Update in Hospice and Palliative Care

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Introduction

THE GOAL OF THIS UPDATE in hospice and palliative care is to summarize and critique research articles published in 2012 that have the highest potential for impact on clinical practice. To identify articles published between January 1 and December 31, 2012, we hand-searched 22 leading journals, the Cochrane Database of Systematic Reviews,¹ and Fast Article Critical Summaries for Clinicians in Palliative Care.² We also performed a PubMed keyword search using the terms “hospice” and “palliative care.” We ranked candidate articles based on study quality, scientific merit, topic area, and potential for impact on the clinical practice of hospice and palliative care. Here we summarize the findings of 10 articles with the highest ratings, and make recommendations for clinical practice based on the strength of the resulting evidence (Table 1).

Communication

Mack JW, Cronin A, Keating NL, Taback N, Huskamp HA, Malin JL, Earle CC, Weeks JC: Associations between end-of-life discussion characteristics and care received near death: A prospective cohort study. J Clin Oncol 2012;30:4387–4395.

Summary and main findings

End-of-life (EOL) discussions are associated with improved quality of life and less aggressive treatment for cancer patients.^{3–6} However, the impact of the timing and location of discussions on EOL care has not been well-characterized. The authors performed a secondary analysis of a large prospective cohort study conducted in health maintenance organizations (HMOs) or Veterans Affairs (VA) sites in five states. Subjects had stage IV lung or colorectal cancer, died 1 to 15 months after diagnosis, and spoke English, Spanish, or Chinese. Authors assessed characteristics of EOL discussions via medical record review and patient or surrogate telephone interviews. The interviews occurred 4 to 6 months and 15 months after cancer diagnosis. Investigators ascertained that an EOL discussion had taken place if patients or surrogates responded “yes” to either of the following questions: (1)

“Has a doctor ever talked to you about whether you would want to be revived or use life-sustaining machines?” and (2) “Was hospice recommended by any doctor or other health care provider?” Investigators also deduced that an EOL discussion had occurred if the patient’s medical record documented advance care discussions or preferences for location of death. The main outcomes were chemotherapy in the last 14 days of life, hospital or intensive care unit (ICU) care in the last 30 days of life, hospice enrollment, and hospice initiation in the last 7 days of life.

The analysis included 1231 patients (46% of 2671 eligible patients): 62% male, 76% white, 50% Medicare enrollees, and 82% diagnosed with lung cancer (versus colorectal cancer). Eighty-eight percent of patients had EOL discussions reported in interviews or medical records. Of the 794 patients with EOL discussions documented in medical records, 39% of these discussions occurred in the last 30 days of life, and 63% took place in a hospital. Patients whose first EOL discussion took place in an outpatient setting or occurred earlier than 30 days before death were significantly less likely to receive aggressive EOL care ($p < 0.001$) and more likely to use hospice ($p < 0.001$).

Strengths and limitations

This was a large, rigorous, multisite, prospective study of cancer patients. Investigators used multivariable logistic regression models to adjust for confounding variables. However, because the study design was observational, we cannot conclude that the associations between EOL discussions and less aggressive EOL care are causal. Further, both the content of the discussions and degree of alignment of EOL care with patient preferences are unknown. The study’s findings may also have limited generalizability to other diagnoses beyond lung and colorectal cancer.

Clinical bottom line

EOL discussions with cancer patients that took place in an outpatient setting or occurred earlier than 30 days before death were associated with less aggressive care and increased use of hospice.

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TABLE 1. RECOMMENDATIONS FOR CLINICAL HOSPICE AND PALLIATIVE CARE PRACTICE EMERGING FROM SELECTED ARTICLES

<i>Recommendation</i>	<i>Reference</i>
Start	
Partnering with pediatric clinicians to help overcome barriers to advance care planning discussions.	Durall et al. ¹⁷
Advocating for payment policies that increase access to hospice care concurrent with skilled nursing facility (SNF) care and referring eligible patients to hospice after SNF.	Miller et al. ¹⁸
Continue	
Advance care planning discussions early in the course of serious illness in nonacute care settings.	Mack et al. ¹⁹
Checking in with surrogates of patients in the ICU to assess their perspectives when conveying poor prognoses.	Zier et al. ²⁰
Counseling families and providers that PEG feeding tubes do not improve survival or prevent pressure ulcers in patients with advanced dementia and feeding problems.	Teno et al. ²¹ Teno et al. ²²
Exploring reasons for patient and family requests for hydration at the end of life.	Bruera et al. ²³ Cohen et al. ²⁴
Consider	
Acupuncture to improve symptoms of dyspnea and quality of life in patients with COPD.	Suzuki et al. ²⁵
Potential harms of ketamine when used as an adjuvant to opioids in patients with refractory cancer pain.	Hardy et al. ²⁶

COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; PEG, percutaneous endoscopic gastrostomy.

Symptom Management

Suzuki M, Muro S, Ando Y, Omori T, Shiota T, Endo K, Sato S, Aihara K, Matsumoto M, Suzuki S, Itotani R, Ishitoko M, Hara Y, Takemura M, Ueda T, Kagioka H, Hirabayashi M, Fukui M, Mishima M: A randomized, placebo-controlled trial of acupuncture in patients with chronic obstructive pulmonary disease (COPD). *Arch Intern Med* 2012; 172:878–886.

Summary and main findings

Dyspnea on exertion (DOE) is common and challenging to manage for patients with chronic obstructive pulmonary disease (COPD). This study was a randomized, placebo-controlled, single-blind, multicenter trial of acupuncture compared with sham (placebo) needling to relieve DOE in patients with COPD. Investigators recruited patients from outpatient respiratory medicine clinics at five hospitals in Japan. Eligible patients had stable moderate-to-very-severe

COPD, no significant comorbidities, ability to walk unassisted, and DOE. Participants received acupuncture or sham needling at the same standardized acupuncture points once per week for 12 weeks. To ensure blinding, sham needles appeared to penetrate the skin, but actually retracted with application of pressure. To test the effectiveness of blinding, investigators asked patients whether they thought they had received real or sham acupuncture, and found that patients were able to correctly identify the treatment received no better than chance. The primary outcome was self-rated DOE on a 10-point scale. Secondary outcomes included distance walked and lowest oxygen saturation during the 6-minute walk test, measures of pulmonary function, and self-reported quality of life.

Of 111 eligible patients, 68 (61%) participated in the study. Demographics (mean age 72 years; 91% to 94% male), and baseline COPD stage, dyspnea score, and pulmonary function measures were similar in both groups. The DOE score on the 6-minute walk test improved 3.6 points in the real acupuncture group, with minimal improvement (0.4 points) in the sham group (mean difference, −3.58 points; 95% confidence interval [CI], −4.27 to 2.90). Additionally, the acupuncture group (versus sham) had significant improvement in 6-minute walk distance, oxygen saturation, and quality of life. There was no difference between groups in pulmonary function measures, such as forced expiratory volume in one second. Adverse events were infrequent and minor in both groups.

Strengths and limitations

This is the first placebo-controlled, randomized study to examine the efficacy of acupuncture in the management of DOE in patients with COPD. The authors standardized their real and sham acupuncture protocols and blinding appeared to be adequate. The authors propose that acupuncture may be effective for DOE in COPD because needling decreases accessory respiratory muscle tone, resulting in increased muscle recoil and rib cage mobility. Though patients and evaluators were blinded, the lack of blinding of acupuncture therapists may have influenced the results. Additionally, due to limited follow-up, the study cannot determine how long the effect persists beyond 12 weeks. Finally, the fact that the study was conducted in Japan and that most subjects were males without significant comorbidities may limit generalizability of the results.

Clinical bottom line

Acupuncture improved dyspnea, 6-minute walk distance, oxygen saturation, and quality of life for patients with COPD.

Hardy J, Quinn S, Fazekas B, Plummer J, Eckermann S, Agar M, Spruyt O, Rowett D, and Currow DC: Randomized, double-blind, placebo-controlled study to assess the efficacy and toxicity of subcutaneous ketamine in the management of cancer pain. *J Clin Oncol* 2012;30:3611–3617.

Summary and main findings

Use of ketamine for refractory cancer pain has become increasingly common. However, previous trials for this use have been small and underpowered. The authors conducted a randomized, double-blind, placebo-controlled trial across 10 Australian palliative care services to assess the efficacy of

ketamine in treating cancer pain. Eligible patients had refractory chronic pain due to cancer or its treatment, and a Brief Pain Inventory score of 3 or more (on a 0 to 10 scale) despite treatment with opioids and coanalgesics. The study excluded patients who had received ketamine within 6 months, had received radiation or other therapy for pain, or had contraindications to ketamine. Authors randomized patients to receive a placebo saline infusion or subcutaneous ketamine infusion over 5 days with ketamine dose escalation and breakthrough medications if pain control was insufficient. Investigators reduced ketamine doses if toxicity occurred. They stopped ketamine altogether if toxicity was intolerable, or no response was observed after delivery of the maximum dose of ketamine (500 mg) for 24 hours. Primary outcomes included reduction in pain scores by at least 2 points (on a 0 to 10 scale), and delivery of less than four breakthrough doses in 24 hours. Secondary outcomes included: daily pain assessments on days 2 to 5 and adverse events. The authors performed an intention-to-treat analysis.

Overall, 185 patients were randomized (95% enrollment rate): 93 to ketamine, and 92 to placebo. Demographics (age 63.0 to 64.3 years; male 55.0% to 58.2%), baseline pain assessment, and opioid dose were similar in both groups. There were no significant differences in pain improvement or use of breakthrough medications between the groups. In the ketamine arm, 22.7% of patients discontinued ketamine due to toxicity, compared with 2.7% in the placebo arm. Nearly twice as many adverse events, such as dizziness, hypoxia, and somnolence, were reported for ketamine than for placebo (incidence rate ratio, 1.95; $p < 0.001$).

Strengths and limitations

This was a high-quality, adequately powered, double-blinded, placebo-controlled trial examining both efficacy and toxicity of ketamine. Investigators recruited a heterogeneous population of cancer patients with clinical characteristics representative of a hospice or palliative care patient population. However, because no studies have compared dosing protocols or routes of administration for ketamine, it is unknown whether the regimen used in this trial is optimal. Additionally, the study did not have sufficient power to detect differences in response to ketamine among pain types.

Clinical bottom line

Compared with placebo, subcutaneous ketamine, as an adjuvant to opioids, did not improve cancer pain and caused considerably more adverse events.

Artificial Nutrition and Hydration

Teno JM, Gozalo PL, Mitchell SL, Kuo S, Rhodes RL, Bynum JPW, Mor V: Does feeding tube insertion and its timing improve survival? *J Am Geriatr Soc* 2012;60:1918–1921.

Teno JM, Gozalo P, Mitchell SL, Kuo S, Fulton AT, Mor V: Feeding tubes and the prevention or healing of pressure ulcers. *Arch Intern Med* 2012;172:697–701.

Summary and main findings

Questions regarding artificial feeding in patients with dementia are common and emotionally charged. Physicians

often recommend percutaneous endoscopic gastrostomy (PEG) feeding tubes based on beliefs that they increase survival and facilitate pressure ulcer healing.^{7–9} Previous studies investigating the benefits and harms of PEG feeding have been small or retrospective. Both studies described here were secondary analyses of the Minimum Data Set, a database that includes all U.S. nursing homes certified by Medicare and Medicaid, merged with corresponding Medicare claims files. The aim of the first study was to determine whether use and timing of PEG tubes affect survival. The aim of the second study was to examine whether PEG tubes prevent or help alleviate pressure ulcers. Eligible patients had advanced dementia and needed assistance with eating. The studies excluded patients who died within 2 weeks of the qualifying assessment, or who had evidence of PEG tubes in the prior 6 months. Primary outcomes were: survival from development of eating problems to death; survival from insertion of a PEG tube to death; development of pressure ulcers stage II or higher in patients with no ulcers at enrollment; and improvement in ulcers for patients with ulcers at enrollment.

The sample for the survival analysis included 36,492 patients: 34,536 did not have PEG tubes, and 1,956 did. The cohort without PEG tubes was older, had a greater proportion of female and white patients, and had a higher proportion of completed living wills compared with the cohort with PEG tubes. There was no significant difference in survival between patients who had a PEG tube placed following development of eating problems and those who did not. Timing of PEG tube placement also did not affect survival.

The sample for the pressure ulcers analysis included 1124 patients with no preexisting ulcers and 461 patients with preexisting ulcers. Demographic characteristics were similar across both pairs of comparison groups. Most patients were in their early 80s, and the majority was female and white. Compared with patients who did not have a PEG tube, those who had a PEG tube were significantly more likely to develop an ulcer (odds ratio [OR] 2.27, 95% CI, 1.95–2.65) and less likely to show improvement in an existing ulcer (OR 0.70, 95% CI, 0.55–0.89).

Strengths and limitations

These secondary analyses of large databases used rigorous methods, including propensity scores, to control for selection bias. Authors used multiple sensitivity analyses to confirm the studies' findings. However, these studies may not be generalizable to settings other than nursing homes. Although eligible patients had total dependence in eating, they may not have had difficulty swallowing. Thus, these results may not apply to patients considered for PEG tube due to difficulty in swallowing.

Clinical bottom line

In patients with advanced dementia who develop eating problems, placement of a PEG tube did not improve survival. Patients with a PEG tube had a higher risk for development of pressure ulcers or decreased healing of preexisting pressure ulcers.

Bruera E, Hui D, Dalal S, Torres-Vigil I, Trumble J, Roosth J, Krauter S, Strickland C, Unger K, Palmer JL, Allo J, Frisbee-Hume S, Tarleton K: Parenteral hydration in patients with advanced cancer: A multicenter, double-blind,

placebo-controlled, randomized trial. *J Clin Oncol* 2012; 31:111–118.

Cohen MZ, Torres-Vigil I, Burbach BE, De la Rosa A, Bruera E: The meaning of parenteral hydration to family caregivers and patients with advanced cancer receiving hospice care. *J Pain Symptom Manage* 2012;43:855–865.

Summary and main findings

Cancer patients often eat and drink less toward the end of life. Dehydration may contribute to fatigue, myoclonus, and delirium.^{10,11} Yet many worry that the harms of parenteral hydration in dying patients include dyspnea, edema, and increased secretions. The authors conducted a randomized, double-blind, placebo-controlled, multicenter trial to determine the impact of hydration on symptoms of dehydration, quality of life, and survival. They also conducted qualitative interviews to explore the meaning of hydration for participating patients and families.

Authors recruited patients with advanced cancer from five hospices in Houston. Eligible patients had mild-to-moderate dehydration, life expectancy of more than one week, and decision-making capacity. Patients with severe dehydration or those who did not have a primary caregiver at home were excluded. Participants in the intervention group received normal saline at 1 L/day over 4 hours, whereas those in the placebo group received normal saline at 100 mL/day over 4 hours. Treatment continued until coma, death, or the end of the study. Primary outcomes were: change in the sum of four dehydration symptoms (fatigue, myoclonus, sedation, hallucinations) between baseline and days 4 and 7, as measured on the Edmonton Symptom Assessment Scale (ESAS, scale of 0 to 10). Secondary outcomes included: delirium, survival, quality of life, and change in symptoms.

Of 905 patients assessed for eligibility, 129 (14%) were enrolled and 102 were included in the final analysis. Demographic and clinical characteristics were similar between the hydration and placebo groups (median age 67 years, 57% to 62% white, ESAS dehydration score 18), with the exception that the hydration group had more males (60% versus 45%). The study found no difference between groups in the main outcome measures, including change in fatigue, myoclonus, sedation, and hallucinations, at day 4 or 7. There were no differences in survival or quality of life.

Qualitative interviews were conducted at baseline and on day 4 with 85 patients and 84 caregivers who participated in the trial. Patients had a mean age of 67 years, 54% were female, and 61% were white. Caregivers had a mean age of 56 years, 79% were female, and 62% were white. Investigators asked patients to describe their experiences with hydration, and asked caregivers for their observations of the impact of hydration on their loved ones. In their qualitative analysis of responses, the authors identified the following themes: hope that hydration would sustain life and facilitate healing; and hydration as a means to promote comfort by lessening pain, augmenting medication efficacy, increasing energy, and improving quality of life.

Strengths and limitations

These studies were a high-quality, randomized control trial and qualitative analysis, respectively. For the experimental study, authors used rigorous blinding methods, including the

use of identical locked backpacks for infusion pumps, counterweights placed in placebo backpacks, and tape placed over infusion rates. The study was slightly underpowered to detect differences in multiple outcomes and may not have adequately assessed potential harms of hydration, such as edema or increased secretions. Additionally, the authors did not monitor enteral fluid intake, potentially influencing results. The qualitative study used well-established phenomenological methods. Finally, the studies included only cancer patients with mild or moderate dehydration and may not be generalizable to cancer patients with severe dehydration, or patients who do not have cancer.

Clinical bottom line

Compared with placebo, intravenous (IV) hydration (1 L/day) did not improve symptoms or survival for hospice patients with cancer and mild or moderate dehydration. Patients and families perceived multiple benefits from hydration.

Pediatrics

Durall A, Zurakowski D, Wolfe J: Barriers to conducting advance care discussions for children with life-threatening conditions. *Pediatrics* 2012;129:975–982.

Summary and main findings

In adult patients, advance care discussions are associated with better quality of life near the end of life.^{12,13} However, little research exists examining such discussions for children with life-threatening conditions. The authors conducted a web-based survey to solicit clinician perspectives on barriers to advance care discussions for children.

Physicians and nurses who cared for children in ICU or oncology settings in a single Boston hospital received a link to the survey via e-mail. The closed-ended, 148-item survey was developed from clinician and parent focus groups and previous surveys. Primary outcomes included clinician perceptions of how often 23 barriers, such as behaviors and attitudes of parents, patients, and clinicians, were impediments to advance care discussions. The actual timing of advance care discussions compared with when clinicians believed these discussions should take place was a secondary outcome.

Of 496 eligible clinicians, 266 (54%) responded, including 107 physicians and 159 nurses. Mean age of physicians was 38.2 years, 50% were female, 78% were white, and 47% reported more than 10 years of clinical experience. Mean age of nurses was 38.6 years, 94% were female, 91% were white, and 64% had more than 10 years of clinical experience. The most common perceived barriers were those related to parent behavior and attitudes, including: “unrealistic parent expectations” (44%), “differences between clinician and patient/parent understanding of prognosis” (39%), and “lack of parent readiness to have the discussion” (38%). Common concerns related to clinician behaviors and attitudes included: “clinician concern about taking away hope” (29%), “clinician uncertainty about prognosis” (27%), and “clinicians not knowing the right time to address the issues” (26%). Most clinicians (60%) reported that advance care discussions occur in critical situations, during a severe illness or near death, but 92% of clinicians believed that such

discussions should take place sooner, when the patient's illness is first diagnosed or is stable.

Strengths and limitations

The authors pilot-tested the survey and evaluated it for face validity, and a large number of physicians and nurses from multiple specialties responded. However, investigators only recruited participants from a single pediatric hospital, and the study did not assess parents' or children's perceived barriers. Another potential limitation is that clinicians chose from a predetermined list of potential barriers and were unable to provide detail about how the various barriers impeded discussions. Palliative care specializes in addressing many of the barriers identified by clinicians, such as mediating differences in goals and prognostic understanding. These results indicate a potential role for palliative care in advance care planning discussions for children.

Clinical bottom line

Most clinicians believed that advance care discussions for children with life-limiting illness occur too late. Clinicians perceived prognostic uncertainty, parent expectations, taking away hope, and timing and readiness for discussions as key barriers.

Prognostication

Zier LS, Sottile PD, Hong SY, Weissfeld LA, White DB: *Surrogate decision makers' interpretation of prognostic information.* *Ann Intern Med* 2012;156:360–366.

Summary and main findings

Prognostic information factors prominently in decisions to withhold or discontinue life-sustaining therapies. Physicians and surrogates frequently have different expectations for patients' recovery.^{14,15} The authors recruited surrogates who participated in decision making for incapacitated patients from ICUs at three hospitals in San Francisco. Eligible surrogates were English speakers, at least 18 years of age, and present in the hospital. Investigators asked surrogates to interpret 16 hypothetical prognostic statements. Some statements were qualitative: "It is very unlikely that he will survive." Others presented a numeric likelihood of survival: "The patient has a 5% chance of surviving." For numeric statements, surrogates who reported that they would interpret the statement differently than its intended meaning were asked to explain why their estimate would differ. Using quantitative and qualitative methods, the authors addressed two questions: (1) Did surrogates interpret statements more optimistically as the stated probability of survival decreased? and (2) What were surrogates' reasons for their interpretations of prognostic statements?

The patients' mean age was 66 years and at least one surrogate was enrolled for each of the 61 eligible patients (enrollment rate, 74%). Of the 80 participating surrogates, mean age was 54 years, 42% were female, 49% were white, and 29% reported a spousal relationship to the patient. As the stated probability of survival decreased, surrogates' interpretations were more optimistic and less accurate ($p < 0.001$). Surrogates' reasons for their optimistic estimates of prognosis most commonly included: the need for optimism, belief

in patients' resilience, mistrust in doctors' prognostic accuracy, and perception of prognosis as an approximate rather than an exact estimate.

Strengths and limitations

This was a well-designed, multicenter, mixed methods study. The use of a single experimental interview composed of hypothetical statements may be a limitation, though presented statements were derived from previous research on actual physician-patient discussions. Results may not be generalizable to patients in non-ICU settings or patients who have decision-making capacity. These results underscore the importance of assessing surrogate perceptions when communicating a poor prognosis.

Clinical bottom line

Surrogates of ICU patients optimistically interpreted prognostic information, especially when a high likelihood of death was presented.

Geriatrics and Long-Term Care

Miller SC, Lima JC, Mitchell SL: *Influence of hospice on nursing home residents with advanced dementia who received Medicare-skilled nursing facility care near the end of life.* *J Am Geriatr Soc* 2012;60:2035–2041.

Summary and main findings

Prior research has demonstrated that most adults (66%) with advanced dementia die in nursing homes.¹⁶ Current Medicare policy disallows concurrent payment for skilled nursing facility (SNF) care and hospice, impeding hospice enrollment for many patients at the end of life. The impact of the timing of SNF care and hospice enrollment on patient outcomes has not been studied. The authors conducted a retrospective cohort study of 3353 U.S. nursing homes. They utilized information from the Minimum Data Set (MDS) and Medicare Part A claims. Eligible patients had advanced dementia, received SNF care in the last 90 days of life, and had a nursing home or hospice length of stay of at least 8 days. Outcomes were: treatments in the week before the last MDS assessment, persistence of pain and dyspnea, and location of death.

The study sample included 4344 decedents in three groups: patients who did not receive hospice ($n = 3258$), patients who received hospice concurrent with SNF care ($n = 381$), and patients who received hospice following SNF care ($n = 705$). Demographic characteristics were similar between both hospice and nonhospice groups (age ≥ 85 years 52.5% to 54.2%, white 80.7% to 83.2%).

Compared with patients who did not receive hospice, patients who received hospice concurrent with or after SNF care received fewer interventions, including fewer medications and lower rates of feeding tube placement (both $p < 0.001$). Patients receiving hospice concurrent with or after SNF care were also less likely to die in the hospital (OR 0.13, 95% CI 0.07–0.26 and OR 0.02, 95% CI 0.01–0.07, respectively). Decedents receiving hospice after SNF care were less likely to report persistent dyspnea (OR 0.63, 95% CI 0.45–0.87), and those receiving hospice concurrent with SNF care were more likely to report persistent pain (OR 1.65, 95% CI 1.23–2.19).

Strengths and limitations

This was a well-designed retrospective cohort study with extensive adjustment for potential confounders. The fact that it was a large, national study strengthens generalizability of the results. Validity of the findings is limited by potential underreporting of pain and dyspnea in the MDS database. Further research should explore why patients receiving hospice concurrent with SNF care were more likely to report persistent pain.

Clinical bottom line

For patients with advanced dementia who died in the nursing home and received SNF care in the last 90 days of life, hospice use concurrent with or after SNF care was associated with fewer interventions and a lower likelihood of in-hospital deaths.

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Author Disclosure Statement

No competing financial interests exist.

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