) ***	2.74 (1.76-4.26)***	1.71 (1.09-2.68)*	0.72 (0.36-1.44)	0.83 (1.09-5.95)	2.05 (0.81-5.23)
Death in the hospital	HSC	492 (57.4%)	15 (83.3%)	45 (72.6%)	169 (62.8%)	90 (52.%9)	82 (51.6%)	44 (60.3%)	30 (43.5%)	17 (45.9%)
	UC	498 (58.1%)	6 (33.3%)	37 (59.7%)	158 (58.7%)	104 (60.8%)	92 (57.9%)	42 (57.5%)	38 (55.1%)	21 (58.3%)

AOR	0.97	2.91	2.04	1.18	0.74	0.77	1.12	0.62	0.54
(95% CI)	(0.79-1.18)	(1.55-3.97)	(0.87-4.8)	(0.82-1.68)	(0.47-1.15)	(0.48-1.21)	(0.58-2.18)	(0.87-4.8)	(0.18-1.6)

Note: The subgroups (ex: G##d) denoted that the patients started to receive HSC ## days before death. The categorical variables and continuous variables were presented as n (%) and mean± standard deviation. We used the binominal generalized linear mixed-effects model for comparing the categorical variables and the generalized linear mixed-effects model for comparing the continuous variables with a normal distribution. In these models, the hospital attributes and death year were placed in the random-effects model for control.

* p < 0.05; ** p < 0.01; *** p < 0.001

Abbreviations: AOR = adjusted odds ratio, ARR = adjusted relative ratio, CI = confidence interval, HSC = hospice shared care, ICU = intensive care unit, QOC= quality of care, UC= usual care

Comparisons of medical expenses between groups

Comparing to the entire UC groups, the entire HSC group had significantly lower total medical expenses after receiving HSC (4069.5 ± 6314.5 versus 5057.0 ± 6673.8 USD, ARR (95% CI) = 0.81 (0.80-0.81), p<0.001).

In the subsequent subgroup comparisons, we found that the significantly lower medical expenses of the HSC group occurred in the "G15-30d," "G31-60," and "G61-90d" subgroups. These results demonstrated that the financial benefits occurred when the patients initiated HSC on 15-90 days before their deaths. (Table 3 and Figure 3)

Furthermore, we found a decreasing daily medical expense decrease following the increasing survival periods in both HSC and UC groups. Moreover, the entire HSC group who received HSC on the last 15th-90th day of their lives had significantly lower daily medical expenses than the entire UC group. (Supplementary figure S1)

Table 3. Comparisons of the total medical expenses after receiving HSC between the HSC and UC groups

	Total patients	Subgroups stratified by survival periods							
		G1-3d	G4-7d	G8-14d	G15-30d	G31-60d	G61-90d	G91-180d	G181-365d
n (UC/HSC)	857/857	18/18	62/62	269/269	171/171	159/159	73/73	69/69	36/36
HSC group	4069.5 ± 6314.5	1047.5 ± 851.2	1492.3 ± 1005.4	2297.6 ± 2315.1	2488.0 ± 7107.0	3748.7 ± 3264.1	6138.6 ± 5018.2	9383.9 ± 7321.6	17393.6 ± 13176.9
UC group	5057.0 ± 6673.8	2364.2 ± 7207.2	1455.6 ± 1382.6	2342.9 ± 3044.5	3520.4 ± 3564.8	5796.2 ± 5163.7	8999.1 ± 8501.4	11581.4 ± 7854.1	16421.8 ± 13879.3
AMD	-$895.20	-$38	$39	-$73	-$1,281	-$2,007	-$2,171	-$1,954	$2,420
ARR (95% CI)	0.81 (0.80-0.81)***	0.95 (0.95-0.95)***	1.03 (1.02-1.03)	0.97 (0.96-0.97)	0.61 (0.61-0.62)***	0.65 (0.64-0.65)***	0.71 (0.71-0.72)*	0.82 (0.80-0.82)	1.26 (1.25-1.3)

Note: The subgroups (ex: G##d) denoted that the patients started to receive HSC ## days before death. The categorical variables and continuous variables were presented as n (%) and mean± standard deviation. We used the log-link function of the gamma generalized linear mixed-effects model to compare the medical expenses that belong to continuous variables with the abnormal distribution. The hospital attributes and year of death were placed in the random-effects model for control in the model. A negative AMD indicated that less medical expenses of the HSC group comparing to the UC group

* p < 0.05; *** p < 0.001

Abbreviations: AMD = adjusted mean difference, ARR= adjusted relative ratio, CI = confidence interval, HSC = hospice shared care, UC= usual care

Subgroup comparisons

In the entire HSC group, 523 patients (61.0%) only received HSC (named as "HSC alone" group), and 334 patients (39.0%) subsequently received home-based or hospital-based hospice care (named as "HSC+HHC" group). At the same time, we generated the other two "UC" groups, which were matched respectively with the "HSC alone" group and "HSC+HHC" group. It is also not surprising that the basic characteristics were not significantly different in the two sets of comparisons (the "HSC alone" group versus the corresponding "UC" group and the "HSC+HHC" group versus the corresponding "UC" group. (Supplementary table S1)

Regarding the QOC in the last month, the significant differences in the four QOC indices ("with emergency room visit," "with ICU admission," "receiving chemotherapy," and "with hospitalization≧14 days") between the entire HSC group and the entire UC group (shown in Table 2) persisted in the two-group comparisons of the two sets ("HSC alone" group versus "UC" group, and "HSC+HHC" group versus "UC" group). Nevertheless, we found that the "HSC+HHC" group had significantly lower total QOC scores than the corresponding "UC" group, whereas the significant difference was not disclosed in the comparison between the "HSC alone" group and its corresponding "UC" group. (Supplementary table S2)

As to the total medical expenses after receiving HSC, the benefit seen in the comparison between the entire HSC group and the entire UC group (shown in Table 3) persisted in the comparison of the "HSC+HHC" group versus the "UC" group but was not disclosed in the comparison between the "HSC alone" group versus the "UC" group. (Supplementary figure S2)

Discussion

The current study has several strengths. First, we took the "survival period" as one factor to match the study group and control group. Also, we made comparisons of paired subgroups stratified by survival periods to demonstrate the association between timing of HSC referral and clinical benefits. It is reasonable that the survival period is significantly related to the patients' illness severity and total medical expenses. Compared to previous studies that did not take the "survival period" into consideration to evaluate the difference between patients with and without palliative care, the current study is much more delicate for figuring out real-world situations. Second, we further subgrouped the HSC group into the "HSC alone" group and the "HSC+HHC" group to different the effect of HSC and subsequent HHC.

In the current study, we found that HSC was associated with a better QOC in the last month of life when the HSC was initiated 8-60 days before death. (Table 2) Also, HSC is associated with a significantly lower "total medical expenses after receiving HSC" when the HSC was initiated 15-90 days before death. (Figure 3) Furthermore, we disclosed that even "HSC alone" could improve QOC in the last month of life (Supplementary table S2), whereas the decreased total medical expenses of the HSC mainly occurred in the patients who received HSC and subsequent hospital-based or home-based hospice care. (Supplementary figure S2)

The QOC at the EOL stage represents a meaningful outcome. Aggressive medical management, such as emergency room visits, hospital and ICU admission, and chemotherapy administration, in the last months of life, are generally considered as indicators of poor QOC [28,29]. It is reasonable that HSC, a practice pattern similar to palliative care consultation, can reduce the probability of receiving aggressive managements, which equals a better QOC at the EOL stage. [30,31] The current study found that the patients received HSC, comparing to those who did not, had a significantly lower proportion of "with emergency room visit," "with ICU admission," "receiving chemotherapy," but a higher proportion of "with hospitalization≧14 days" and the similar probability of "death in the hospital." Most of these results were supported by the studies of Cheung et al. [32] and Triplett et al. [33]. However, the higher proportions of "with hospitalization≧14 days" and "death in the hospital" of the HSC group in our study were different from these studies' findings [32,33]. The high medical service availability and high medical insurance coverage rate in Taiwan mainly attribute to these disagreements [34], which somehow encourage terminal cancer patients to seek medical aids in hospitals [26].

The current study found that HSC referral was associated with a significantly lower medical expense after initiating HSC. Some previous studies investigated the influences of HSC on medical costs in a hospitalization period [35,36] or the last month of life [31], but both of them did not precisely reflect the influence of HSC as our study. Previous works also demonstrated that hospice care consultation effectively saved daily inpatient medical costs in terminal patients' terminal hospitalization [35,36]. Since the daily medical cost varied widely following the evolving stages of illness (Supplementary figure S1), it might be less clinically relevant to compare groups using an average value. We compared the total medical cost after receiving HSC between two groups matched with the same survival periods in the current study. Although both the previous studies agreed with our results, the current study provided a better overview of the total medical expense and HSC than the previous studies [35,36]. In contrast with our results, a study reported that palliative care did not affect medical expenses in the last month of terminal cancer patients' lives [31]. The discordant results might be related to different study designs. In the current study, the HSC group had significantly lower total medical costs after HSC than the UC group, but not in the last month. These findings might be because the medical expense in the last month consisted of medical expenses before HSC and after HSC since the patients' median survival period was about 21 days. Just like the explanation addressed in our previous work, the higher medical cost before the HSC initiation would dilute the expense saving after the HSC initiation [26].

Furthermore, our results were in line with Lin et al. [37], which also demonstrated an effectively saved medical expenditure of cancer patients after receiving hospice care. Nevertheless, the current study further demonstrated that medical costs saving occurred in those who subsequently receive home-based or hospital-based hospice care (Supplementary figure S1).

To date, the exactly optimal timing for palliative care initiation is unclear. The current concept prefers early referral of palliative care because of vast benefit [33], but the widely varied definitions of early referral, as well as various definitions of QOC indices and medical expenses, prohibit the generation of a solid consensus [21,28,30,38,39]. Among the previous studies evaluating the QOC and timing of palliative care consultation defined by the survival period from consultation to death, the referral before the last 90 days [28,40] or 30 days [22,30] of patients' lives were considered "early palliative care consultation" and were associated with lower probabilities of receiving aggressive care in terminal cancer patients. In the current study, the better QOC in the HSC group started to occurred when they received HSC earlier than the eight days before their deaths. Nevertheless, the trend of better QOC in the HSC group persisted in those who received HSC earlier than 60 days before death. The relatively small number of patients who received HSC earlier than the last 60 days might be a cause that failed to make the difference statistically significant (Table 2 and figure 2). Regarding the benefit of saving medical expenses, Nevadunsky et al. [16] found that palliative care consultation occurring > 30 days before death was associated with a significantly lower inpatient direct medical expenses for the last 30 days and 14 days of life. The current study found that medical cost benefits occurred when the HSC initiated as late as the 15th day before death. The benefit went less significantly when the patients received HSC earlier than 90 days before death. We proposed two reasons to explain this finding. First, the daily medical expenses decreased gradually following the increased survival periods. The relatively fewer daily medical costs in both groups with survival period longer than 90 days diluted the benefit of medical cost saving for the HSC group (Supplementary figure S1). Second, the relatively small number of patients who received HSC before the last 90 days of life was responsible for the insignificancy (Table 3 and figure 3).

Several limitations should be addressed. First, the nature of a retrospective study is subject to bias. Second, we only enrolled patients with terminal cancer who were covered by the NHI, and did not include self-paid medical expenses into the total expenses. However, owing to the extremely high coverage rate of NHI and high coverage range of medical expenses items, the patients enrolled in the current study was still representative of the target population. Third, our target population was terminal cancer patients, thus the results could not be extrapolated to patients with terminal diagnoses other than cancer. Fourth, the decision of accepting HSC is associated with the preferences of physicians and patients and families. However, the nationwide population within the same period minimized this bias. Fifth, the cultures and insurance coverage are two crucial aspects affecting the decision of choosing hospice and palliative care. Besides, the religions, traditional philosophies and values were unavailable from the database. Thus the results should be applied to cancer patients with caution regarding to cultures and insurance coverage range.

Conclusion

Among patients with terminal cancer, HSC can effectively improve QOC in those who received it before the last eight days of life and save medical expense in those who received it before the last 15 days of life.

Abbreviations

AMD = adjusted mean difference, AOR = adjusted odds ratio, ARR = adjusted relative ratio, CCI = Charlson comorbidity index, CI = confidence interval, EOL = end-of-life, GLMM = generalized linear mixed-effects model, HSC = hospice-shared care, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, ICU = intensive care unit, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database, QOC = quality of care, SD = standard deviation, UC = usual care.

Declarations

Acknowledgments:

Funding:

YMD, YTH, MYL, HEL, CCS

Authors' Contributions:

Conceptualization: YMD, YTH, MYL, HEL, CCS; Data curation: YMD, YTH, MYL, HEL, CCS; Formal analysis: YMD, YTH, CCS; Funding acquisition: YTH; Investigation: YMD, YTH, MYL, HEL, CCS; Supervision: CCS; Writing – original draft: YMD, YTH, MYL, HEL, CCS; Writing – review & editing: YTH and CCS.

Competing interests:

The authors declare that they have no competing interests.

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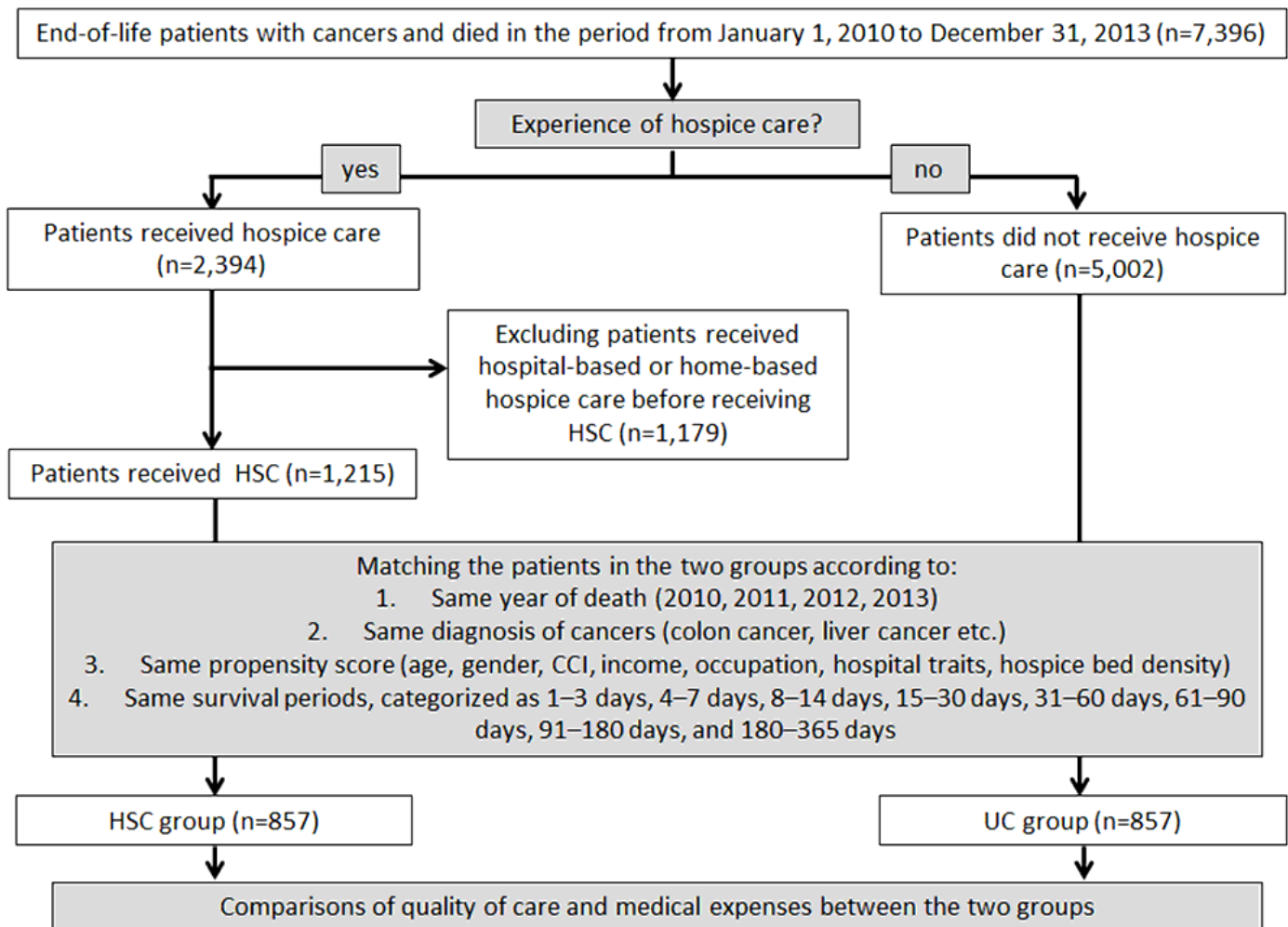
Figures

Figure 1

Flowchart of patient selection and matching Abbreviations: CCI= Charlson comorbidity index, HSC= hospice-shared care, UC= usual care
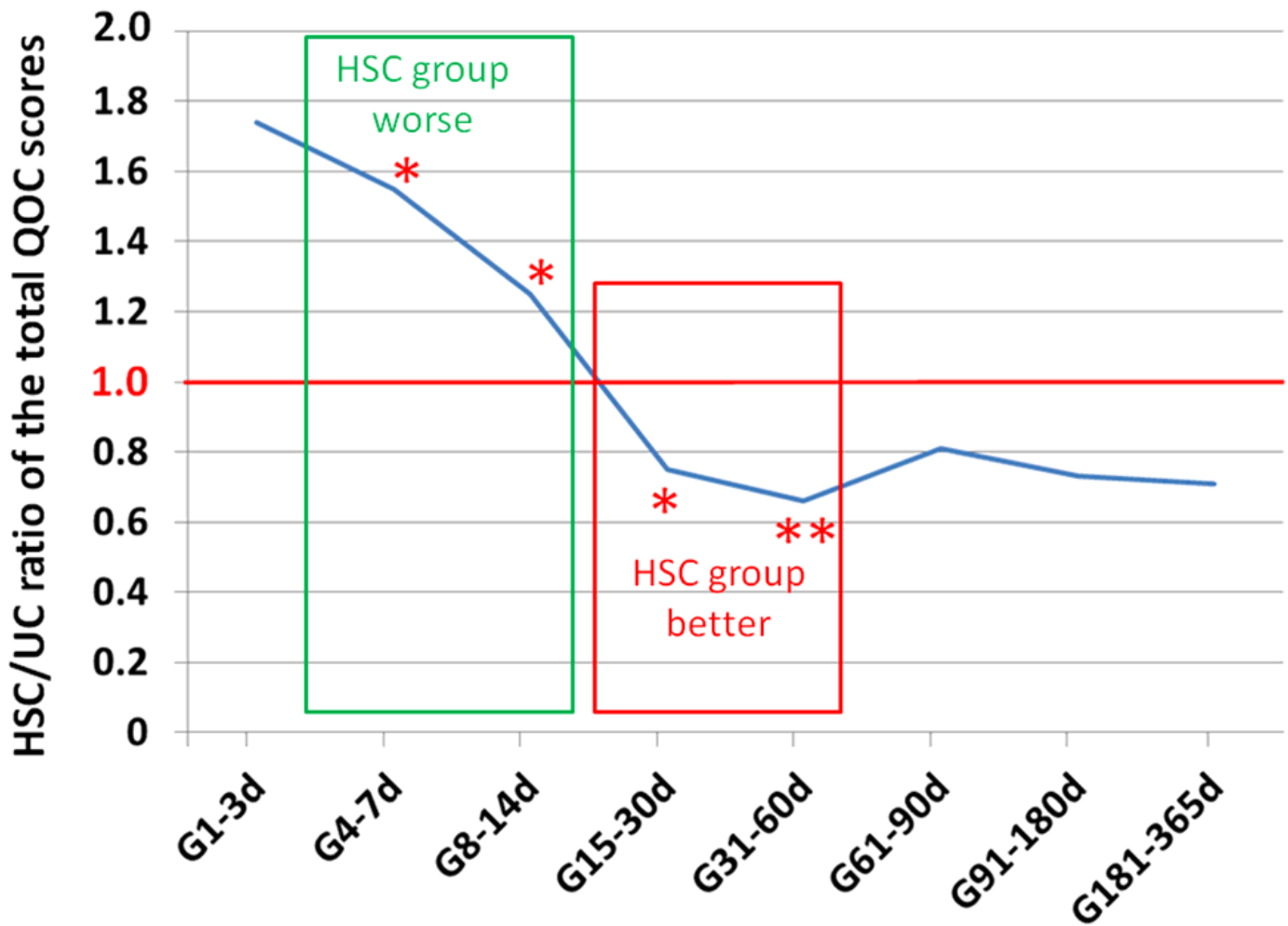
Figure 2

Comparisons of QOC between the HSC and UC groups Note: A ratio >1 or < 1 denoted that the HSC has worse or better QOC than the UC group, respectively. * p < 0.05; ** p < 0.01 Abbreviations: HSC = hospice shared care, QOC= quality of care, UC= usual care
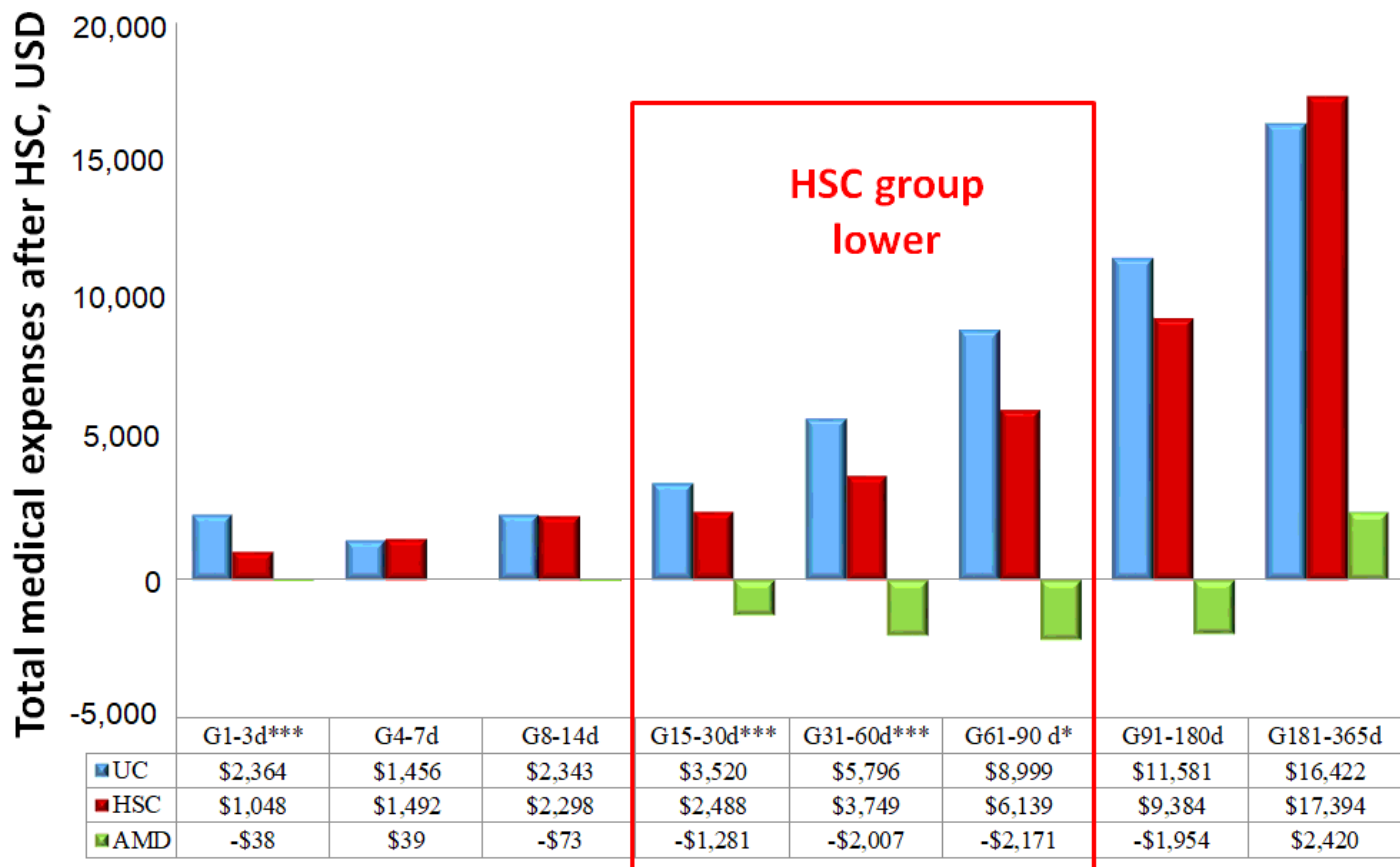
	G1-3d***	G4-7d	G8-14d	G15-30d***	G31-60d***	G61-90 d*	G91-180d	G181-365d
UC	$2,364	$1,456	$2,343	$3,520	$5,796	$8,999	$11,581	$16,422
HSC	$1,048	$1,492	$2,298	$2,488	$3,749	$6,139	$9,384	$17,394
AMD	-$38	$39	-$73	-$1,281	-$2,007	-$2,171	-$1,954	$2,420

Figure 3

Comparisons of the total medical expenses after receiving HSC in subgroups categorized by survival periods Note: * p < 0.05; *** p < 0.001 Abbreviations: AMD = adjusted mean difference, HSC = hospice shared care, UC= usual care, USD= United States dollar

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