

Quality of life changes and intensive care preferences in terminal cancer patients

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ABSTRACT

Objective: There is scarce research on the short-term fluctuations in end-of-life (EoL) care planning for seriously ill patients. The aim of our study was to investigate the stability of preferences regarding treatment in an intensive care unit (ICU) and identify the factors associated with changes in preferences in terms of quality of life (QoL).

Method: A prospective examination on preference changes for ICU care in 141 terminal cancer patients was conducted. Patients were categorized according to their change in preference during the final two months of their lives into four categories: (1) the *keep-accept* group, (2) the *keep-reject* group, (3) the *change to accept* group, and (4) the *change to reject* group. Using multiple logistic analyses, we explored the association between patient demographics, health-related QoL, and changes in ICU preference.

Results: The overall stability of ICU preferences near the end of life was 66.7% ($\kappa = 0.33$, $p < 0.001$). Married patients were more likely to change their preference regarding ICU care [adjusted odds ratio (aOR) toward *accept* 12.35, $p = 0.021$; aOR toward *reject* 10.56, $p = 0.020$] than unmarried patients. Patients with stable physical function tended to accept ICU care (aOR = 5.05, $p = 0.023$), whereas those with poor performance (aOR = 5.32, $p = 0.018$), worsened QoL (aOR = 8.34, $p = 0.007$), or non-aggravated fatigue (aOR = 8.36, $p = 0.006$) were more likely to not accept ICU care.

Significance of results: The attitudes of terminally ill cancer patients regarding ICU care at the end of life were not stable over time, and changes in their QoL were associated with a tendency to change their preferences about ICU care. Attention should thus be paid to patients' QoL changes to improve medical decision making with regard to EoL care.

KEYWORDS: Changes, Intensive care unit, Preference, Quality of life, Terminal care

INTRODUCTION

The application of aggressive end-of-life (EoL) care for cancer patients has recently become more and more popular (Cooke et al., 2014; Ho et al., 2011). Discussions between terminal cancer patients and their

physicians about preferences for EoL care can lead to such care being less aggressive (Wright et al., 2008; Mack et al., 2010). The current guidelines recommend that physicians discuss EoL care planning with terminal cancer patients early on in the course of the disease, during periods of physical and mental stability, rather than when the patient is undergoing acute deterioration (Peppercorn et al., 2011; Smith et al., 2012). Patients who have discussed their preferences for EoL care with their physicians are more likely to choose less-aggressive palliative care

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(Wright et al., 2008; Weeks et al., 1998), and such less-aggressive care has been associated with better quality-of-life (QoL) close to the time of death (Wright et al., 2008; 2010).

When EoL care planning is discussed with patients early on in the course of their disease, care plans can be modified over time during disease progression (Straton et al., 2004; Fried et al., 2006; Witting et al., 2008). Even after advanced directives have been signed, patients can change their minds and update those directives. EoL care planning may be modified for various reasons, which can determine aggressiveness of care and quality of death (Earle et al., 2008; Wright et al., 2008). Although much previous research has investigated the stability of long-term EoL care preference in both the general population and specific clinical settings (Mukamel et al., 2013; Barrio-Cantalejo et al., 2013; Janssen et al., 2012; Cotter et al., 2009; McParland et al., 2003; Weissman et al., 1999; Danis et al., 1994; Everhart & Pearlman, 1990), there are very little data regarding short-term fluctuations in EoL care planning in seriously ill patients (Rosenfeld et al., 1996). Identifying the factors related to these changes in patient preference for EoL care in terms of QoL could help improve the decision-making process in EoL care.

We evaluated the stability of terminally ill cancer patients' preferences regarding EoL care over time. We hypothesized that serial changes in QoL over time could affect EoL care planning, thus representing changes in attitude toward intensive care unit (ICU) care. We investigated the stability of preferences regarding ICU care and identified the factors associated with changes in QoL preferences.

PATIENTS AND METHODS

Study Design and Recruitment

The Study to Understand Risks, Priority, and Issues at the End of Life (SURPRISE), a prospective cohort

study, enrolled terminal cancer patients in the Republic of Korea. Patients were recruited from 11 university hospitals and the National Cancer Center during the period from July of 2005 to October of 2006. Patients were eligible to participate if they were 18 years or older, had been diagnosed as terminal by their physicians, were capable of communicating with an interviewer or filling out questionnaires, and had been deemed competent to understand the purpose of the study and provide informed consent. They were enrolled within days of being diagnosed and informed of being in a terminal state. We defined a terminal patient as one with progressive, advanced disease who was likely to die within months. Patients were not eligible to participate if they continued anti-cancer treatment after enrollment, their disease status was non-evaluable, had changed their treatment plan, or could not complete the questionnaire because their condition had deteriorated. All participants provided informed consent, and our institutional review boards approved the protocol. The details of the study design have been published (Yun et al., 2010a; 2011).

We identified 481 terminal cancer patients who completed baseline questionnaires in SURPRISE (Figure 1). Of these, 473 were followed throughout their EoL period. During the 2-month follow-up, 330 patients died, and 2 were deemed incompetent. The data from 141 patients were subsequently analyzed.

Data Collection

SURPRISE collected demographic data and clinical information about the patients. Questionnaires were administered within days of initiation of the study by face-to-face interviews. The same questionnaires were administered two months later by mail and took about 20 minutes to complete. SURPRISE gathered demographic information (i.e., age, sex, education level, religion, marital status, employment details, the person paying for treatment, and monthly household income) to evaluate previous discussions

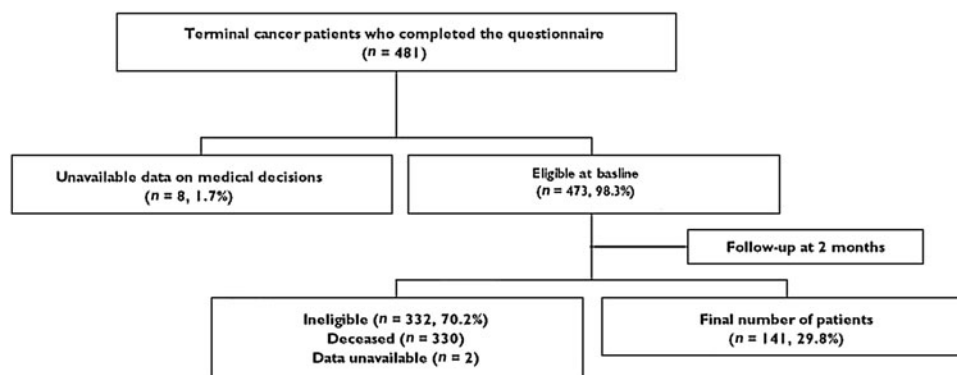


Fig. 1. Flowchart of patient recruitment.

with physicians and patients about intentions regarding ICU care near death and other EoL issues. Following a previous investigation (Wittink et al., 2008), the response on ICU care was coded as the dichotomous variables *reject* (“No, I would not want”) or *accept* (“Yes” or undetermined).

To measure QoL, we employed the validated Korean version of the European Organization for Research and Treatment of Cancer instrument (EORTC QLQ–C30) (Aaronson et al., 1993; Yun et al., 2004). The EORTC QLQ–C30 is a brief, self-reported, cancer-specific measure of QoL and is comprised of five, multiitem, functional scales that evaluate physical, role, emotional, cognitive, and social function, and one global health status/QoL scale. The three symptom scales measure fatigue, pain, and nausea/vomiting, and the six single items assess other symptoms (i.e., dyspnea, insomnia, appetite loss, constipation, and diarrhea) and financial difficulties. According to the EORTC scoring manual, all scales are then linearly transformed into a numerical score (0 to 100), with 100 representing the best global health status or functional status, or the worst symptom status, as appropriate. We handled incomplete questionnaires according to the developer’s recommendations. We defined a meaningful difference in health-related QoL as a 10-point difference in mean score (Osoba et al., 1998).

Each variable was categorized as follows: monthly income was categorized into “< 2,000 US dollars (USD)” and “≥ 2,000 USD”; education level into “high school or lower” and “college or beyond”; marital status into “married” and “unmarried,” which included “single” and “divorced/separated/widowed”; religion into “no religion” and “professing a religion,” including non-Catholic Christians, Buddhist, Catholics, and others; and the person paying for treatment into “patient” and “others,” including spouse, parents, offspring, relatives, and others. Patients also provided clinical information regarding their awareness of the terminal diagnosis and Eastern Cooperative Oncology Group (ECOG) performance status. ECOG performance status is an observer-rated scale of a patient’s physical ability that utilizes numbers ranging from 0 (able to carry out all normal activities) to 4 (completely disabled) (Oken et al., 1982). We divided patients into two groups: those with scores of 0–2 and those scoring 3–4.

Statistical Analysis

Overall preference stability was assessed by kappa statistics. The primary outcome was the direction of the changed preference for ICU care near death. We categorized subjects into four groups according to changed preference: *accept–accept* group, *reject–reject* group, change to *accept* group, and change to *reject* group. Assuming that patients who accepted ICU

care at baseline would have different reasons to change their preference at follow-up compared with patients who rejected ICU care at baseline, we compared patients in the *accept–accept* and *accept–reject* groups with those in the *reject–reject* with *reject–accept* groups (Rosenfeld et al., 1996).

We employed a logistic regression model in order to assess the impact of patients’ QoL changes or demographic/clinical characteristics on a shift of preference for ICU care near death. In addition, each independent factor that was statistically significant ($p \leq 0.10$) in the univariate analysis was entered into the final multivariate logistic regression model to calculate adjusted odds ratios (aORs). Using a forward stepwise elimination procedure, we obtained a best-fit multivariate logistic regression model. In multivariate logistic analyses, we considered p values less than 0.05 generated in two-tailed tests to indicate statistical significance. All statistical tests were performed using SAS software (v. 9.2) (SAS Institute, Cary, North Carolina).

RESULTS

Patient Characteristics

Table 1 summarizes the demographic and clinical characteristics of participants. The mean age was 56.2 years (range 20–79 years), and nearly 50% were male. More than half of our subjects were aware of their terminal status (58.7%), and a large proportion of patients had not discussed ICU care near death with their physicians (79.7%).

Changes of Preference for ICU Care

Figure 2 depicts preference stability for ICU care during the 2 months prior to death ($\kappa = 0.33$, $p < 0.001$). In brief, the preference for ICU care during this time period did not change for 94 patients (66.7%; 48 for *keep–accept* and 46 for *keep–reject*), shifted to *accept* in 24 patients (17.0%), and shifted to *reject* in 23 patients (16.3%). At baseline, answers were 32 for “yes,” 70 for “no,” and 39 for “undetermined.” Among the 32 patients who answered “yes,” only 10 (31.3%) replied “yes” after the two-month follow-up (22 switched to “no” or “undetermined”). For those who answered “no” initially, the second answer was “yes” in 10%, “no” in 65.7%, and “undetermined” in 24.3%. Regarding subjects who answered “undetermined” at baseline, the response shifted to “yes” in 23.1% and to “no” in 30.8% (data not shown).

Impact of QoL Changes on the Direction of Altered Preference

The data presented in Table 2 show the relationships between QoL changes and change in preference for

Table 1. Characteristics of patients

Characteristics	n	%
Age, years (n = 141)		
≤ 55	64	45.4
> 55	77	54.6
Sex (n = 141)		
Male	72	51.1
Female	69	48.9
Education level (n = 139)		
High school	113	81.3
College or beyond	26	18.7
Has a religion (n = 139)		
Yes	100	71.9
No	39	28.1
Marital status (n = 140)		
Married	109	77.9
Not married	31	22.1
Job status (n = 132)		
Employed	17	12.9
Unemployed	115	87.1
Who pays for treatment (n = 114)		
Patient	33	29.0
Other	81	71.1
ECOG performance status (n = 138)		
0–2	99	71.7
3–4	33	28.3
Monthly family's income, USD (n = 111)		
< 2,000	102	64.9
≥ 2,000	39	35.1
Cancer site (n = 141)		
GI	57	40.4
Other	84	59.6
Metastasis (n = 140)		
Yes	123	87.9
No	17	12.1
Aware of terminal diagnosis (n = 138)		
No	57	41.3
Yes	81	58.7
Pre-discussion for ICU treatment with physicians (n = 128)		
No	102	79.7
Yes	26	20.3

ECOG = Eastern Cooperative Oncology Group.

USD = United States dollars.

ICU = intensive care unit.

ICU care near death. Patients who had maintained physical function changed their preference toward *accept* ($OR = 0.34$, $p = 0.086$), whereas those whose global health had deteriorated ($OR = 2.37$, $p = 0.095$) or those with non-aggravated fatigue ($OR = 0.31$, $p = 0.031$) altered their preference toward *reject*.

Factors Related to the Altered Preference for ICU Care

Table 3 lists the demographic or clinical factors significantly associated with a changed preference for ICU care near death. Married patients were more

likely to change their preference (OR for *accept* 0.10; OR for *reject* 0.22). Patients who were unaware of their terminal diagnosis tended to change their preference toward *accept* ($OR = 2.49$, $p = 0.083$), whereas those with poor performance were more likely to change their preference toward *reject* ($OR = 2.45$, $p = 0.100$).

Multivariate Analyses of Factors Related to Changes in Preference Regarding ICU Care

Table 4 shows the results of a multivariate analysis of factors associated with preferences regarding ICU care. Married patients were more likely to change their preference regarding ICU care (a OR toward *accept* 12.35, $p = 0.021$; a OR toward *reject* 7.87, $p = 0.020$). The likelihood of switching to *reject* was significantly higher in patients with poor performance (a $OR = 5.32$, $p = 0.018$), worsened QoL (a $OR = 8.34$, $p = 0.007$), or non-aggravated fatigue (a $OR = 8.36$, $p = 0.006$). The maintenance of physical function was a significant predictor of a change in preference toward *accept* (a $OR = 5.05$, $p = 0.023$).

DISCUSSION

In this multicenter prospective study, we found that patient attitudes regarding ICU care at the end of life changed over time, and that deteriorating function was associated with this change. When patients were able to maintain physical function during their final two months, they tended to change their preference toward ICU care. However, when patients had worsening global health or stable symptoms such as fatigue, they tended to change their preference against ICU care. Interestingly, married patients were more likely to change their preference in either direction.

To the best of our knowledge, there is very little research on changes in preference for EoL care in seriously ill patients (Janssen et al., 2012; Rosenfeld et al., 1996; Fried et al., 2007). The treatment preferences of patients who are confronting death should be given priority over those of healthy individuals imagining some future illness (Ditto et al., 2006). A recent study identifying predictors of preference changes regarding life-sustaining treatments reported that decreased health status and mobility were associated with a change in preference (Janssen et al., 2012), whereas we found that a deterioration in global QoL and physical function were related to a preference to reject ICU care. This discrepancy could be explained by the course of the disease and/or duration of follow-up, as the cited study investigated one-year stability of preferences in patients with advanced chronic organ failure. Since the functional decline

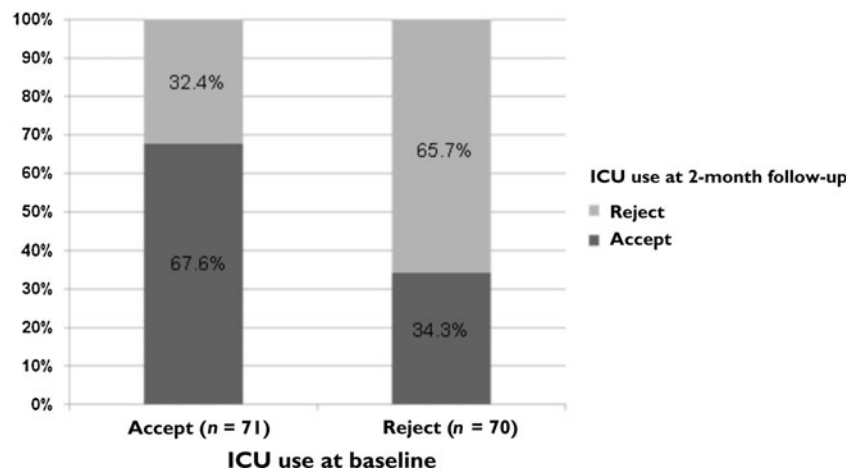


Fig. 2. Stability of ICU preference 2 months before death ($N = 141$). Degree of agreement was 66.7% ($\kappa = 0.33, p < 0.001$) by kappa statistics. ICU = intensive care unit.

associated with chronic organ failure is gradual compared to patients with terminal cancer, the reported preferences may be influenced by the individual’s affective state rather than situational factors.

In our study, preferences toward ICU care at the EoL were significantly influenced by aggravated symptoms. Patients with stable symptoms tended to reject ICU care at the end of life. Patients who suffered from symptoms appeared to regard ICU care as another type of intensive care for management of their symptoms. However, actual ICU care at the

EoL has been found to not be associated with prolonged survival (Yun et al., 2011), and terminal cancer patients have been found to not benefit from ICU care (Kim et al., 2014). Hence, sufficient management of symptoms is important not only for quality of life but also for appropriate EoL care planning.

Since patients who had earlier discussions about EoL care received less-aggressive treatment before death (see Mack et al., 2012), early EoL care planning should be undertaken in terminal cancer patients. The same study found that use of aggressive care

Table 2. Association between QoL changes* and preferences for ICU care

EORTC QLQ-C30	Change to Accept (n=24)			Change to Reject (n=23)		
	n (%)	OR (CI _{95%})	p	n (%)	OR (CI _{95%})	p
Deteriorated function						
Physical	4 (16.7)	0.34 (0.10–1.17)	0.086	5 (21.7)	0.39 (0.12–1.22)	0.106
Role	8 (33.3)	0.85 (0.30–2.41)	0.764	10 (43.5)	0.91 (0.33–2.47)	0.852
Emotional	8 (33.3)	1.14 (0.40–3.28)	0.804	12 (52.2)	1.99 (0.72–5.46)	0.182
Cognitive	7 (29.2)	0.59 (0.20–1.69)	0.321	9 (39.1)	0.83 (0.30–2.28)	0.712
Social	9 (37.5)	1.13 (0.40–3.14)	0.822	11 (47.8)	1.28 (0.47–3.49)	0.625
Global health/QoL	9 (37.5)	2.47 (0.82–7.42)	0.108	13 (56.5)	2.37 (0.86–6.54)	0.095
Aggravated symptom						
Fatigue	12 (50.0)	1.30 (0.48–3.50)	0.603	7 (30.4)	0.31 (0.11–0.90)	0.031
Nausea/vomiting	11 (45.8)	1.93 (0.70–5.36)	0.205	8 (34.8)	0.58 (0.21–1.62)	0.299
Pain	11 (45.8)	1.93 (0.70–5.36)	0.205	7 (30.4)	0.73 (0.25–2.11)	0.560
Dyspnea	11 (45.8)	0.65 (0.24–1.76)	0.396	7 (30.4)	0.44 (0.15–1.25)	0.124
Insomnia	10 (41.7)	2.02 (0.71–5.75)	0.186	7 (30.4)	0.88 (0.30–2.56)	0.807
Appetite loss	6 (25.0)	0.76 (0.25–2.32)	0.633	8 (34.8)	0.97 (0.34–2.76)	0.958
Constipation	10 (41.7)	1.11 (0.41–3.03)	0.837	6 (26.1)	0.59 (0.20–1.77)	0.344
Diarrhea	13 (54.2)	2.02 (0.74–5.49)	0.170	6 (26.1)	0.78 (0.26–2.36)	0.656
Financial problem	8 (33.3)	0.65 (0.23–1.82)	0.412	9 (39.1)	1.17 (0.42–3.27)	0.761

QoL = quality of life.
 ICU = intensive care unit.
 OR = odds ratio.
 CI = confidence interval.
 * More than 10 points.

Table 3. Characteristics related to a change in preference for ICU near death

	Change to Accept		Change to Reject	
	OR (CI _{95%})	p	OR (CI _{95%})	p
>55 years	1.87 (0.65–5.37)	0.246	1.29 (0.48–3.49)	0.617
Female	0.85 (0.31–2.31)	0.750	0.92 (0.34–2.50)	0.875
Education, college or beyond	1.05 (0.31–3.59)	0.935	2.41 (0.68–8.54)	0.173
Having a religion	1.97 (0.56–6.88)	0.288	1.00 (0.34–2.98)	0.994
Unmarried	0.10 (0.01–0.81)	0.031	0.22 (0.05–1.09)	0.064
Unemployed	0.44 (0.10–1.95)	0.277	0.95 (0.21–4.21)	0.946
Other pays for treatment	0.59 (0.18–1.92)	0.381	0.71 (0.21–2.41)	0.588
Family's income, ≥2,000 USD	1.33 (0.41–4.28)	0.637	0.97 (0.30–3.20)	0.965
Non-GI cancer	0.76 (0.28–2.06)	0.589	0.78 (0.28–2.14)	0.630
No metastasis	1.14 (0.25–5.26)	0.864	0.23 (0.03–1.94)	0.175
Not aware of terminal diagnosis	2.49 (0.89–6.99)	0.083	0.89 (0.32–2.49)	0.819
Poor performance (ECOG 3–4)	1.27 (0.42–3.87)	0.671	2.45 (0.84–7.11)	0.100
No advanced discussions	0.66 (0.20–2.20)	0.495	1.37 (0.33–5.77)	0.668

ICU: intensive care unit.

USD = United States dollars.

ECOG: Eastern Cooperative Oncology Group.

OR=odds ratio.

CI = confidence interval.

was much less frequent when EoL discussions took place before the last 30 days of life, and that the odds of hospice utilization were nearly twice as high. We found that patient attitudes toward ICU care at the end of life changed over time over the course of the disease, and that a preference for ICU care near the end of life changed in a third of terminally ill cancer patients. These results suggest a need for continuous discussions regarding EoL care planning as patient preferences for ICU care continue to change.

Generally, married patients have been found to be more likely to make predictable treatment decisions (Nielsen et al., 2013; Erci & Ozdemir, 2009), which might be limited to when their conditions are stable (Janssen et al., 2012). In our cohort of terminal cancer patients at the end of life, married patients were very vulnerable in the face of decisions regarding

ICU care. Especially in Korea, an individual's health decisions are frequently made within a strong family context, where interdependence among family members is a prime value in decision making (Kwak & Salmon, 2007; Mo et al., 2012). Stronger interrelationships within a patient's family tend to have a great deal of influence on medical decisions at the end of life when the patient's condition is highly unstable.

Our study has several limitations. First, our participants were enrolled from selected university hospitals and might not represent the general population of terminal cancer patients. Nevertheless, our large multicenter-based setting and high participation rate should have minimized selection bias. Second, among our 481 participants, serial data for only 141 participants were available, for various reasons,

Table 4. Predictors of a change in preference for ICU near death

	Change to Accept			Change to Reject		
	aOR	CI _{95%}	p	aOR	CI _{95%}	p
Married	12.35	1.47–103.8	0.021	10.56	1.46–76.45	0.020
Poor performance				5.32	1.34–21.26	0.018
Worsened QoL				8.34	1.80–38.52	0.007
Maintained physical function	5.05	1.25–20.38	0.023			
Non-aggravated fatigue				8.36	1.84–38.0	0.006

ICU = intensive care unit.

QoL = quality of life.

aOR=adjusted odds ratio.

CI = confidence interval.

introducing a potential selection bias. Third, we serially evaluated attitudes toward ICU care as part of EoL care planning. However, the intention to employ the ICU does not reflect all aspects of EoL care planning. Finally, other potential confounding factors were not considered (i.e., the influence of caregivers or the psychological aspects of individual patients) (Rosenfeld et al., 1996; Yun et al., 2010b).

In conclusion, patient attitudes regarding treatment in an intensive care unit at the end of life are not stable over time, and changes in symptoms or function are associated with a tendency to changing attitudes. To improve medical decision making for EoL care, we believe that it is necessary to continue and broaden discussions about EoL care planning over time and thereby hopefully provide adequate care for cancer patients to preserve quality of life.

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