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Terminal delirium: families' experience

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Background: Although delirium is a common complication in terminally ill cancer patients and can cause considerable distress to family members, little is known about the actual experience of family members. The primary aims of this study were thus to explore: (1) what the family members of terminally ill cancer patients with delirium actually experienced, (2) how they felt, (3) how they perceived delirium and (4) what support they desired from medical staff. **Methods:** A single-center in-depth qualitative study on 20 bereaved family members of cancer patents who developed delirium during the last two weeks before death. Content analysis of transcribed text was performed. **Results:** Families experienced various events including other than psychiatric symptoms, such as 'patients talked about events that actually occurred in the past', 'patients were distressed as they noticed that they were talking strangely,' 'patients talked about uncompleted life tasks', and 'patients expressed physiologic desires such as excretion and thirst'. Family emotions were positive, neutral, or negative (eg, distress, guilt, anxiety and worry, difficulty coping with delirium, helplessness, exhaustion and feeling a burden on others). Families perceived the delirium to have different meanings, including positive meanings (eg, relief from real suffering), a part of the dying process, and misunderstanding of the causes of delirium (effects of drugs, mental weakness and pain). Families recommended several support measures specifically for delirium, in addition to information and general support: 'respect the patients' subjective world', 'treating patients as the same person as before', 'facilitating preparations for the patients' death', and 'relieving family's physical and psychological burden'. **Conclusions:** From the results of this study, we generated a potentially useful care strategy for terminal delirium: respect the patients' subjective world, treat patients as the same persons as before, explore unmet physiological needs behind delirium symptoms, consider ambivalent emotions when using psychotropics, coordinate care to achieve meaningful communication according to changes in consciousness levels during the day, facilitate preparations for the patients' death, alleviate the feelings of being a burden on others, relieve family's physical and psychological burden and information support. *Palliative Medicine* 2007; **21**: 587–594

Key words: palliative care; delirium; family; neoplasm; end-of-life care

Introduction

Delirium occurs in 85–90% of terminally ill cancer patients, and persists until death in 50–70%.[1,2] Therefore, many families spend their last days with delirious patients, and recent studies have demonstrated that this can cause great emotional distress.[3,4] Thus, understanding the experience of families of delirious terminally ill patients is important to explore effective care strategies.

To date, several empirical studies have explored the experience of delirious patients and their families in the intensive care unit setting and the transient delirium of elderly patients,[5–10] but there have been few reports on delirium in the terminal stage.[11–13] One qualitative study revealed various experiences of the families, such as their ambivalent feelings (ie, wish to relieve patient distress but hesitating to use sedative medication), wish for medical information concerning delirium and wish for respect and dignity in patient care.[11] Another preliminary study on the effectiveness of psycho-educational intervention for families of delirious terminal patients suggests that advance information could give family members confidence and a sense of security in their communication with patients.[12] However, these studies do not cover the full aspects of the family experience,

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especially the type of support they actually desire from nurses and physicians.

The primary aims of this study were thus to explore (1) what the family members of terminally ill cancer patients with delirium actually experienced, (2) how they felt, (3) how they perceived delirium and (4) what support they desired from medical staff. The ultimate purpose of this study was to obtain in-depth insights to generate a potentially useful care strategy for terminal delirium.

Subjects and methods

Methods

This was a qualitative interview study of the bereaved families of cancer patients who developed delirium during the last two weeks. Semi-structured interviews were performed between September, 2003 and March, 2004 once for each subject for an hour, and the contents were tape-recorded. The interviewers were nurses at Seirei Hospice who had not been involved in direct patient care. In the interviews, questions concerned the actual experience of delirium by the families, their feelings and perceptions of delirium, and family-recommended support provided by medical staff, when the patients had delirium.

Subjects

Primary physicians initially identified potential participants following these inclusion criteria: (1) bereaved family members of an adult cancer patient diagnosed with delirium during the last two weeks on retrospective chart review on the basis of DSM-IV criteria,[14] (2) aged 20 or more and (3) no serious psychological distress recognized. Among 250 families of patients who died at Seirei Hospice between January, 1999 and December, 2000, 184 met the inclusion criteria and cooperation with the study was requested by mail. Of them, 37 families gave consent and were interviewed.

On initiation of the interview, the interviewers confirmed that family members acknowledged that patients had experienced delirium. Delirium was paraphrased as 'the rapid development of difficulty in concentration, forgetfulness, disorientation about time and place, hallucinations and delusions, incoherent speech, clouding of consciousness and difficulty communicating, emotional instability, reversal of daytime and nighttime activities (drowsy during the day and a wake during the night), and inconsistent behavior, with these conditions changing even within a day'. As 17 families denied that the patients had had delirium, 20 family members were finally interviewed. The final sample consisted of 9 men and 11 women who ranged in age from 42 to 75 years, with a mean of 55 years (SD = 9.4). The family relationship to the deceased consisted of 11 spouses, 8 children, and 1 sibling. The patients were 12 men and 8 women and the age ranged from 58 to 78 years with a mean of 65 years (SD = 11). Primary tumor sites were: lung (n = 7), gastrointestinal (n = 6), genitourinary (n = 4) and others.

Despite a substantial delay between patient death and the interview, we decided to choose this population, because the institutional review board recommended this time-interval to avoid unnecessary emotional burden on the bereaved family. The institutional review board approved the ethical and scientific validity of this study and each participant gave written consent.

Analyses

Content analysis was performed using the transcribed data obtained. First, the parts containing the experience, feelings, perceptions and family-recommended support related to delirium were extracted from the transcriptions using the phenomenological method. Then, two of the authors carefully conceptualized and categorized the contents of the transcription based on similarities and differences. Another two investigators then independently coded whether each transcription included remarks that belonged to any of the attributes according to their definitions. The initial Cohen's kappa coefficients were greater than 0.40 for 26 categories and lower than 0.40 for 7 categories. Finally, the authors jointly reviewed and discussed each coded data set under the supervision of an experienced palliative care specialist (TM) until all discrepancies were resolved.

Results

As shown in Table 1, the data were classified as experience, emotions, perception and support.

Experience of delirium

Family-reported experiences were classified into: Symptoms of delirium as described in the DSM-IV criteria of delirium,[14] and Experiences other than symptoms of delirium.

Symptoms of delirium. Families reported that the patients had decreased consciousness levels (n = 10, 50%), communication difficulty (n = 9, 45%), inappropriate/agitated behavior (n = 9, 45%), hallucination/delusion (n = 8, 40%), and unstable mood (n = 6, 30%).

Experiences other than symptoms. Besides 'psychiatric symptoms', the families reported various experiences.

Patients talked about events that actually occurred in the past or that they used to do. Five families (25%) noticed that,

Table 1 Categories identified in the interview with bereaved family members

Experience of delirium
Symptoms of delirium
Experiences other than symptoms
Patients talked about events that actually occurred in the past or that they used to do
Patients were distressed as they noticed that they were talking strangely
Patients talked about uncompleted life tasks
Patients expressed physiologic desires such as excretion and thirst
Mental activity was normal in some situations
Emotion
Positive or neutral emotion
Negative emotion
Distress
Guilt
Anxiety and worry
Difficulty in coping with delirium, helplessness and exhaustion
Burden on others
Ambivalent emotion
Perception of delirium
Positive or neutral meanings
Relief from real suffering
Same as usual and dreaming
Part of the dying process
Misunderstanding the causes
Recommended support
Recommended support specifically for delirium
Respect the patients' subjective world
Treating patients the same as before
Facilitating preparations for the patients' death
Relieving families' physical and psychological burden
Information support
Non-specific general recommended support

although what the patients talked about in the episodes of delirium appeared 'strange' to nurses and doctors, it actually related to past real events or the work that the patients used to do.

> 'Since (the patient) said, "... on the wheelchair..., on the wheelchair ... , in fact, he was talking about his trip to Korea.' (Bereaved 3)
> (The patient) moved her hands like she would do when binding flowers. That was her work. She grew flowers.' (Bereaved 17)

Patients were distressed as they noticed that they were talking strangely. Two families (10%) reported that the patients felt distress as they at times noticed that they were delirious.

> 'When the patient talked about strange things, he noticed that he was out of his mind and seemed distressed. So, he stopped talking.' (Bereaved 8)

Patients talked about uncompleted life tasks. Six families (30%) experienced patients expressing uncompleted life tasks in the episodes of delirium, such as confessing and apologizing for past events, or aftermath concerns.

> '(The patient) was saying, "I am sorry. That was my fault," although I am not sure whom she was saying that to.' (Bereaved 3)
> '(The patient) said to his daughter that he was sorry for not having been a good husband and asked her to apologize to his wife for him.' (Bereaved 1)
> '(The patient) talked a lot about how to make preparations for the funeral.' (Bereaved 17)

Patients expressed physiologic desires such as excretion and thirst. Three families (15%) saw the patients behaving 'inappropriately' to fulfill their physiologic desires.

> '(The patient) suddenly woke up even at night and removed the diapers by himself. I could not initially understand what he wanted, but after he went to the toilet, every time he settled down.' (Bereaved 9) '(The patient) became agitated at night, often saying, "Give me water."' (Bereaved 3)

Mental activity was normal in some situations. Six families (30%) noted that there were changes in the patients' mental activity during the day, and thus the patients could achieve normal mental activity for some periods of the day or with some people.

> '(The patient) was not like that all day. When he was sound, he was clear-minded.' (Bereaved 2)

Emotion

Family emotion evoked by the experience of delirium varied from positive or neutral, negative and ambivalent.

Positive or neutral emotion. Seven families (35%) reported positive emotions with the episodes of delirium, such as 'happy', 'relieved', 'not distressing at all', 'feeling bound to the patient', or 'feeling meaningful by staying at the patient's side'. One bereaved person said, 'I was happy to hear such wandering talk, rather than pain or suffering.' (Bereaved 4)

In addition, five families (25%) reported that they just accepted the delirium. One bereaved person said, 'I knew such a condition would occur as the disease advanced, so I accepted it as it was.' (Bereaved 5). Three families (15%) stated that the delirium was just 'mysterious.'

Negative emotion Distress. Fourteen families (70%) expressed some level of distress on seeing delirious patients. They felt distress to see the patient changed from what he was before, being physically restrained, and therefore did not want to have other families see the patient. A bereaved family member said, 'Everything was distressing.' (Bereaved 3)

> 'My father was once a distinguished person who would always look sharp in a well-tailored suit and be on the stage with a flower in his lapel. So, it was miserable, or rather painful to see him this way.' (Bereaved 3)

'I thought I should never let my daughters see their father behaving like that.' (Bereaved 11)

Guilt. Six families (30%) expressed guilt concerning 'not taking good care of the patient', 'not facing the patient,' 'having driven the patient into a corner' or 'having made the patient fall.'

'I could not be of sufficient help to the patient. I might have been able to maintain a more relaxed relationship with the patient. I blamed myself later.' (Bereaved 3)

Anxiety and worry. Nine families (45%) expressed anxiety and worry that 'they could not leave the patient alone so that s/he might do something unexpected,' 'staying with the patient alone at night,' and 'the soul of the patient was splitting.'

Difficulty in coping with delirium, helplessness and exhaustion. Ten families (50%) expressed difficulty in coping with delirium, helplessness and exhaustion, such as 'difficult to accept,' 'I made an effort to persuade myself it was real,' 'not sure what was happening,' 'at a loss how to deal with it,' 'I wanted to escape from reality,' and 'so exhausted both physically and mentally.'

'I had no idea what was happening. That was my honest feeling.' (Bereaved 16)
'I was at a loss what to do. I thought the situation was out of control.' (Bereaved 3)
'Honestly, I wished to kill (the patient) by choking her and kill myself. Just hearing those cries wore me out.' (Bereaved 16)

Burden to others. Five families (25%) expressed their emotional burden, because they felt the patient had become a burden on others.

'The nurses told the patient that, if he stayed in a large room, the roommates would be disturbed if he had those attacks. It must have been disturbing to others.' (Bereaved 1)
'The patient made a lot of noise at night. The person in the next bed was also very sick, and I felt sorry for him.' (Bereaved 12)

Ambivalent emotion. One family referred to ambivalent wishes that the patient would remain conscious but at the same time sleep or die in peace, saying that 'I certainly wanted the patient to live longer, but it was also true that I felt the patient should be quickly relieved of this horrible situation.' (Bereaved 16)

Perception of delirium

Families perceived the delirium as having different meanings, including positive or neutral meanings, a part of the dying process and misunderstanding of the causes.

Positive or neutral meanings.

Relief from real suffering. Six families (30%) believed that delirium alleviated physical and psycho-existential suffering of the patient, and interpreted the state as a comfort to the patient.

'The patient said he had been out having fun or met such and such people. Maybe, he forgot his pain and suffering while he was talking. He was relaxed, being able to talk like that.' (Bereaved 4)

Same as usual and dreaming. Four families (20%) thought that the patients were the same as usual even when they were delirious, saying '(the patient) had always had a bad temper, so I felt nothing about it.' (Bereaved 3)

Three families (15%) interpreted the symptoms of delirium as dreaming.

Part of the dying process. Fourteen (70%) families referred to delirium as part of the dying process; families recognized delirium as a sign that death was approaching, a natural part of the dying process, or a transcendence experience (ie, the patient visiting the next world).

'We had been told about the signs that many patients show before death. So, we felt it was about time.' (Bereaved 19)
'The patient died naturally as she was drowsing. So did my brother. I understand it as a natural thing.' (Bereaved 13) 'I felt that the patient would be able to go to the next world, because he had someone to guide him.' (Bereaved 9)

Misunderstanding of the causes. Nine (45%) families attributed the causes of delirium to the effects of drugs, mental weakness and death anxiety, or pain and physical distress, without physicians' confirmation.

'Was it morphine? I thought it was a symptom caused by such drugs.' (Bereaved 20)
'I wondered if the patient became more and more like that, because of fear of death as a human being.' (Bereaved 16)
'I wondered if it was because the patient was in pain.' (Bereaved 12)

Recommended support

We identified four family-recommended support activities specifically for delirium and information support and four few general support.

Recommended support specifically for delirium.

Respect the patients' subjective world. Six families (30%) wanted the staff not to correct or deny the patients' 'unrealistic' remarks, but to try to understand what they wanted to say and respect what they experienced.

'When, for example, the patient says, "I have just been on an airplane. It was a pleasant flight," and if a nurse responds, "Weren't you cold? Be careful not to catch cold," it's good to give positive responses. But if a nurse

says, "No, this is a hospital," it ruins everything.' (Bereaved 4)

Treating patients the same as before. Four families (20%) wished the patients, even when they had delirium, to be treated with respect for their past lives and uniqueness, and to be treated as individuals, not as a 'delirious patient,' 'child,' or 'object.' A bereaved person additionally referred to the loss of dignity in using physical restraints.

'The staff treated the patients according to what kind of people they were: for a person in a high position, with the right attitude to ward such a person, and for a craftsman, with the right attitude to ward such a person.' (Bereaved 3)

Facilitating preparations for the patients' death. Three families (15%) reported they were supported by the in-advance advice from medical professionals to prepare for the patients' death, such as confirming the patients' preference about end-of-life care or to complete unfinished tasks before delirium.

'They advised us that the patient's consciousness would begin to decrease at such and such a time, so please be prepared. It was very important for us that we had enough time to say what we had to say to the patient.' (Bereaved 2)

Relieving family's physical and psychological burden. Seven families (35%) listed care strategies to relieve the family's physical burden as helpful, such as 'leave the physical care to hospital staff,' 'facilitating support from other family members,' 'good environment for the family to stay,' and 'encouraging families to maintain their normal daily activities.'

Five families (25%) reported they obtained comfort from medical professionals who reassured the families that they were doing their best and the right things.

'Since the staff did so well, we left everything to them with great trust.' (Bereaved 10)

'(On the general ward), nurses told us that they could not take care of the patient if she got excited, and insisted that we look after the patient.' (Bereaved 1)

'Since we were more worried about what would become of us after my father's death, we had to maintain our daily routine. They understood our situation, and even told us we would not have to look after him everyday.' (Bereaved 3)

'I felt reassured when I was told, "You are not wrong," "You will feel better that way," or "That is the best way."' (Bereaved 4)

Information support. Twelve families (60%) reported that good information was very helpful. The helpful information included the causes, pathologies (consciousness disturbance), possible treatments, expected course (eg, imminent death), how to treat the patients and the universality of delirium.

'Without understanding the cause of hallucination, we wondered if the patient had lost her soul, and we simply stopped talking, not being able to talk any longer.' (Bereaved 8)

'Whatever the outcome may be, the most worrying thing is the uncertainty of what will happen. So, I think we can feel more assured if we are informed in advance what drugs will be used if symptoms worsen.' (Bereaved 2)

'We had been told in advance that death was close. It was hard at that time, but I appreciated being informed.' (Bereaved 19)

'I was not sure how I should talk to the patient, but the nurses showed me how loud we should talk into the patient's ears. That was helpful.' (Bereaved 2)

'The phrase, "Everybody is like this toward the end," made me feel a lot better.' (Bereaved 16)

Concerning the helpful timing of information, they wished for information at appropriate points depending on changes in the patients' condition by medical staff before asking, easily understood information, an atmosphere they could feel easy to ask questions, and being reassured to be able to discuss mental or spiritual issues.

'It was helpful that, now and then, they explained the latest condition very well.' (Bereaved 14)

'We can talk to the doctor about pain, but we cannot consult with him about matters like hallucinations or the soul.' (Bereaved 8)

Non-specific general recommended support. Non-specific general recommended support by the families included: symptom control ($n = 7$, 35%), human attitude of the medical staff, such as friendliness, sincerity, cheerfulness, warmth, professional pride and genuine regard ($n = 7$, 35%), high-quality professional care ($n = 6$, 30%; 'professional psychiatric and palliative care', 'do everything they could do'), prompt response and excellent teamwork ($n = 6$, 30%), and good environment ($n = 2$, 10%; private and comfortable room). A bereaved family stated, 'nurses were always close to the patient and talked to us, and the doctor would also come quickly whenever wanted. That was the best.' (Bereaved 5)

Discussion

This is, to our best knowledge, the first systematic study to explore the actual experiences of the family members of cancer patients with terminal delirium, what they felt, how they perceived delirium and what support they desired. This study suggests large variations in the experience of families concerning terminal delirium, their emotions, perceptions and support they desired. Therefore, in the care of terminal delirium, it could be of great importance to provide care tailored to the individual needs of each patient and family. From the results of this study, we generated a care strategy for

terminal delirium: respect the patients' subjective world, treat patients the same as before, explore unmet physiological needs behind delirium symptoms, consider ambivalent emotions when using psychotropics, coordinate care to achieve meaningful communication according to changes in consciousness levels during the day, facilitate preparations for the patients' death, alleviate the feelings of being a burden on others, relieve the family's physical and psychological burden and information support.

Respect the patients' subjective world

This recommendation is important because (1) the families noticed that, during episodes of delirium, the patients talked about events that actually occurred in the past, talked about uncompleted life tasks, and were distressed when they noticed that they were talking strangely, (2) some families and patients experienced delirium with positive emotions and meanings and (3) the families directly recommended respect for the patients' subjective world. These results indicate that, if medical professionals aim to understand the 'strange' behavior of delirious patients as a potentially meaningful experience of patients and families, they may find a cue to share important landmark events with patients and family members, and achieve uncompleted life tasks. In addition, although intentional correction of patient orientation is often recommended in psychiatric literature,[15,16] this study suggests that repeated correction of patients' 'misconceptions' might ignore patient dignity, because terminal delirium is intrinsically untreatable and patients are often distressed to notice their 'symptoms' of delirium. Rather, efforts to allow the patients to stay in their subjective world, for example, not asking the time or place, might be appropriate for at least some patients.

Treat patients the same as before

This recommendation is based on the families' suggestion that, even when patients have delirium, they should be treated with respect for their past lives and uniqueness as individuals. This finding is consistent with a study on bereaved family members of sedated patients that identified 'to treat unconscious patients with dignity' is an essential care.[17,18] Treating a patient as a unique individual is a basic principle in palliative care, and it should be more stressed in the care of delirium, because families see the 'same' individual through 'delirious' patients.

Explore unmet physiological needs behind delirium symptoms

This recommendation is based on the families' observation that patients behaved 'inappropriately' to fulfill their physiologic desires. Palliative care textbooks stress the importance of urinary retention and fecal impaction as aggravating factors of agitated delirium.[19–21] This study confirms these experts' recommendations, and suggests that general physiologic unmet needs, such as the wish to drink, eat, to be cleaned and take a bath may be remediable elements of terminal delirium.

Consider ambivalent emotions when using psychotropics

Some families reported ambivalent emotions as to whether the patients should remain conscious but at the same time sleep or die in peace. This finding is consistent with a preliminary finding.[11] Clinicians should note that patients and families want not only symptom palliation but also much broader elements of quality of life, such as maintaining cognitive control, communicating with others and living as long as possible.[22–24] Clinically, if symptomatic sedation is applied, the depth and duration of sedation should be closely adjusted for each situation.

Coordinate care to achieve meaningful communication according to changes in consciousness levels during the day

This is recommended on the basis of the families' observation that mental activity was normal in some situations. This indicates daily changes in symptoms of delirium, as well-described in psychiatric literature.[19] In palliative clinical care situations, this phenomenon encourages clinicians to carefully monitor the patterns of changes in the patients' consciousness levels and allow the families to communicate with patients in a relatively good state of consciousness.

Facilitating preparations for the patients' death

This recommendation is based on the families' suggestion that advance advice from medical professionals to prepare for the patients' death, such as confirming the patients' wishes or completing unfinished tasks before delirium, was useful, and actually many families perceived delirium as a part of the dying process. Previous studies about palliative sedation therapy revealed that the family burden in participating in decision making instead of patients, and insufficient consideration to provide an opportunity to say important things to patients before sedation was a source of great distress.[17,18] These findings indicate that coordinating opportunities for families to communicate sufficiently with patients before they develop delirium, confirm the patients' preference in end-of-life care, and ensure a chance to give thanks and say good-bye, is important for palliative care clinicians.[22–24]

Alleviate the feelings of being a burden on others

Some families reported that feeling a burden on others was a distressing aspect of agitated delirium. Therefore,

clinicians should alleviate the family feelings of being a burden on others by modifying the environment (eg, transfer to a private room), not directly saying 'the patient can disturb other patients,' and stressing the universality of delirium.

Relieving families' physical and psychological burden

This recommendation is important because (1) many families reported negative feelings such as distress, guilt, anxiety, difficulty in coping with delirium, helplessness and exhaustion, and (2) families themselves listed this as a useful care strategy. The family is an important target in palliative care, and, in terminal delirium, clinicians should give intensive care to family members, not only patients. Care strategies can include: reassuring the families that they could leave the patients' care to the staff, making the hospital environment comfortable for the families, and coordinating support from other members of the family, reassuring them that they did their best and the right things, and allowing them to share information with other families undergoing a similar experience.

Information support

Information needs are a well-established concept, and a significant indicator of patient and family satisfaction with palliative care.[25] This study especially highlights misunderstandings about the causes of delirium, as well-documented in non-empirical literature.[20] Many family believed the patients developed delirium due to opioids, mental weakness and death anxiety or physical pain. These findings therefore stress the importance of information focusing on the cause, pathologies and the universality of delirium.

Limitations and conclusion

This study has several limitations. First, the subjects were recruited from a single institution. Second, the interviews were held a considerably long time after the actual experience, and some families denied the episodes of delirium. This suggests the possibility of recall bias, but we believe the use of DSM-diagnosis of delirium, ie, inclusion of hypoactive delirium, could lead to under-recognition of delirium by lay persons, and recall bias had minimal influence on the conclusion of this study. Finally, this is a qualitative study on a small number of subjects, and the generalizability of the findings should be explored in a future study.

In conclusion, this study revealed the experience of families concerning terminal delirium, their emotions and perceptions, and the support they desired. The clinical efficacy of potentially useful interventions generated from this study should be tested in future.

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Development of a National Clinical Guideline for Artificial Hydration Therapy for Terminally Ill Patients with Cancer

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ABSTRACT

***Background*: Although differences in physician practices of artificial hydration therapy for terminally ill patients with cancer can cause unnecessary suffering from overhyrdration or underhydration of patients, no clinical guideline is available in Japan. This paper illustrates a summary of a nationwide project to construct a clinical guideline for artificial hydration therapy.**

***Methods*: The Japanese Society of Palliative Medicine constructed a national multidisciplinary committee to develop a clinical guideline for artificial hydration therapy for terminally ill patients with cancer, using evidence-based and formal consensus-building methods with the Delphi technique.**

***Results*: After systematic literature review, three sequential sessions of discussion using the Delphi method, and an external review, a clinical guideline was established. This guideline includes general recommendations, specific recommendations (31 recommendations for medical aspects, 9 recommendations for nursing, and 7 recommendations for ethics), background descriptions, case examples, communication examples, a complete reference list, and structured abstracts of all relevant original articles.**

***Conclusion*: The Japanese Society of Palliative Medicine constructed a clinical guideline for artificial hydration therapy for terminally ill patients with cancer, using evidence-based and formal consensus-building methods. The clinical efficacy of this guideline should be tested in the future.**

INTRODUCTION

RECENT LITERATURE revealed many differences in physician practice of artificial hydration therapy for terminally ill patients with cancer.[1] This means that patients may undergo unnecessary suffering from overhydration or underhydration. The establishment of a clinical guideline can contribute to patient well-being by clarifying the best practice recommended from empirical evidence and expert experience available. To date, there are several clinical practice guidelines[2–7]; however, they are general recommendations rather than for specific clinical questions and, in Japan, relevant guideline is unavailable.

In this paper, we report the methodology of developing a clinical guideline for artificial hydration therapy, general recommendations, and specific recommendations regarding quality-of-life–related medical

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aspects of the guideline. The original paper (available from the authors, in Japanese) further includes specific recommendations from nursing, psychosocial, and ethical aspects, background descriptions, case studies, and structured abstracts of all relevant original articles.

METHODS

We first decided to focus our discussion on artificial hydration therapy, not all artificial nutrition therapies, because enteral nutrition is rarely performed in our current practice. The primary aim of the guideline is thus to help clinicians make a clinical decision about artificial hydration therapy to ensure better quality care for terminally ill patients.

The target population is adult patients with incurable cancer, except for those of head and neck, esophagus, and liver primary origin, without adequate oral intake refractory to appropriate palliative treatments who are likely to die within 1 to 2 months. We defined "terminally ill patients with cancer" as those patients with estimated survival of 1 to 2 months or less, and recommended the clinical estimation of patient prognoses to be assessed by a multidisciplinary team on the basis of validated methods (e.g., the Palliative Prognostic Score, Palliative Prognostic Index[8,9]). The targeted users are health care professionals who treat the target population as described above.

The objective for this guideline is to improve quality of life, dying, and death. We assume that the determinants of the quality of life, dying, and death vary among individuals, and individuality is essential to define what is important for each patient. Palliation of physical distress, peace of mind, having a good family relationship, not being a burden to others, completion of life, fighting against cancer, maintaining hope, and not being aware of death are good death elements that could be related to decision-making process for artificial hydration therapy for Japanese.[10]

CONCEPTUAL FRAMEWORK

Second, we determined the conceptual framework used in this guideline (Fig. 1). We strongly recommend that clinicians respect patient and family values; to individualize the treatment suitable for each patient; to assess the situation comprehensively from a medical, practical, psychosocial, ethical, and legal point of view; and to reevaluate the treatment efficacy periodically. On the basis of this conceptual framework, clinicians should first clarify the general treatment goal consistent with patient and family values. Second, clinicians should comprehensively assess the situation, especially the potential effects of artificial hydration therapy on patient physical symptoms, survival, daily activities, psychoexistential well-being, and ethical and legal issues. Third, clinicians should decide one treatment plan after discussion with patients and families. Finally, and most importantly, clinicians should periodically reevaluate the treatment efficacy at planned intervals, and adjust the treatment suitable for each patient.

DEVELOPMENT PROCESS

The Hydration Guideline Task Force developed this guideline, following the Japanese national recommendation to develop a clinical guideline.[11] The Task Force consisted of 32 experts: 6 palliative care physi-

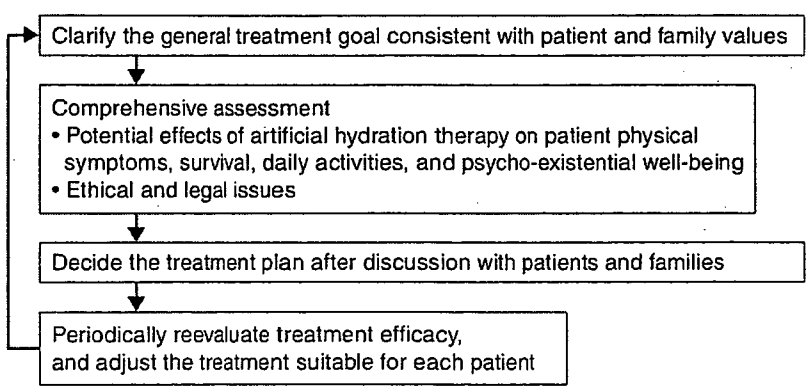

FIG. 1. Conceptual framework.

cians, 6 surgeons, 4 anesthesiologists, 3 medical oncologists, 2 home care physicians, 5 nurses, 1 social worker, 2 bioethicists, 1 lawyer, and 2 epidemiologists (Appendix A). The Japanese Society of Palliative Medicine approved each member as having enough clinical and professional competency to complete this task.

First, the Task Force gathered more than 100 clinical questions using a questionnaire survey on the members of the Japanese Society of Palliative Medicine and brain-storming session among the pane members. The questions were then restructured into 28 questions.

Next, the Task Force performed a systematic literature review using PubMed, and obtained 116 original articles and 6 relevant clinical guidelines. The principle search terms were "palliative OR hospice OR end-of-life OR terminal OR advanced OR cachexia OR cachexic AND neoplasms OR neoplastic OR cancer OR carcinoma OR malignant OR malignancy AND nutritional support [MeSH] OR nutrition OR fluid therapy [MeSH] OR rehydration OR dehydration OR hydration." All articles were formulated into structured abstracts and distributed to all members with the full texts. Evidence-level tables were: I: systematic review, meta-analyses; II: one or more randomized controlled trials; III: nonrandomized intervention trials; IV: observational studies; V: descriptive studies; VI: expert opinion, physiologic findings.[11] The Task Force decided to use an original recommendation table for this project to articulate the levels of each recommendation (Table 1).

After drafting recommendations, the Delphi technique was performed to examine the validity of each statement.[12,13] The members were requested to rate the validity of all recommendation statements on a 9-point Likert-type scale from 1 (not appropriate) to 9 (appropriate). In the first evaluation, the median value was 8 or more in 131 items (the difference between the minimum and maximum was 5 or less in 94 items and 6 or more in 37 items), and in the remaining 6 items the median values were 7 or 7.5. The median, minimum, and maximum values were disclosed to each member, and differences in opinions were discussed and resolved in a face-to-face conference. In the second evaluation, in all statements, the median value was 8 or more and the difference between the minimum and maximum was 5

Finally, six external reviewers (three palliative care physicians, a medical oncologist, and two nurses) and five family members of patients with cancer made comments. After those comments were circulated to all members, the final Delphi evaluation achieved a median value of 8 or more and the difference between the minimum and maximum was 5 or less in all statements. We determined that the major differences had been resolved, and adopted this as the final version.

RESULTS

The committee ultimately defined general and specific recommendations (31 recommendations for medical aspects, 9 recommendations for nursing, and 7 recommendations for ethics), in addition to background descriptions, case examples, communication examples, a complete reference list, and structured abstracts of all relevant original articles. Of them, we here report the general recommendations and specific recommendations regarding quality-of-life-related medical aspects.

TABLE 1. RECOMMENDATION TABLES

A. Sufficient research evidence (level I or consistent findings from level II evidence) and sufficient clinical agreement. We strongly recommend the intervention, when the treatment is consistent with patient preference and the treatment effect is monitored.

B. Fair research evidence (single or inconsistent findings from level II or level III–VI evidence) and sufficient clinical agreement. We recommend the intervention, when the treatment is consistent with patient preference and the treatment effect is monitored.

C. No research evidence available but fair clinical agreement. We can recommend the intervention, if the treatment is consistent with patient preference and the treatment effect is monitored.

D. No research evidence to support the intervention available and inadequate clinical agreement. We recommend the indication of the intervention only in the specific situation that the patient wants the treatment after being fully informed and the treatment effect is closely monitored.

E. Sufficient or fair research evidence and sufficient clinical agreement about the ineffectiveness or harmfulness of the treatment. We recommend not performing the intervention.

General recommendations

[Respect for patient and family values, wishes, and individuality]

1. The aims of artificial hydration therapy should be consistent with the overall treatment goal on the basis of each patient and family value. Improvement of laboratory findings and nutritional status alone is not a primary end point for artificial hydration therapy.
2. Patient and family wishes should be respected in the treatment decision.
3. Artificial hydration therapy should be individualized for each patient and family situation. Routine use or nonuse of artificial hydration therapy is not supported.
   [Evaluation]
4. The indication of artificial hydration therapy should be based on comprehensive assessment of the patient's overall quality of life, satisfaction, physical symptoms, survival, psychoexistential well-being, daily activities, and ethical and legal issues.
5. Dehydration and/or water depletion in the terminal stage does not always cause discomfort for patients. Improvement in objective findings, such as laboratory findings, urine volume, and central venous pressure, are not primary end points in artificial hydration therapy.
6. Periodical reevaluation and timely adjustment of treatment regimens is essential to maximize the treatment benefit of artificial hydration therapy. [Maximization the balance between benefits and burdens].
7. Artificial hydration therapy should maximize the balance between benefits and burdens of artificial hydration therapy.
   [Importance of nursing and psychosocial care]
8. For terminally ill patients with cancer suffering from decreased oral intake, not only artificial hydration therapy, but pharmacologic treatment to improve appetite, nursing care, psychosocial interventions, and support in the decision-making and daily activity are of great importance.
   [Summary of medical recommendations]
9. For terminally ill patients with cancer with decreased oral intake from progressive malignancy-related etiology other than bowel obstruction and/or poor performance status, artificial hydration therapy alone is unlikely to improve overall quality of life.
10. For terminally ill patients with cancer with better performance status and decreased oral intake due to bowel obstruction, artificial hydration therapy can improve overall quality of life.
11. Artificial hydration therapy can deteriorate distress related to ascites, pleural effusion, and peripheral edema in terminally ill patients with cancer.
12. Artificial hydration therapy is unlikely to alleviate the sensation of thirst in terminally ill patients with cancer. Intensive nursing care is of most importance to alleviate the sensation of thirst.
13. In some terminally ill patients with cancer, artificial hydration therapy can contribute to improvement in quality of life through alleviating opioid-induced delirium and acute dehydration/water depletion.
14. Subcutaneous hydration can be appropriate for terminally ill patients with cancer in whom an intravenous line is difficult to pace and/or is distressing.

Specific recommendations

1. General Quality of Life

Rationale

In patients with a poor performance status, a preliminary randomized controlled trial demonstrated no significant improvement in patient-reported general well-being of 1000 mL/d hydration compared to 100 mL/d hydration,[14] which is consistent with several observation studies.[15,16]

On the other hand, some audit trials demonstrated that artificial hydration therapy could contribute to maintaining quality of life in patients with a better performance status.[17–22] The backgrounds of patients who received considerable benefits from this intervention include a better performance status, bowel obstruction, and estimated survival of several months or longer.

Available empirical evidence thus suggests that (1) artificial hydration therapy is ineffective in improving overall quality of life in patients with cancer close to death and (2) artificial hydration therapy can be effective in improving overall quality of life (QOL) in patients with cancer with a better performance status, bowel obstruction, and estimated survival of several months.

Recommendations

R010: To improve general QOL in terminally ill patients with cancer who are expected to live for 1–2 months, are incapable of oral fluid intake due to intestinal obstruction, but show a performance status of 2 or better:

- Simple hydration at 1000–1500 mL/d (400–600 kcal/d, nitrogen: N, 0 g/d). [C]
- Hyperalimentation at 1500 mL/d (1000 kcal/d, N 5 g/d). [C]
- Simple hydration at 2000 mL/d (800 kcal/d, N 0 g/d). [D]
- Hyperalimentation at 2000 mL/d (1600 kcal/d, N 10 g/d). [D]

R011: To improve general QOL in terminally ill patients with cancer who are expected to live for 1–2 weeks, are incapable of oral fluid intake due to intestinal obstruction, and show a performance status of 3 or worse

- Simple hydration at 1000–1500 mL/d (400–600 kcal/d, N 0 g/d). [D]
- Hyperalimentation at 1000–2000 mL/d (800–1600 kcal/d, N 5–10 g/d). [E]

R012: To improve general QOL in terminally ill patients with cancer who are expected to live for 1–2 weeks, are incapable of oral fluid intake due to progressive cachexia, and show a performance status of 3 or worse:

- Simple hydration at 1000–1500 mL/d (400–600 kcal/d, N 0 g/d). [E]
- Hyperalimentation at 1000–2000 mL/d (800–1600 kcal/d, N 5–10 g/d). [E]

2. Ascites
Rationale

We have had no intervention trials with a primary end point of ascites. One large multicenter prospective observational study suggested that patients receiving 1000 mL/d or more hydration during the last 3 weeks experienced significantly more severe ascites than those receiving no or less than 1000 mL/d hydration.[23] This is consistent with another multicenter retrospective observational study, a nationwide opinion survey, and other small observation studies.[24–26]

Available empirical evidence thus suggests that (1) less than 1000 mL/d hydration is unlikely to deteriorate ascites, (2) 1500–2000 mL/d hydration can deteriorate ascites, and (3) volume reduction can alleviate ascites.

Recommendations

R020: To minimize ascites-related distress in terminally ill patients with cancer who are expected to live for 1–2 months, are capable of oral fluid intake of 500 mL/d or more, and have symptomatic ascites:

- No artificial hydration therapy. [B]
- Artificial hydration therapy is limited to 500–1000 mL/d or less, if performed. [C]

R021: To minimize ascites-related distress in terminally ill patients with cancer who are expected to live for 1–2 months, are incapable of oral fluid intake, and have symptomatic ascites:

- Artificial hydration therapy is limited to the volume of vomiting + 500–1000 mL/d or less, if performed. [C]

R022: To minimize ascites-related distress in terminally ill patients with cancer who are expected to live for 1–2 months, are incapable of oral fluid intake, are receiving artificial hydration therapy at 2000 mL/d, and show exacerbation of ascites:

- Artificial hydration therapy is limited to 1000 mL/d or less. [C]

3. Nausea/vomiting
Rationale

One small randomized controlled trial demonstrated no clear benefits of an additional 1000 mL/d hydration compared to pharmacologic treatment in terminally ill patients with cancer with a median survival of 4 days.[27] On the other hand, several audit trials on patients with better performance status and bowel obstruction suggested that artificial hydration therapy could contribute to alleviating nausea and vomiting resulting in better quality of life.[19,22] This finding was consistent with several observation studies and case series.[18,28–32]

Available empirical evidence thus suggests that (1) adequate hydration may contribute to alleviating nausea and vomiting in patients with cancer with a better performance status and bowel obstruction and (2) artificial hydration therapy has no clinical benefits in alleviating nausea and vomiting in patients with cancer with a poor performance status, or the irreversible underlying etiology of nausea and vomiting other than bowel obstruction (e.g., cancer cachexia).

Recommendations

R030: To alleviate nausea/vomiting in terminally ill patients with cancer who are expected to live for 1–2

months, are incapable of fluid intake due to intestinal obstruction, and show no fluid retention symptoms:

- Artificial hydration therapy at 1000 mL/d (in combination with pharmacologic therapy). [B]
- No artificial hydration therapy (pharmacologic therapy only). [D]
- Artificial hydration therapy at 2000 mL/d (without pharmacologic therapy). [E]

Recommendation

R031: To alleviate nausea/vomiting in terminally ill patients with cancer who are expected to live for 1–2 months, are incapable of fluid intake due to intestinal obstruction, and have fluid retention symptoms:

- Artificial hydration therapy at 500–1000 mL/d or less (in combination with pharmacologic therapy). [B]
- No artificial hydration therapy (pharmacologic therapy only). [C]
- Artificial hydration therapy at 2000 mL/d (without pharmacologic therapy). [E]

Recommendation

R032: To alleviate nausea/vomiting in terminally ill patients with cancer who are expected to live for 1–2 weeks or less:

- No artificial hydration therapy (pharmacologic therapy only). [B]
- Artificial hydration therapy at 500–1000 mL/d or less (in combination with pharmacologic therapy). [D]
- Artificial hydration therapy at 2000 mL/d (without pharmacologic therapy). [E]

4. Thirst

Rationale

One small randomized controlled trial demonstrated no significant benefits of an additional 1000 mL/d hydration compared to nursing care in terminally ill patients with cancer with a median survival of 4 days,[27] and this result is consistent with a well-conducted audit study that showed that nursing care without artificial hydration alleviated the sensation of thirst in most terminally ill patients.[15,33] A large observation study demonstrated that patients receiving 1000 mL/d or more hydration during the last 3 weeks showed significantly less objective findings of dehydration than those receiving no or less than 1000 mL/d hydration, but the absolute difference was small and both groups demonstrated consistent deterioration in objective dehydration.[23] Several small observation studies revealed that the sensation of thirst was not linearly associated with the levels of blood urea nitrogen, sodium, protein, and hematocrit, but could be significantly associated with hyperosmolality, decreased intravenous volume (measured by artrial natriuretic peptides), stomatitis, oral breathing, and anticholinergic medications.[34–37]

Available empirical evidence thus suggests that (1) sensation of thirst in terminally ill patients with cancer is a multietiology symptom, and hyperosmolality and decreased intravenous volume may contribute to symptom development and (2) artificial hydration can alleviate objective findings of dehydration to some degree, but a subjective sensation of thirst can be sufficiently alleviated by nursing measures without artificial hydration therapy. In patients with better performance status and correctable dehydration, artificial hydration therapy appears effective in alleviating thirst, despite lack of no clinical observations on this selected study population.

Recommendations

R040: To alleviate thirst in terminally ill patients with cancer who are expected to live for 1–2 months, are incapable of oral fluid intake because of intestinal obstruction, and have no fluid retention symptoms:

- Artificial hydration therapy at 1000–1500 mL/d. [C]

R041: To alleviate thirst in terminally ill patients with cancer who are expected to live for 1–2 weeks or less, are capable of oral fluid intake, and have no fluid retention symptoms:

- Artificial hydration therapy at 500–1000 mL/d. [D]
- No artificial hydration therapy (nursing oral care only).

R042: To alleviate thirst in terminally ill patients with cancer who are expected to live for 1–2 weeks or less, are hardly capable of oral fluid intake because of intestinal obstruction (peritonitis carcinomatosa), and have fluid retention symptoms:

- Artificial hydration therapy at 500–1000 mL/d. [D]
- Artificial hydration therapy increased from 1000–2000 mL/d. [E]

- No artificial hydration therapy (nursing oral care only). [B]

5. Pleural effusion
Rationale

There are no intervention trials with a primary endpoint of pleural effusion. One large multicenter prospective observation study suggested that patients receiving 1000 mL/d or more hydration during the last 3 weeks experienced significantly more severe pleural effusion than those receiving no or less than 1000 mL/d hydration.[23] This was consistent with a nationwide opinion survey.[25]

Available empirical evidence thus suggests that (1) less than 1000 mL/d hydration is unlikely to deteriorate pleural effusion, (2) 1500–2000 mL/d hydration can deteriorate pleural effusion, and (3) volume reduction may alleviate pleural effusion.

Recommendations

R050: To prevent pleural effusion-related distress in terminally ill patients with cancer who are expected to live for 1–2 months, are capable of oral fluid intake, and have symptomatic pleural effusion:

- No artificial hydration therapy. [B]
- Artificial hydration therapy is limited to 500–1000 mL/d or less, if performed. [C]

R051: To prevent pleural effusion-related distress in terminally ill patients with cancer who are expected to live for 1–2 months, are capable of oral fluid intake but are receiving artificial hydration therapy at 2000 mL/d, and show exacerbation of pleural effusion-related distress:

- Artificial hydration therapy is gradually reduced to 500–1000 mL/d or less or discontinued. [B]

6. Bronchial secretion
Rationale

We have had no intervention trials with a primary end point of bronchial secretion. One large multicenter prospective observational study revealed no significant difference in prevalence of bronchial secretion between the patients receiving 1000 mL/d or more hydration during the last 3 weeks and those receiving no or less than 1000 mL/d hydration.[23,38] In that study, however, all patient had abdominal malignancy, and the median hydration volume was relatively small (700 mL/d). Terminally ill patients with cancer receiving a median of 1500 mL/d hydration experienced significantly more frequently bronchial secretion than those receiving a median of 250 mL/d.[39] This is consistent with an opinion survey and case report, suggesting that increased levels of hydration therapy could increase the risk of developing bronchial secretion.[25,33]

Available empirical evidence thus suggests that (1) a relatively large volume of hydration (e.g., 1500 mL/d or more) can deteriorate bronchial secretion and (2) in patients receiving a relatively small volume of hydration (e.g., <500–1000 mL/d), the hydration volume is minimally associated with the development of bronchial secretion.

Recommendations

R060: To alleviate bronchial secretion-related distress in terminally ill patients with cancer who are expected to live for a few days and have bronchial secretion-related distress:

- Artificial hydration therapy is reduced to 500 mL/d or less or discontinued. [B]

7. Delirium
Rationale

For patients with opioid-induced delirium, no controlled trials examined the accurate effects of hydration therapy. Some observation studies suggested that dehydration was significantly associated with the reversibility of delirium, although the association seemed dependent on opioid use.[24,40,41]

On the other hand, in patients close to death, a small randomized controlled trial demonstrated no significant benefits of 1000 mL/d hydration in the improving cognitive function of terminally ill patients with cancer with a median survival of 4 days.[27] A multicenter observation study failed to demonstrate beneficial effects of hydration to prevent agitated delirium,[23] and a Japanese historical control study also failed to demonstrate a decrease in the occurrence of agitated delirium using aggressive hydration and opioid rotation, contrary to a previous report from the other group.[42,43] These findings are consistent with several observations and case series suggesting that artificial hydration did not appear beneficial in improving cognitive function in terminally ill patients with cancer very close to death on a mass level.[24,33,41,44]

Available empirical evidence thus suggests that (1) artificial hydration therapy can be useful in selected

patients in combination with opioid rotation with opioid-induced delirium through the rapid clearance of toxic metabolites and (2) artificial hydration therapy has no benefits in improving delirium for most patients with organ failure.

Recommendations

R070: To alleviate delirium caused by dehydration and morphine in terminally ill patients with cancer, when other symptoms have been sufficiently palliated:

- Artificial hydration therapy (and opioid rotation, e.g., fentanyl). [B]

R071: To alleviate delirium caused by identifiable cause other than dehydration in terminally ill patients with cancer, when other symptoms have been sufficiently palliated:

- Artificial hydration therapy at 1000 mL/d. [B]

R072: To alleviate delirium caused by hypoxemia in terminally ill patients with cancer with multiple lung metastases who are expected to live for 1–2 weeks, and have symptomatic pleural effusion and/or edema:

- Artificial hydration therapy at 1000 mL/d. [E]

R073: To alleviate delirium due to hepatic encephalopathy in terminally ill patients with cancer with multiple liver metastases who are expected to live for 1–2 weeks, have symptomatic ascites and/or edema:

- Artificial hydration therapy at 1000 mL/d. [E]

8. Fatigue
Rationale

In patients with poor performance status, a preliminary randomized controlled trial demonstrated no significant benefits in alleviating fatigue of 1000 mL/d hydration compared with 100 mL/d hydration.[14]

On the other hand, an audit trial demonstrated that artificial hydration therapy could contribute to alleviating fatigue resulting in better quality of life in patients with better performance status.[20] The backgrounds of patients who received some benefits from this intervention included better performance status, bowel obstruction, and estimated survival of several months or longer.

Available empirical evidence thus suggests that (1) artificial hydration therapy is ineffective in improving fatigue in patients close to death (2) artificial hydration therapy can be effective in improving fatigue in patients with better performance status, bowel obstruction, and estimated survival of several months.

Recommendations

R080: To alleviate fatigue in terminally ill patients with cancer who are expected to live for 1–2 months, are incapable of oral fluid intake due to intestinal obstruction, but show a performance status of 2 or better:

- Artificial hydration therapy at 1000–2000 mL/d. [B]

R081: To alleviate fatigue in terminally ill patients with cancer who are expected to live for 1–2 weeks or less, and show a performance status of 3 or worse:

- Artificial hydration therapy at 1000–1500 mL/d. [E]

9. Peripheral edema
Rationale

We have had no intervention trials with a primary end point of peripheral edema. One large multicenter prospective observation study suggested that patients receiving 1000 mL/d or more hydration during the last 3 weeks experienced significantly more severe peripheral edema than those receiving no or less than 1000 mL/d hydration.[23,41] This is consistent with a small observation and a nationwide opinion survey.[25,33,45]

Available empirical evidence thus suggests that (1) more than 1000 mL/d hydration is likely to deteriorate peripheral edema and (2) volume reduction can alleviate peripheral edema.

Recommendations

R090: To prevent edema-related distress in terminally ill patients with cancer with no fluid retention symptoms:

- Artificial hydration therapy is limited to 1000 mL/d or less, if performed. [B]

R091: To alleviate edema-related distress in terminally ill patients with cancer who have edema-related distress:

- Artificial hydration therapy reduced to 1000 mL/d or less. [C]

COMMENTS

This paper illustrates the process of developing a clinical guideline for artificial hydration therapy for terminally ill patients with cancer in Japan, along with the general and specific recommendations for QOL sections of the guideline. The recommendations are generally consistent with existing clinical guidelines published in Western countries,[2–7] but this is, to our best knowledge, the first clinical guideline constructed using formal evidence-based and consensus-building methodology. A prospective observation study to assess the efficacy of this guideline is now ongoing, and the results could contribute to revising the recommendations.

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