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Feature Editor: Mellar P. Davis, MD, FCCP, FAAHPM



PC-FACS (Fast Article Critical Summaries for Clinicians in Palliative Care) provides hospice and palliative care clinicians with concise summaries of the most important findings from more than 100 medical and scientific journals. If you have colleagues who would benefit from receiving PCFACS, please encourage them to join the AAHPM at aahpm.org. Comments from readers are welcomed at pc-facs@aahpm.org.

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Summaries With Commentaries

Why Does Chronic Neuropathic Pain Reduce Opioid Receptor Availability?

Background. Studies show reduced brain opioid receptor availability in patients with chronic pain.^{1,2} Are these changes because of the chronic pain itself or pre-existing or medication-induced differences in the endogenous opioid system?

Design and Participants. This study sought to identify the neurobiological substrate of reduced brain opioid receptor availability in chronic pain and investigated whether this change is a result of the chronic pain or pre-existing or medication-induced differences in the endogenous opioid system. A rat model of neuropathic pain (spared nerve injury [SNI]) was employed. In sham vs. SNI rats, testing for mechanical and cold sensitivity was performed presurgery, 1 week postsurgery, and 12 weeks postsurgery. Rats were tested for sucrose preference as an index of anhedonia/depression presurgery and 12 weeks postsurgery. Positron emission tomography with opioid tracer [¹⁸F]-FDPN was used (week 13), and tissue was extracted and immunohistochemically evaluated (week 14) to investigate the cellular-molecular basis of the observed changes. Analyses included Shapiro-Wilk and nonparametric Mann-Whitney U tests, one- and two-way repeated measures ANOVA, and Bonferroni correction.

Results. SNI rats (n=17) showed hypersensitivity to touch and cold (lower withdrawal thresholds vs. sham [n=17]; $P<.001$) and had lower sucrose preference ($P=.030$). SNI reduced insula, caudate-putamen, and motor cortex opioid receptor availability ($P<.01$), meaning painful neuropathy altered the endogenous opioid system. Caudate-putamen ($P=.048$) and insula

($P=.031$) mu-opioid receptor MOR1 immunoreactivity decreased with SNI (chronic pain was associated with reduced MOR1 expression), but opioid peptide enkephalin and neuron count were unchanged. SNI rat sucrose preference correlated with caudate-putamen opioid receptor availability ($P=.041$) and MOR1-immunoreactivity ($P=.017$).

Commentary. Chronic neuropathic pain can be challenging to manage and often is accompanied by negative emotions. Down-regulation of opioid receptor has been reported in chronic pain patients.³ This study used a widely accepted neuropathic pain animal model and demonstrated decreased opioid receptor expression in multiple brain sites, as opposed to concentration of endorphins or neuron density, which was proportionally associated with decreased sucrose preference, a surrogate marker for anhedonia. Decreased opioid receptor expression may likely explain, at least in part, why chronic neuropathic pain is inadequately responsive to opioid treatment. In addition, a decrease in opioid receptor expression was proportionately associated with diminished engagement in pleasurable activities, which may underpin why patients undergoing chronic opioid therapy may develop pain-induced anhedonia and depressed mood.^{4,5}

Bottom Line. In an animal model, chronic neuropathic pain results in decreased opioid receptor expression at 3 months, which was proportionally associated with decreased preference for sucrose.

Reviewer. Amy L. Davis, DO MS FACP FAAHPM, Drexel University School of Medicine, Philadelphia, PA.

Source. Thompson SJ, Pitcher MH, Stone LS, et al. Chronic neuropathic pain reduces opioid receptor availability with associated anhedonia in rat. *Pain*. 2018;159(9):1856-1866.

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Effects of Hip Fracture Surgical Repair in Nursing Home Residents With Advanced Dementia

Background. Hip fractures commonly occur among nursing home (NH) residents.^{1,2} How do outcomes for NH residents with advanced dementia and hip fracture differ based on whether they undergo surgical repair?

Design and Participants. This retrospective cohort study used nationwide Medicare claims data linked with Minimum Data Set assessments (2008-2013) to compare outcomes among NH residents with advanced dementia and hip fracture (unenrolled in hospice care) according to whether they underwent surgical hip repair. Among 6-month survivors, documented pain, antipsychotic drug use, physical restraint use, pressure ulcers, and ambulatory status were compared between groups. Analyses included multivariable Cox proportional hazards and inverse probability of treatment weighting (IPTW) adjusted for differences in prefracture characteristics.

Results. Residents ($N=3,083$; 85% underwent surgical repair) were mean (SD) age 84 (7.2) years, 79% female, 89% white, and 29% ambulatory. Mortality differences between surgically managed and nonsurgically managed residents were greatest ≤ 30 days post-fracture (12% vs. 31%), and median survival was 1.4 vs. 0.4 years, respectively. By 6-month follow-up, 32% and 54% of surgically and nonsurgically managed residents died. Nineteen percent of surgically managed residents used hospice care, vs. 34% of nonsurgically managed residents. After IPTW, surgically managed residents were less likely to die than residents without surgery (adjusted hazard ratio [aHR]=0.88; 95% CI=0.79-0.98), reported less pain (aHR=0.78; 95% CI=0.61-0.99), and had fewer pressure ulcers (aHR=0.64; 95% CI=0.47-0.86). In adjusted Cox proportional hazards models, among 2,007 6-month surviving residents, there was no between-group difference in documented pain, pressure ulcers, antipsychotic drug use, or physical restraint use. Few survivors remained ambulatory (11% of surgically managed vs. 4.8% without surgery).

Commentary. Although there appears to be important differences between the two groups, this study

offers information to facilitate thoughtful discussions regarding treatment options. This study noted survival that appears to be improved for those patients who had surgical repair; however, other factors that affect quality of life appear to be the same whether surgery is performed after 6 months or not. No matter the treatment option taken though, the high rate of death within 6 months should serve as a reminder for the importance of goals of care discussions and use of palliative and hospice services.

Bottom Line. The need to address goals of care early in the disease course as well as earlier use of hospice is key when making treatment decisions for patients with advanced dementia who sustain a hip fracture.

Reviewer. Marissa Galicia-Castillo, MD FAAHPM, Eastern Virginia Medical School, Sentara Norfolk General Hospital, Norfolk, VA.

Source. Berry SD, Rothbaum RR, Kiel DP, Lee Y, Mitchell SL. Association of clinical outcomes with surgical repair of hip fracture vs. nonsurgical management in nursing home residents with advanced dementia. *JAMA Intern Med.* 2018;178(6):774-780.

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Hospice Use and End-Of-Life Spending Trajectories in Medicare Beneficiaries on Hemodialysis

Background. The current Medicare hospice program may be underequipped to care for beneficiaries dying of conditions other than cancer.^{1,2} What are the hospice use patterns among beneficiaries on hemodialysis?

Design and Participants. This study used 2017 US Renal Data System data (Medicare Parts A and B) to determine rates and timing of hospice referral among Medicare beneficiaries with differing premorbid illness trajectories. Among beneficiaries on hemodialysis who died between 2000 and 2014, four last-year-of-life spending trajectories (T1-4) representing different care intensities were identified using group-based trajectory modeling. Characteristics and patterns of inpatient, skilled nursing facility, and hospice use (by patients within each trajectory) were described.

Results. In this study, 60,881 patients (9%) had escalating last-year-of-life spending (T1), 260,132 (41%) had relatively low spending with late escalation (T2), 236,291 (37%) had moderate

spending with late escalation (T3), and 82,162 (13%) had persistently high spending (T4). T1-4 patients were mean (SD) age 70 (12), 71 (13), 70 (13), and 67 (13) years; 52%, 56%, 51%, and 50% male; and 65%, 68%, 65%, and 59% white, respectively. Median spending was \$193,930 (T1), \$78,670 (T2), \$149,408 (T3), and \$279,321 (T4). Healthcare intensity was lowest for T2 and highest for T4. The median number of days spent in-hospital among those admitted ranged from 14 (T2; IQR=7-25) to 86 (T4; IQR=60-120). The percentages of patients enrolled in hospice at the time of death were uniformly low (19% of those with persistently high costs; 21% of those with moderate costs), and the median number of days spent in-hospice was virtually the same (5-6 days).

Commentary. This study used spending patterns of Medicare beneficiaries on hemodialysis as a proxy for clinical trajectory. Four groups were identified. Three groups had variable levels of early spending with late escalation and one had persistently high spending. Astonishingly, there was hardly any variation in low and late hospice use among groups. The Medicare Hospice Benefit does not easily encompass continued hemodialysis; however, if dollar expenditure mirrors clinical debilitation, these patients are hospice appropriate months before death. So, is hemodialysis appropriate for them? Approaches to end-of-life care for these patients may be insufficient compared to other terminal illnesses, and palliative care potentially can play a vital role in curtailing hospital days, prompting earlier hospice transition, and meeting patients' goals of care.

Bottom Line. Hospice use remained consistently low among Medicare beneficiaries on chronic hemodialysis in their last year of life. Efforts are needed to increase palliative care interventions for appropriate goals in this patient population.

Reviewers. Natalee Noche, DO, Cleveland Clinic, Cleveland, OH; Renato V. Samala, MD HMDC FACP FAAHPM, Cleveland Clinic, Cleveland, OH

Source. O'Hare AM, Hailpern SM, Wachterman M, et al. Hospice use and end-of-life spending trajectories in Medicare beneficiaries on hemodialysis. *Health Aff (Millwood).* 2018;37(6):980-987.

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Effect of Prognosis Communication in Adolescents and Young Adults With Cancer

Background. Prognostic awareness helps adult cancer patients and family members psychologically cope.¹⁻³ What preferences/experiences do adolescents and young adults (AYAs) with cancer have regarding prognosis communication with oncologists?

Design and Participants. This study (2014-2017) surveyed AYAs with cancer and their oncologists to evaluate their experiences with prognosis communication. At a large, academic cancer center, patients were asked within 6 weeks postdiagnosis to report on their preferences/experiences with prognosis communication, their beliefs about cure likelihood, and psychosocial outcomes of communication, including trust (Trust in Physician Scale), peace of mind (Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being Scale), and anxiety/depression (Hospital Anxiety and Depression Scale). Oncologists reported cure likelihood. McNemar and χ^2 tests were used as well as multivariable logistic regression.

Results. Patients ($N=203$) were age 15-17 (25%), 18-21 (21%), and 22-29 (54%) years and 87% white. Diagnoses included lymphoma (32%) and sarcoma (16%). Eighty-three percent considered prognostic information extremely/very important (no age-related difference), and 88% reported having had prognosis communication. Patients with oncologist-reported cure likelihood $\geq 50\%$ were more likely to consider prognostic information important ($P=.01$), and oncologists were more likely to discuss prognosis with these patients ($P<.001$). Patients with poorer prognoses were more likely to want additional prognostic information ($P=.008$). There were no differences by prognosis in patient reports in which oncologists volunteered prognostic information or provided written/numeric information. Patients receiving more extensive disclosure had higher odds of trust in the oncologist (odds ratio=1.30; 95% CI=1.01-1.67; $P=.05$), peace of mind (2.13; 1.29-3.51; $P=.002$), hope related to physician communication

(1.27; 1.01-1.59; $P=.04$), and lower prognosis knowledge–related distress (0.65; 0.44-0.95; $P=.03$). Depression/anxiety were unassociated with disclosure. Sixty-two percent overestimated prognosis relative to oncologists ($P<.001$); agreement was unassociated with more extensive disclosure.

Commentary. Prognosis communication in the AYA population can be challenging because parental needs may overshadow the patient's needs, and providers and families may try to protect the patient from "bad news." But this study shows that—contrary to the popular maxim—when it comes to cancer, children (or at least AYAs) really are little adults. AYAs generally desire prognostic information, with greater detail being associated with improved trust, hope, and peace of mind and lower prognosis-related distress. But the subset of patients with $<50\%$ chance of cure deserves special attention. Although most thought prognosis communication was important, nearly one-third did not, and oncologists were less likely to discuss prognosis with them. Ninety-five percent of these patients ultimately overestimated their prognosis, potentially impacting decision making.

Bottom Line. Prognosis communication generally has extremely positive effects on the AYA cancer population, and for patients with poor prognosis, tailored inquiry ("How much information do you want...") is both respectful and empowering.

Reviewer. Robert Macauley, MD FAAP FAAHPM, Oregon Health and Science University, Portland, OR.

Source. Mack JW, Fasciano KM, Block SD. Communication about prognosis with adolescent and young adult patients with cancer: information needs, prognostic awareness, and outcomes of disclosure. *J Clin Oncol*. 2018;36(18):1861-1867.

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Perceptions of Care and Support in the Intensive Care Unit

Background. Communication breakdown between clinicians and patients' surrogates in intensive care units (ICUs) may contribute to surrogates' psychological

distress.^{1,2} Can a newly developed intervention improve decision making and clinician-family communication?

Design and Participants. This stepped-wedge, cluster-randomized trial compared an interprofessional ICU team—delivered multicomponent family-support intervention vs. usual care in patients with a high risk of death and their surrogates in five ICUs. The primary outcome was the surrogates' 6-month mean Hospital Anxiety and Depression Scale (HADS) score. Secondary outcomes were the surrogates' mean scores on the Impact of Event Scale (IES), the Quality of Communication (QOC) scale (range 0-100; higher scores indicate better clinician-family communication), a modified Patient Perception of Patient Centeredness (PPPC) scale (range 1-4; lower scores indicate more patient- and family-centered care), and mean ICU length of stay (ILOS). Analyses (intention-to-treat) included Gray's semiparametric survival regression model, Student's t-test, and Pearson's chi-square test.

Results. Intervention (N=547) and control (N=873) patients were mean (SD) age 68 (15) and 63 (16) years and 53% and 46% female ($P<.05$). Intervention (N=429) and control (N=677) surrogates were mean (SD) age 57 (14) and 56 (14) years and 66% and 71% female. There was no adjusted between-group difference in the surrogates' mean HADS score or symptoms of post-traumatic stress disorder (IES). The intervention-group surrogates' mean QOC score was improved (69 vs. 63; beta coefficient=6.39, 95% CI=2.57-10.20; $P=.001$) as was the surrogates' mean modified PPPC score (1.7 vs. 1.8; beta coefficient=-0.15, -0.26-0.04; $P=.006$). Mean intervention-group ILOS was shorter (6.7 days vs. 7.4 days; incidence rate ratio=0.90, 0.81-1.00; $P=.045$).

Commentary. The psychological costs for family members during and after ICU stays is well documented. This is a well-executed multisite study with sophisticated statistical analysis of an enhanced emotional support intervention, including daily meetings with family delivered by ICU staff under the supervision of specially trained nurses. Although there were no significant differences in the primary outcome, the surrogates' burden of anxiety and post-traumatic stress disorder at 6 months, surrogates in the intervention group rated the quality of clinician-family communication during the hospitalization as well as the patient- and family-centeredness of care as significantly better. Mean length of stay in the ICU also was significantly shorter in the ICU in the intervention group.

Bottom Line. Enhancing quality of ICU staff-family communication and providing ongoing emotional support results in significantly improved perceptions

of care and communication and reduces length of stay in the ICU.

Reviewer: Ronit Elk, PhD, University of Alabama at Birmingham, Birmingham, AL.

Source. White DB, Angus DC, Shields AM, et al. A randomized trial of a family-support intervention in intensive care units. *N Engl J Med.* 2018;378(25):2365-2375.

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Analyzing the Correlation Between Pain and Common Mental Disorders

Background. Nineteen percent of the adult European population suffers from moderate/severe pain.¹ Is pain a risk factor for common mental disorders?

Design and Participants. This study investigated an association between pain and symptoms of depression/anxiety. Data were used from the baseline and 3-year follow-up timepoints of the Netherlands Mental Health Survey and Incidence Study-2, a psychiatric epidemiological cohort study among the Dutch general population age 18-64 years. Three different baseline at-risk groups were selected: (1) subjects without any 12-month mood disorder; (2) subjects without any 12-month anxiety disorder; and (3) subjects without any 12-month substance-use disorder. The Short Form Health Survey measured baseline pain severity and interference due to pain (IDP), and the Composite International Diagnostic Interview v3.0 assessed mental disorders at both timepoints. Logistic regression analyses were performed.

Results. Participants (N=5,303; 94%, 94%, and 95% were in groups 1-3, respectively) were 25% age 35-44 years, 51% male, and 29% university educated. Respondents with moderate to very severe baseline pain vs. no pain had 2X higher odds of developing any mood disorder (OR=2.10; 95% CI=1.33-3.29) or any anxiety disorder (2.12; 1.27-3.55). Respondents with little IDP vs. no pain had 2X higher odds of developing any mood disorder (1.73; 1.19-2.53) or any anxiety disorder (1.90; 1.21-2.99). Respondents with moderate to very severe IDP vs. no IDP also had 2X higher odds of developing any mood disorder (2.14; 1.30-3.54) or any anxiety disorder (1.92; 1.05-3.52). Pain was unassociated with substance-use disorders.

No interaction effects were found between pain severity or IDP and a previous history of mental disorders.

Commentary. This is a well-designed, large, population-based study that, unlike most previous studies in this field, implemented standardized interviews to evaluate pain as a risk factor for mood, anxiety, and substance-use disorders. The participants were young (only 20% age 55 years or older), well-educated (70.5% with higher secondary or higher professional education), and ethnically homogeneous (if the participants' ethnicity reflected the Netherlands' general population, 79.3% Dutch).² The association between pain and first-onset or relapse of mood or anxiety disorder was found to be proportional to the severity of the pain. When evaluating for IDP, the strong relationship persisted but, surprisingly, was not severity related. Also, since the survey questionnaire only asked about pain in the previous 4 weeks, any association with chronic pain could not be assessed.

Bottom Line. In a younger and ethnically homogeneous general population, pain seems to have an impact in the development of mood and anxiety disorders.

Reviewer. Giovanni Elia, MD FAAPM, University of California San Francisco, San Francisco, CA.

Source. de Heer EW, Ten Have M, van Marwijk HWJ, et al. Pain as a risk factor for common mental disorders. Results from the Netherlands Mental Health Survey and Incidence Study-2: a longitudinal, population-based study. *Pain.* 2018;159(4):712-718.

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Rave Reviews

Balasubramaniam M. Rational suicide in elderly adults: a clinician's perspective. *J Am Geriatr Soc.* 2018;66(5):998-1001.

Is suicide ever rational? Maybe. This article gives a framework on caring for older adults who express the desire to end their lives in the absence of a diagnosable mental illness. These older adults who are

considering "rational suicide" may have medical illnesses that affect their quality of life but are not "terminally ill" as often defined by state physician assisted death laws.

Massimo L, Kales HC, Kolanowski A. State of the science: apathy as a model for investigating behavioral and psychological symptoms in dementia. *J Am Geriatr Soc.* 2018;66 Suppl 1:S4-S12.

Apathy rarely is discussed as a problematic behavioral symptom of dementia; however, when you ask caregivers which symptoms are most distressful, apathy ranks near the top. This in-depth review discusses where we are with our knowledge of apathy and promising treatments for it.

Briscoe J, Casarett D. Medical marijuana use in older adults. *J Am Geriatr Soc.* 2018;66(5):859-863.

This is a succinct review on marijuana's clinical indications and adverse effects in older adults, including a table on the advantages and risks of various forms of cannabinoids.

PC-FACS Feedback

We appreciate your feedback. Help us help you—send your comments to pc-facs@aaahpm.org.

PC-FACS was created in 2005 by Founding Editor-in-Chief *Amy P. Abernethy, MD, PhD, FACP, FAAHPM*. The Academy is deeply grateful to Dr. Abernethy for creating this important publication and for her many contributions to the field of hospice and palliative medicine.

PC-FACS is edited by Editor-in-Chief, *Mellar P. Davis, MD, FCCP, FAAHPM*, of the Geisinger Health System, and Associate Editor-in-Chief, *Robert M. Arnold, MD, FAAHPM*, of the University of Pittsburgh Medical Center. All critical summaries are written by *Jeff Fortin, MD*. AAHPM thanks the following PC-FACS Editorial Board members for their review of the critical summaries and preparation of the commentaries:

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