

Update in Palliative Medicine

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The goal of palliative medicine is to prevent and relieve suffering and to support the best quality of life for patients and their families, regardless of the stage of the disease or need for other therapies (1). Palliative care expands traditional disease model medical treatments to include the goals of enhancing quality of life, optimizing function, and helping with decision making, and unlike hospice it is delivered simultaneously with any appropriate life-prolonging treatments. The articles selected for this update were drawn from a keyword search followed by a review of more than 17 000 citations from 20 leading journals in general medicine, palliative medicine, anesthesia, oncology, nursing, and social work spanning September 2005 to June 2007. We rated a subset of these manuscripts on the basis of the quality of the science, innovativeness, and applicability to clinicians who practice palliative medicine. This last criterion applies not only to specialists in palliative medicine, but also to internists, family medicine clinicians, nurse practitioners, and subspecialists in internal medicine—all of whom care for patients with a wide range of advanced, chronic illnesses. We selected the articles ranked highest by these criteria, using a consensus process to resolve ratings discrepancies. The Table summarizes changes to clinical practice that should emerge from these articles.

Pain Management

Portenoy RK, Sibirceva U, Smout R, et al. Opioid use and survival at the end of life: a survey of a hospice population. *J Pain Symptom Manage.* 2006;32:532-40. [PMID: 17157755]

Question: Does opioid use hasten death in patients with advanced disease?

Study Design: Secondary data analysis of a prospective cohort study.

Patients: 725 patients (mean age, 77 years; 42% male) who received opioids and had at least 1 dose change before death (55.5% of the total sample of 1306 patients enrolled in National Hospice Outcomes Project).

Setting: 13 hospices across the United States.

Outcome: Time until death after the last opioid dose change.

Follow-up: Mean length of stay in hospice, 30.25 days (SD, 37.8).

Results: There was no association between percent change in dose and time until death. There was an association

between shorter survival and higher opioid dose ($P = 0.010$), but in multivariable analysis (adjusted for pain score, diagnosis, lack of consciousness, and performance status), this accounted for 10% of the variance, at most.

Conclusion: The association between higher final opioid dose and shorter survival was weak, but it explains only a very small percentage of variation in survival.

Commentary: Fears that opioid medications might hasten death contribute to the undertreatment of pain in patients with advanced illness (2). This study's findings help strengthen existing claims that opioids are safe to use in patients with advanced illness (3–5). However, because this was a hospice population, the findings are subject to referral and selection biases. Also, the higher opioid dose subgroups were relatively small, so the study may have lacked statistical power to find associations in these groups. Nevertheless, these findings demonstrate that concerns about hastening death through the use of opioids (“opiophobia”) seem exaggerated and do not justify the undertreatment of symptoms in patients with advanced illness.

Clinical Bottom Line: Stop withholding opioids from hospice patients and others nearing the end of life because of fears that these medications might accelerate death.

Tremont-Lukats IW, Challapalli V, McNicol ED, et al. Systemic administration of local anesthetics to relieve neuropathic pain: a systematic review and meta-analysis. *Anesth Analg.* 2005;101:1738-49. [PMID: 16301253]

Question: Are intravenous lidocaine and oral mexiletine effective and safe for the treatment of neuropathic pain?

Study Design: Systematic review and meta-analysis.

Patients: 706 patients with neuropathic pain participating in 19 randomized, double-blind, controlled trials with par-

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Table. Changes to Practice Emerging from Articles Important to Palliative Medicine Practitioners between 2005 and 2007

Start	
Using the Seattle Heart Failure model, available at http://depts.washington.edu/shfm , to predict survival in and to counsel patients with advanced heart failure	Levy et al.
Consider	
Using intravenous lidocaine or oral mexiletine for treating refractory neuropathic pain	Tremont-Lukats et al.
Referring patients with malignant gastroduodenal obstruction to endoscopists experienced in luminal stenting as an alternative to gastroenterostomy	Hosono et al.
Using the clinical pathway described by Loeb et al. to treat nursing home patients with lower respiratory tract infections or pneumonia to prevent unnecessary transfers and hospitalizations	Loeb et al.
Requesting palliative care consultation for patients with advanced illness as soon as they are admitted to the intensive care unit	Norton et al.
Stop	
Withholding opioids from patients nearing the end of life because of fears that opioids will hasten their death	Portenoy et al.

allel or crossover design. Ten trials studied lidocaine and 9 studied mexiletine.

Intervention: Intravenous lidocaine or oral mexiletine.

Outcomes: Reduction in neuropathic pain, measured on a continuous scale and reported as the weighted mean difference on a 0- to 100-mm visual analogue scale. Prevalence and severity of side effects were also analyzed.

Results: Lidocaine and mexiletine were superior to placebo (weighted mean difference, -10.60 mm [95% CI, -14.52 to -6.68 mm]; $P < 0.001$). Separate analyses of studies of lidocaine and mexiletine yielded similar results. Five studies compared the agents with active control; no significant differences were found in pain relief (weighted mean difference, -0.60 mm [CI, -6.96 to 5.75 mm]) or adverse events. No serious adverse events were reported in any trial with these agents.

Conclusion: Intravenous lidocaine and oral mexiletine seem to be effective and safe treatments for neuropathic pain.

Commentary: Neuropathic pain syndromes remain a clinical challenge for internists and pain specialists. This article pools data from randomized trials and supports previous uncontrolled studies (6, 7) demonstrating that intravenous lidocaine and oral mexiletine are a viable choice for treating patients with difficult-to-control neuropathic pain. Several caveats must be considered in interpreting this meta-analysis, however. Cause of pain was the greatest source of heterogeneity in the analysis, and only 6 of the trials included patients with the neuropathic pain syndromes most

frequently encountered in palliative medicine (for example, cancer, HIV, stroke, and spinal cord injury). The pain syndromes studied in most of the included trials (painful diabetic neuropathy and postherpetic neuralgia) present less often in palliative care settings. Finally, the clinical significance of an 11-mm change in a visual analogue scale is difficult to interpret.

Clinical Bottom Line: Consider using intravenous lidocaine or oral mexiletine for refractory neuropathic pain, although further studies are needed to better define efficacy and to clarify the appropriate place of these agents in treatment algorithms.

Nonpain Symptom Management

Hosono S, Ohtani H, Arimoto Y, et al. Endoscopic stenting versus surgical gastroenterostomy for palliation of malignant gastroduodenal obstruction: a meta-analysis. *J Gastroenterol.* 2007;42:283-90. [PMID: 17464457]

Question: Is endoscopic stenting as effective as surgical gastroenterostomy for treating malignant gastroduodenal obstruction?

Study Design: Meta-analysis.

Patients: 307 patients (age range, 64 to 79 years) with gastroduodenal obstruction due to inoperable malignant disease, studied in 1 randomized, controlled trial and 8 retrospective studies. Primary malignant conditions were pancreatic, duodenal, stomach, and bile duct cancer.

Intervention: Endoscopic stenting or surgical gastroenterostomy.

Outcomes: Clinical success, defined as improved dietary status, adequate gastric emptying, or tolerance of at least a light diet; number of days from procedure to clinical improvement; overall complications; delayed gastric emptying after intervention; length of hospital stay; and 30-day mortality.

Results: Pooled data showed that endoscopic stenting was associated with a higher clinical success rate than gastroenterostomy (odds ratio, 2.97 [CI, 1.34 to 6.57]; $P = 0.007$). Time from procedure to oral intake was 5.4 days shorter for stenting than for surgery ($P < 0.001$), but there was significant heterogeneity between studies for this result. Although the overall frequency of complications was less for stenting (17 complications [14%] for stenting vs. 38 complications [31%] for surgery; $P = 0.02$), the authors did not consider this to be significant because of concerns that selection and publication bias in favor of stenting influenced the result. Stenting reduced the risk for delayed gastric emptying (odds ratio, 0.08 [CI, 0.02 to 0.41]), although not all studies reported the outcome. Length of hospital stay after intervention was 9.7 days shorter (CI, 7.7 to 11.6 days) with stenting. Thirty-day mortality was lower with stenting but did not statistically significantly differ from that with surgery.

Conclusion: Endoscopic stenting seems to be superior to surgical gastroenterostomy for the treatment of malignant gastroduodenal obstruction.

Commentary: Patients with malignant gastroduodenal obstruction have limited life expectancy (8, 9), so it is important that palliative procedures are effective and not overly burdensome and minimize hospital length of stay. These data demonstrate that stenting of gastroduodenal obstruction confers these advantages better than surgery to relieve the obstruction. However, the studies in the meta-analysis were small, they were subject to publication and language biases, and the clinicians performing the interventions had different levels of expertise. Also, laparoscopic gastrojejunostomy has gained popularity in recent years. Studies of this procedure were not included in the meta-analysis, and laparoscopic procedures may offer a reasonable alternative to open surgery for patients who have an obstruction that cannot be relieved through endoscopic stenting.

Clinical Bottom Line: Refer patients with malignant gastroduodenal obstruction to endoscopists experienced in luminal stenting.

Nursing Home Care

Loeb M, Carusone SC, Goeree R, et al. Effect of a clinical pathway to reduce hospitalizations in nursing home residents with pneumonia: a randomized controlled trial. *JAMA*. 2006;295:2503-10. [PMID: 16757722]

Question: Can an algorithm for treating nursing home residents with lower respiratory tract infections prevent acute hospitalizations?

Study Design: Cluster-randomized trial.

Patients: 680 residents age 65 years or older (mean age, about 85 years; about 70% female) from 20 nursing homes, who met a standardized definition of a lower respiratory tract infection or pneumonia and, if randomly assigned to intervention, could eat and drink and had stable vital signs. Patients with a life expectancy fewer than 30 days, a history of severe allergic reaction to fluoroquinolones, or an advance directive precluding hospital transfer were excluded.

Setting: Nursing homes throughout Canada.

Intervention: Clinical pathway (10 nursing homes, 327 residents) or usual care (10 nursing homes, 353 residents). Patients treated by the clinical pathway remained on site; received levofloxacin, 500 mg orally, for 10 days; and received subcutaneous fluid infusion as needed for dehydration.

Outcomes: The primary outcomes were hospital admission and emergency department visits. Secondary outcomes were death, health-related quality of life, change in functional status, days to normalization of vital signs, skin or soft tissue infections, and falls. A separate analysis examined resource utilization and costs.

Follow-up: Daily for 10 days, then twice weekly for up to 30 days.

Results: Intervention patients had fewer hospitalizations (adjusted weighted mean hospital admission rate, 8% for the intervention vs. 20% for usual care; weighted mean difference, 12% [CI, 5% to 18%]; $P = 0.001$), shorter hospital stays (mean hospital length of stay, 0.79 day vs. 1.74 days; weighted mean difference, 0.95 day per resident [CI, 0.34 to 1.55 days]; $P = 0.004$), and equal numbers of emergency department visits (1.2% for the intervention vs. 1.6% for usual care; weighted mean difference, 0.4% [CI, -1.9% to 2.8%]; $P = 0.72$). Results were similar in analyses restricted to patients with radiographically defined pneumonia. There were no differences in secondary outcomes. Initially higher costs for patients in the intervention group were offset by reduced professional billings, resident transportation, and hospitalization costs, with an overall cost savings with the intervention of \$1016 (Canadian) per resident. In U.S. dollars, the savings were estimated to be \$1517 per resident.

Conclusion: An algorithm for treating nursing home residents with lower respiratory tract infections on site prevents acute hospitalizations and reduces overall health care costs.

Commentary: The question asked by this study is important because pneumonia and other lower respiratory tract infections occur frequently in nursing home residents (10, 11). One limitation is that research nurses at the participating institutions were not blinded to the intervention, which may have biased data collection. Another is that the study was undertaken within the single-payer Canadian health care system, so the results are more generalizable to systems where costs are contained within a single-payer structure, such as Kaiser Permanente and Veterans Affairs medical centers, and less generalizable to most other nursing homes in the United States, in which the initially increased costs of on-site treatment may not be offset by later savings. In these facilities, supplemental funding from insurance providers may be needed to implement the pathway and keep residents in the nursing home for treatment. In addition, the findings may not be generalizable to nursing homes with fewer than 100 beds.

Clinical Bottom Line: Consider using the clinical pathway described in this study to treat nursing home patients with lower respiratory tract infection who otherwise resemble study participants.

Prognosis

Levy WC, Mozaffarian D, Linker DT, et al. The Seattle Heart Failure Model: prediction of survival in heart failure. *Circulation*. 2006;113:1424-33. [PMID: 16534009]

Question: Can a risk model that uses readily obtainable clinical information accurately predict the survival of patients with heart failure?

Study Design: Development and validation of a prediction model using data from clinical trials and observational studies and databases.

Patients: The derivation cohort comprised 1125 patients from a single randomized trial (12). The validation cohort comprised 9942 patients from 3 trials and 2 observational cohorts (13–17). Mean age ranged from 53 to 71 years, 69% to 80% of patients were male, and mean ejection fraction ranged from 0.22 to 0.35.

Outcomes: Survival without left ventricular assist device implantation, cardiac transplantation, or death.

Results: The final model incorporates demographic, clinical, medication, laboratory, and echocardiographic data; provides 1-, 2-, and 5-year survival data; and is available at <http://depts.washington.edu/shfm>. Predicted probabilities of survival closely matched observed probabilities in the validation cohorts. The model was fairly good at discriminating patients who survived from those who did not (area under the receiver-operating characteristic curve for the derivation cohort, 0.73 [CI, 0.71 to 0.74]).

Conclusion: The Seattle Heart Failure model accurately predicts survival of patients with heart failure by using easily available clinical characteristics.

Commentary: Accurate assessment of prognosis helps patients and their families make decisions about treatment and helps clinicians plan patient discharges and referrals to appropriate services, such as hospice. Previous risk models for heart failure have been notoriously inaccurate at predicting prognosis (18). The Seattle Heart Failure model not only accurately predicts survival but shows changes in prognosis over baseline based on interventions, specifically medications (such as angiotensin-converting enzyme inhibitors) and devices (such as implantable cardioverter defibrillators). However, the model has some limitations. It was developed by using data from outpatients and thus may not be generalizable to inpatients. The statistical derivation of the model uses estimations of hazard ratios for some treatments, which may introduce error into the model predictions. Finally, because the model does not take into account patients' other medical conditions, it may not be generalizable to patients with competing comorbid conditions.

Clinical Bottom Line: Use the Seattle Heart Failure model to predict survival in and to counsel patients with heart failure.

Question: Can earlier palliative care consultation in the medical intensive care unit (ICU) reduce length of stay for patients at a high risk for death?

Study Design: Before–after, prospective cohort study.

Patients: 191 patients (65 from before and 126 from after the start of the intervention) identified as having a high risk for death, defined as 1 or more of the following: current hospital stay greater than 10 days, age greater than 80 years and the presence of 2 or more life-threatening conditions (such as end-stage renal failure or severe heart failure), diagnosis of active stage IV cancer, recent cardiac arrest, or diagnosis of intracerebral hemorrhage requiring mechanical ventilation.

Setting: Single, adult ICU (17 beds) at an academic medical center in upstate New York.

Intervention: Automatic palliative care consultation on admission to the ICU to provide ICU providers with recommendations for treating symptoms and creating plans of care.

Outcomes: The primary outcome was length of stay (in ICU, for entire hospitalization, and from ICU admission to hospital discharge). Death was a secondary outcome.

Follow-up: Mean, 41 days (control group) or 36 days (intervention group).

Results: The ICU length of stay was shorter for the intervention group than the usual care group (mean length, 8.96 vs. 16.28 days; $P < 0.001$). Overall hospital length of stay, time from ICU admission to hospital discharge, and mortality did not differ.

Conclusion: Palliative care consultation early in the course of a patient's ICU stay is associated with decreases in length of stay but no increase in mortality among patients at high risk for death.

Commentary: This study adds to the data demonstrating that early palliative care consultation in the ICU setting can reduce length of stay for hospitalized patients (19–21). The reduction in ICU bed-days presumably resulted from enhanced communication about overall goals and alignment of treatment to those goals. Mortality in both groups was high (60% in the palliative care group, 55% in the usual care group); however, these data suggest that palliative care consultation does not increase mortality but is instead a marker for patients who were likely to die soon. The authors estimate that the intervention would save about 1400 ICU bed-days per year, which would improve bed turnover and lead to substantial cost savings. The most well known of previous interventions that aimed to improve outcomes for end-of-life care in the ICU, SUPPORT (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment) (22), was a communication intervention in which a nurse tried to determine patients' desires for life-sustaining treatment and communicated those to the primary care provider. The intervention used in this study might have been more successful than that in the SUPPORT trial because it was a multidisciplinary palliative care intervention that included recommendations for symptom control and clarification of goals of care.

Quality of Care

Norton SA, Hogan LA, Holloway RG, et al. Proactive palliative care in the medical intensive care unit: effects on length of stay for selected high-risk patients. *Crit Care Med*. 2007;35:1530-5. [PMID: 17452930]

Clinical Bottom Line: Obtain palliative care consultation for patients with advanced illness who are admitted to an ICU early in their stay.

Teno JM, Mor V, Ward N, et al. Bereaved family member perceptions of quality of end-of-life care in U.S. regions with high and low usage of intensive care unit care. *J Am Geriatr Soc.* 2005;53:1905-11. [PMID: 16274371]

Question: Is greater resource utilization near the end of life associated with perceptions of better quality of care?

Study Design: Cross-sectional.

Patients: 778 contacts of deceased patients: 413 from low ICU use regions and 365 from high ICU use regions of the United States.

Setting: Hospital service areas in the highest and lowest deciles of ICU use in the United States.

Outcomes: Quality of end-of-life care measured in 5 domains: unmet needs, shared decision making between physician and patient or family, respectful treatment of the patient, attending to family needs for information, and emotional support (23). Zero was the worst possible score, and 50 was the best possible score.

Results: Contacts of patients who died in the higher utilization areas reported insufficient assistance with pain control, dyspnea relief, and emotional support. They were also more likely to report concerns with physician communication about decision making (relative risk, 1.8 [CI, 1.0 to 2.9]), that the decedent was not always treated with respect (relative risk, 1.4 [CI, 1.0 to 1.9]), that they did not know what to expect while the patient was dying (relative risk, 1.5 [CI, 1.3 to 1.8]), and less overall satisfaction with the quality of end-of-life care (rating care, on average, 2.7 points lower [CI, 0.0 to 5.5] on the 50-point scale).

Conclusion: Greater resource utilization near the end of life is not associated with perceptions of better quality of care.

Commentary: Although this study's findings support the claim that quantity of care does not improve quality of care, the study has important limitations. First, it was retrospective and relied on reports from the deceased patients' family members and friends, who may have inaccurately recalled events. In addition, proxies may not fully appreciate the distress of patients who are near the end of life. Although these data show an association between greater care utilization and lower quality of care, other attributes in these hospital service areas (such as greater fragmentation of care or a predominance of academic medical centers) may contribute to these regional differences. It is reassuring that family members in lower utilization areas did not report more concern about the amount of life-sustaining treatment used, so it does not seem that the use of these treatments in these lower utilization areas was constrained.

Clinical Bottom Line: None specifically, but greater re-

source utilization at the end of life does not correlate with perceptions of higher quality of care.

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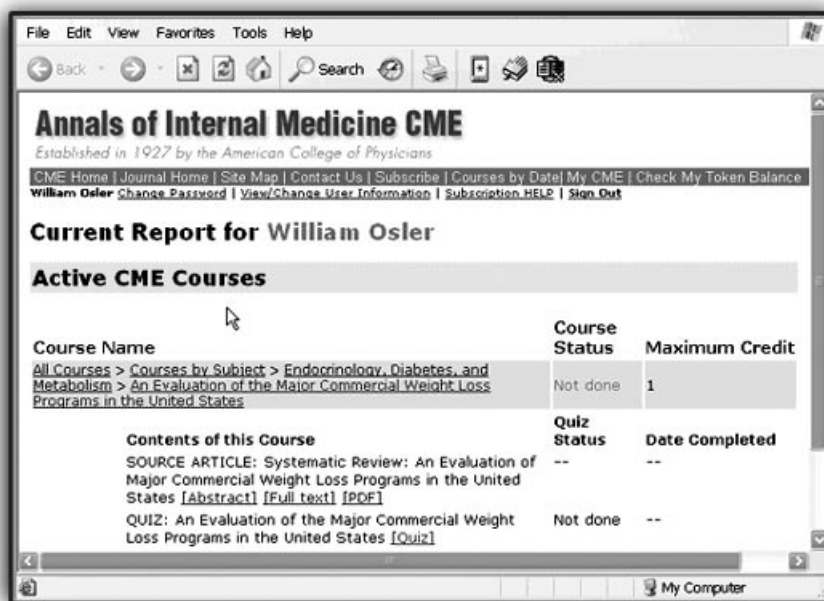
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