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Tissue Donation after Withdrawal of Life-Sustaining Treatment as an Advanced Care Plan is One of the Options in End-of-Life Care

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Abstract

Background: Withdrawal of life-sustaining treatment (WLST) is an option in end-of-life of critical illness in a surgical/neurosurgical intensive care unit (SNICU). In addition to lessen the patient's suffering and to comfort the surrogates' grief, there is something meaningful, such as tissue donation, for others to pursue.

Aim: The aim of this study is to investigate the relationship between surgical intervention and the willingness of patients and/or their surrogates to donate tissue after WLST.

Design: Retrospective cohort study of 368 patients who died in a SNICU in the past 3 years

Setting/participants: Twenty-eight adult patients had life-sustaining treatment withdrawn from a total of 368 patients. We analyzed patient demographics and time courses of WLST in SNICU using the Student t-test.

Results: Fourteen patients (50%) received surgical interventions, and 19 patients (67.86%) were admitted due to neuro-critical diseases. Tissue procurement for donation is significantly higher in patients underwent surgery than patients without surgery (21% *vs.* 0%, P=0.041) after the scheduled WLST and consequent verification of cardiac death.

Conclusions: Our study uniquely demonstrates that patients who underwent surgical intervention with sufficient time for bidirectional discussions between physicians and the patients' families were more likely to have tissues donated after WLST. Importantly, tissue donation after WLST is one of the options for end-of-life care in advanced care plan of SNICU.

Keywords: End of life care; Tissue and organ procurement; Advanced care plan; Withdrawal of life-sustaining treatment

Introduction

Over recent decades, rapid advances in medical technology, including surgery, have allowed critically ill patients to survive longer than they would have in the past. At the same time, critically ill patients are treated in different or mixed intensive care units (ICUs). Great efforts have been devoted to intensive care in the ICU to treat diseases with advanced equipment and skills. Neurocritical illness has been regarded as a more abrupt and catastrophic event than other critical diseases are, not only for patients but also for their families [1]. For those who survive with permanent disabilities, recovery from neurologic injury can be prolonged, and even prolong dying. Surrogates may therefore decide to withdraw life-sustaining treatment from critically ill patients in order to decrease suffering or pain, based on the laws in different countries. Futility issues in end-of-life care have thus gradually become clear in recent years [1,2].

In Taiwan, euthanasia has not been approved to date. However, palliative care at the end of life has been well developed in the most recent two decades. An order of DNR (Do Not Resuscitate) is usually regarded as withholding treatment. In Western and European countries, there is no difference assumed between withdrawal of and withholding life-sustaining treatment. However, in Eastern countries, withdrawing life-sustaining treatment is classified as an active decision to shorten the dying process or to relieve pain [3]. In 2013, a law was approved to allow withdrawing life-sustaining treatment for end-of-life care in Taiwan.

To date, organ donation after cardiac death has been legally prohibited in Taiwan. In contrast, tissue donation such as corneas, skin, or bone after cardiac death is allowed. Many researchers have investigated behaviors and factors related to organ donation after cardiac death after the withdrawal of life-sustaining treatment (WLST), including predicting the time to death after WLST [1, 4-7]. However, the relationship between surgical intervention and the willingness of patients and/or their surrogates to donate after WLST has not yet been clarified. Moreover, the characteristics of neuro-

critical diseases related to the WLST have not been investigated in Taiwan. We therefore retrospectively investigated the WLST from critical care patients in surgical/neurosurgical ICU (SNICU).

Materials and methods

Study design

The Institutional Review Board approved this study (TSGHIRB No: 1-105-05-084). We performed an observational retrospective investigation at the Tri-Service General Hospital in Taipei, Taiwan. The ICU is a combined surgical ICU (SICU) and neurosurgical ICU (NICU) with a 25-bed capacity. All patients admitted to the SNICU from 1 January 2013 to 10 November 2015 were enrolled. Three hundred sixty-eight patients died in the SNICU. Patients were excluded if they died during the natural disease course, if life-sustaining treatment was withheld, or if they donated organs after brain death. Only 28 patients completed the family meeting and experienced WLST.

Data collection

We used the following databases to obtain data for this study: the patient service record, the electronic medical chart, and the IntelliVue Clinical Information Portfolio (ICIP; Philips) system. We summarized patient demographics including age, sex, condition on ICU admission, severity of illness using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, diagnosis, length of stay in the ICU, time course for the WLST (including number of days in the ICU before the final family meeting and the number of days from the WLST before the final family meeting), and the number of hours from WLST to death. Diagnoses were further categorized as hemorrhagic cerebrovascular accident, traumatic brain injury, medical disease, brain surgery, major operations (excluding the brain), and multiple trauma (excluding the brain). Surgical interventions, medical management before WLST, the location at which the patient died, and whether tissues were donated were also recorded.

Study definitions

All patients and/or surrogates signed the DNR consents at or before the final family meeting. End-of-life was confirmed by two specialists before the final family meeting. A social worker usually attended the meeting to manage paramedical issues (such as bereavement counseling, financial problems, legal norms, or medical ethics). The willingness to participate in organ/tissue donation, palliative care, and/or continued futile treatment (including post-withdrawal care) were also discussed in the final family meeting if patients met the criteria for approval under Taiwanese law. The WLST included the termination of mechanical ventilation and vasopressor drugs.

Management before withdrawal was defined as the prescription of sedatives and analgesics and/or adjusting the setting on ventilators. However, if patients presented delayed death, they were transferred to a ward or discharged to home, depending on the family's willingness and local culture. Surgical interventions included laparotomy with bowel resection and anastomosis, laparotomy to check bleeding, open reduction and internal fixation, craniotomy/craniectomy with hematoma evacuation, craniotomy with tumor removal, craniotomy with clipping of an aneurysm, or external ventricular drainage.

Statistical analysis

Statistical analysis was conducted using Microsoft excel. Results are presented in numbers and percentages, or mean ± standard deviation for parametric variables. Difference testing between two groups was performed with the Student t-test, as appropriate. Statistical significance was set at $P<0.05$.

Results

General outcomes

During the observation period, 368 consecutive patients who died in the SNICU or after critical discharge from the SNICU were reviewed. We excluded 340 patients who died in natural disease course, did not receive the WLST at the end of life, or for whom list-sustaining treatment was withheld. During the almost 3-year period, 28 patients were enrolled and experienced the WLST at the end of their lives under approval by Taiwanese law and a final family meeting in the SNICU. The mean patient age was 60.82 years (range, 23–86 years) and the sex ratio was 50:50 (Tables 1 and 2). All patients were admitted to our hospital from the emergency room (100%) and received adequate treatment either in the ICU (67.86%) or in the general ward before being transferred to the ICU (32.14%). The mean APACHE II score on ICU admission was 26.14 ± 7.16 (range, 15–51 scores). There were 14 patients who received surgical intervention (50%) (Table 3), and 19 patients (67.86%) (Table 4) were admitted in service of the neurosurgical department. Hemorrhagic cerebrovascular accident (28.6%), traumatic brain injury (21.4%), and medical disease (21.4%) were common diagnoses for ICU admission (Table 2). Despite aggressive medical treatment, patients deteriorated to a futile medical condition, as confirmed by two specialists, and the family meetings (regarding patient prognosis at the end of life) were held during hospitalization. The mean duration was 16.5 days (median time, 9.5 days) from ICU admission to the final family meeting (defined as discussing issues related to the WLST to decrease patients' suffering and regain dignity at the end of life). Before the final family meeting, at least one type of vasopressor was maintained (39.28%), including extracorporeal membrane oxygenation support (3.57%). The mean time from the final family meeting to the WLST was 1.57 days. Some families decided to withdraw support immediately after the meeting (10.71%), while the majority decided to withdraw it the next day (57.14%) or 2–6 days later (32.14%) in order to prepare the funeral and/or legal proceedings or to have a final moment with the patient before death.

Management before WLST was performed in 24 patients (85.71%) to prescribe morphine and sedation (propofol or midazolam). The median time to death was 0.55 hours after WLST (including mechanical ventilation and vasopressors), with a range of 0.1 hour to 8.3 days (Table 1). The percentage of patients who died within one hour of WLST was 71%, and that of patients who died within 24 hours of WLST was 82%. A small proportion (14%) of patients was discharged from our ICU prior to death to the ward or to home. One patient (3.57%) with a previous ventriculoperitoneal shunt lived in a vegetative state after WLST. Corneas and skin were donated by three patients (10.71%) after cardiac death.

No.	Age (yrs). Sex	ICU APACHE II scores	Time 1 (days)	Time 2 (days)	Time 3 (days)	Time 4 (hours)	Management before withdrawal	No. of vasopressors	Place of death	Tissue donation
1	23.M	22	13	136	4	0.5	Yes	0	ICU	
2	36.M	26	29	21	1	0.4	Yes	1	ICU	Cornea+Skin
3	79.M	23	13	26	1	1.4	Yes	0	ICU	
4	71.F	32	0	19	0	58.1	Yes	0	ward	
5	64.F	25	9	8	3	0.1	No	ECMO	ICU	
6	57.F	32	0	3	1	0.2	Yes	3	ICU	
7	39.F	17	0	45	1	0.7	Yes	0	ICU	
8	53.F	15	13	11	2	0.1	Yes	1	ICU	
9	55.F	18	49	6	2	0.6	Yes	1	ICU	
10	57.F	21	0	6	1	25.6	No	0	ICU	
11	69.M	27	0	12	1	0.4	No	0	ICU	
12	78.F	32	6	29	1	0.6	Yes	1	ICU	
13	79.M	30	52	9	1	0.2	Yes	1	ICU	
14	57.M	36	1	7	1	0.8	Yes	1	ICU	
15	58.M	25	0	2	1	0.6	Yes	1	ICU	
16	70.F	27	0	2	1	0.4	Yes	0	ICU	
17	53.M	51	0	14	2	0.2	Yes	0	ICU	
18	53.M	33	0	1	6	1.5	Yes	0	ICU	Cornea+Skin
19	64.F	31	0	15	3	15.5	Yes	0	ICU	
20	86.M	30	0	18	1	0.1	Yes	2	ICU	
21	60.F	20	0	22	1	0.9	Yes	0	ICU	
22	46.M	23	0	7	3	0.1	Yes	0	ICU	
23	84.M	24	11	3	0	0.2	No	2	ICU	
24	79.M	27	0	2	3	0.1	Yes	0	ICU	
25	46.F	18	0	5	0	0.1	Yes	2	Critical AAD	
26	56.F	19	0	4	1		Yes	0		
27	62.M	22	0	10	1	201.3	Yes	0	Ward	
28	69.F	26	0	19	1	56.3	Yes	0	ICU	Cornea+Skin

Time 1=days before transferring to the ICU; Time 2=number of days in the ICU days before final family meeting; Time 3=days from withdrawal of life support before final family meeting; Time 4=hours from withdrawal of life support to death; §, Patient did not die. AAD, against-advice discharged; APACHE II, Acute Physiology and Chronic Health Evaluation II; ECMO, extracorporeal membrane oxygenation; F, female; ICU, intensive care unit; M, male.

Table 1: Summary of cases experiencing withdrawal of life-sustaining treatment.

Admission diagnosis	n	%
CVA-hemorrhage	8	28.6%
Traumatic brain injury	6	21.4%

Medical disease	6	21.4%
Brain surgery	4	14.3%
Major operations (excluding the brain)	3	10.7%
Multiple trauma (excluding the brain)	1	3.6%
Total	28	100.0%

Table 2: Reason for admission to the intensive care unit.

Outcomes following the WLST in patients who underwent prior surgery

The characteristics of patients experiencing WLST stratified by whether or not they underwent prior surgery are shown in Table 3. The ICU APACHE II scores were significantly higher in the surgery group than in the non-surgery group (28.7 ± 7.9 *vs.* 23.5 ± 5.1, respectively, P=0.031).

The number of days before WLST was significantly longer in the surgery group than in the non-surgery group (28.4 ± 34.0 *vs.* 8.7 ± 6.7, respectively, P=0.03).

Patients were more likely to participate in tissue donation in the surgery group than in the non-surgery group after cardiac death (21% *vs.* 0%, respectively, P=0.041).

Variables	**Surgery**	**No surgery**	**P value**
	(n=14)	**(n=14)**	
Age (Mean ± SD)	58.4 ± 16.2	63.2 ± 12.5	0.204
Sex (Female Predominant)	36% (5)	64% (9)	0.070
Neuro-critical diseases	57% (8)	79% (11)	0.120
ICU APACHE II scores	28.7 ± 7.9	23.5 ± 5.1	0.031*
Time 1	8.7 ± 14.4	5.2 ± 12.8	0.256
Time 2	28.4 ± 34.0	8.7 ± 6.7	0.030*
Time 3	1.8 ± 1.4	1.4 ± 1.0	0.200
Time 4	18.9 ± 52.6	7.9 ± 16.3	0.256
Dependent on vasopressors	50% (7)	43% (6)	0.343
Management before withdrawal	86% (12)	86% (12)	0.437
Died in the ICU	86% (12)	86% (12)	0.470
Tissue donation	21% (3)	0	0.041*

Time 1=number of days before transferring to the ICU; Time 2=number of days in the ICU before the final family meeting; Time 3=number of days from the final family meeting to the withdrawal of life-sustaining treatment; Time 4=number of hours from withdrawal of life-sustaining treatment to death.

*P<0.05. APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; SD, standard deviation.

Table 3: Characteristics of patients from whom list support was withdrawn stratified by whether or not they underwent surgery.

Different outcomes in patients experiencing WLST with neurocritical diseases or other critical diseases

Table 4 shows the characteristics of patients who experienced the WLST stratified by whether or not they had a neurocritical disease. The number of days before transfer to ICU hospitalization from the emergency room was significantly shorter in patients with neurocritical diseases than in those without neurocritical diseases (1.7 ± 4.1 *vs.* 18.1 ± 19.3 days, P=0.022).

Vasopressors were used significantly less often before the moment of WLST in patients with neurocritical diseases than in patients without them (26% *vs.* 78%, P=0.006). In patients with neurocritical diseases, withdrawal management was not routinely performed before WLST (P=0.021).

In contrast to patients in other departments, patients with neurocritical diseases did not always die in the ICU (83% *vs.* 100%, P=0.041).

Variables	NCD (n=19)	Non-NCD (n=9)	P value
Age (Mean ± SD)	56.3 ± 16.0	62.4 ± 17.5	0.204
Sex (Female Predominant)	53% (10)	44% (4)	0.352
ICU APACHE II scores	26.6 ± 7.2	25.2 ± 7.0	0.328
Receiving surgical intervention	42% (8)	67% (6)	0.122
Time 1	1.7 ± 4.1	18.1 ± 19.3	0.022*
Time 2	15.3 ± 29.2	19.1 ± 12.1	0.319
Time 3	1.7 ± 1.5	1.2 ± 0.4	0.098
Time 4	20.1 ± 47.5	0.5 ± 0.4	0.054
Dependent on vasopressors	26% (5)	78% (7)	0.006*
Management before withdrawal	79% (15)	100% (9)	0.021*
Died in the ICU	83% (15)	100% (9)	0.041*
Tissue donation	11% (2)	11% (1)	0.483

Time 1=number of days before transferring to the ICU; Time 2=number of days in the ICU before the final family meeting; Time 3=number of days from the final family meeting to the withdrawal of life-sustaining treatment; Time 4=number of hours from withdrawal of life-sustaining treatment to death. *P<0.05. APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; NCD, neurocritical disease; SD, standard deviation.

Table 4: Characteristics of patients from whom life support was withdrawn who did or did not have neurocritical diseases.

Discussion

This study investigated the behaviors related to and the time courses of WLST in the SNICU. Interestingly, the results showed that longer lengths of stay for critical patients undergoing surgical intervention were associated with a greater likelihood of surrogates choosing to have tissues donated following withdrawal. To our knowledge, this is the first study to address the relationship between surgical intervention and tissue donation after WLST.

There are many factors that influenced the decisions for organ donation. First, our study (Time 2 in Table 3) showed that a factor contributing to the decision to donate tissue was that, the longer families accompanied their loved ones through end-of-life care, the more they trusted the medical staff. In 1969, Elisabeth Kübler-Ross published the five stages of grief model to explain how families cope with bereavement and the loss of a loved one [8]. Her model indicated that there is no normal or average time frame for grieving, that the length of grieving can differ from person to person, and that sharing the loss with others, wherever the support comes from, makes grief easier to carry. In a study by Marsha Exley [9], families that did not choose tissue/organ donation usually reported that there was not enough time to make a final decision about donation. At the same time, some non-donating families complained of an unpleasant experience from the coordinator and/or that the coordinator hurried them. In a study by Elizabeth A. Boyd [10], on days 3 and 5 of the patient's ventilator support in the ICU, the surrogates' predictions for prognosis differed from those of the physician because of complex systems of interpretation, personal experience, or beliefs. Bidirectional discussions should be aimed at reaching a shared understanding, including of the patient's physical condition, personal characteristics, and unique life experience. The additional time to earn trust and build relationships with the families was equally important as the additional time that families could spend with their loved ones. At the same time, explaining and introducing the option of organ or post-WLST tissue donation early or during the final family meeting is feasible when the physician-family relationship has relatively less tension. In our experience, when medical staff allows families to accompany the patient during the end-of-life, these families may be more accepting of considering tissue or organ donation.

Second, our study (Time 1 in Table 4) showed that neurocritical illnesses developed more abruptly than did other critical illnesses (1.7 ± 4.1 *vs.* 18.1 ± 19.3 days, P=0.022), indicating that neurosurgical staff and surrogates may experience an abrupt increase in stress and decision-making. Without a doubt, the unique features of neurocritical illnesses are different from those of other life-threatening illness. Neurocritical diseases occur suddenly and may follow a catastrophic trajectory from healthy independence to serious and permanent disability, and even the prospect of death (1). The families of such patients may experience increased sadness and hopelessness in the face of the precipitous loss of physical and cognitive function of their loved ones. Previous studies showed that, compared to medical staff treating patients with other diseases, medical staff treating patients with neurocritical diseases experience greater stress because they are not only dealing with devastating neurocritical diseases but are also helping the patient's families/surrogates cope with the disease's impact and the decision-making process, both within a short time frame [4,5].

Third, the time to death after WLST may not always be predictable for those without brainstem dysfunction. Most of the patients in our series were predicted to die within one hour. However, some cases were unexpectedly prolonged more than one hour, and some were even bed-ridden for more than one week. It is very important for clinicians to deliver advanced care planning for patients and their surrogates to prepare for death.

In our study (Table 1), we found that the number of vasopressors used for hemodynamic instability is a good predictor of a WLST-to-death duration of one hour. Moreover, Laveena Munshi [5] found that neurological function and respiration were the most consistent variables for predicting the time to death within one hour. Therefore, a catastrophic neurologic injury with brainstem dysfunction and controlled mechanical ventilation with oxygenation impairment may lead to a hastened death within one hour post-WLST.

In some Eastern countries, organ donation after withdraw life-sustaining treatment is allowed. However, not every country approves this policy in end-of-life care. In contrast, patients underwent WLST can only donate tissues, but not include organs in Taiwan's law. Therefore, patients were excluded if they donated organs after brain death in this study.

Our study was the first to describe the behaviors and time courses of WLST in a neuro-surgical ICU in Taiwan, despite the limitations of a retrospective study. Future, prospectively enrolled large-scale studies are warranted to further promote the success of tissue or organ donation after WLST.

Conclusions

Uniquely, our study demonstrated that patients who underwent surgical intervention with sufficient time for a bidirectional discussion between physicians and patients/surrogates had a greater willingness to donate tissues after WLST. Importantly, tissue donation after WLST is one of the options in end-of-life care in the surgical/neurosurgical ICU.

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Declaration of Conflicting Interests

The authors declare that there is no conflict of interest.

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