AAHPM PC-FACS

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Biologic Cost of Caregiving

Biologic Cost of Caring for a Cancer Patient: Dysregulation of Pro- and Anti-Inflammatory Signaling Pathways

Background: Caring for a seriously ill family member carries psychological and physical morbidity risks. Do biomarkers of stress and inflammation occur in family caregivers of patients with cancer?

Design and Participants: Family caregivers (n = 18) of adult patients with brain cancer treated with radiation and age-matched healthy controls (n = 19) were assessed for psychological distress and mediators of systemic inflammation four times during each patient's first year of treatment. The Perceived Stress Scale (PSS) and the Center for Epidemiologic Studies Depression Scale (CES-D) were used to assess psychological distress. Hypothalamus-pituitary-adrenal axis and sympathetic nervous system activity were assessed by salivary cortisol and amylase, systemic inflammation by blood levels of C-reactive protein (CRP) and interleukin-6 (IL-6), pro- and anti-inflammatory signaling pathways by leukocyte expression of related signaling proteins, and in vitro regulation of inflammation by leukocyte glucocorticoid sensitivity. The mean age ($\pm$SD) of caregivers was 50.4 years ($\pm$3.5); 61% were female and 83% were white. Controls had similar demographics.

Results: At baseline, caregivers reported more perceived stress and depression than controls (P = .020 and P = .003, respectively). Diurnal variation of amylase declined in caregivers over the first 18 weeks, but did not decline in controls. Cortisol and IL-6 levels did not significantly differ between groups at baseline or during the study period. CRP increased in caregivers and slightly declined in controls during the study period (P = .004). Markers of proinflammatory signaling pathways declined in caregivers but increased in controls, while anti-inflammatory markers declined in caregivers, reaching a nadir at approximately 18 weeks. There was a trend toward decreased glucocorticoid sensitivity in caregivers, but not in the controls (P = .094).

Commentary: Being the family caregiver of someone with glioblastoma is stressful. This study helps us understand the level of their stress and its physiological sequelae. Previous caregiver studies, largely in dementia, have revealed wide-ranging effects on physiology, including slower wound healing, greater autonomic and neuroendocrine dysregulation, and impaired cellular immune function. The evolving field of psychoneuroimmunology has elucidated the connection between the central nervous system (CNS) and immune function. The biologic markers in this study reflect changes in the regulation of inflammatory control by the hypothalamic-pituitary-adrenal axis, which may affect processes such as the development of cardiovascular and other diseases. This study adds to a growing body of data studying the biologic effects of caregiving and concerns that it may contribute to more than just psychological duress. With estimates of more than three million unpaid caregivers for terminally ill patients in the United States, information about the health effects resulting from caregiving are of great significance.

Bottom Line: As hospice and palliative care providers, readers should be comfortable affirming for caregivers that the toll they are experiencing is real and should be taken seriously.

Reviewer: Gail Gazelle, MD FACP FAAHPM, Harvard Medical School, Boston, MA

Source: Rohleder N, Marin TJ, Ma R, Miller GE. Biologic cost of caring for a cancer patient: dysregulation of pro- and anti-inflammatory pathways. *J Clin Oncol*. 2009 May 11 [epub ahead of print]. To access the abstract of this article, link to NLM—PubMed here.

Coronary Intervention and Quality of Life

Quality of Life After Late Percutaneous Coronary Intervention Versus Medical Management for Myocardial Infarction

Background: Patients with persistent occlusion of arteries after acute myocardial infarction (MI) are at risk for impaired quality of life (QOL). Does percutaneous coronary intervention (PCI) with stenting improve outcomes? If so, at what cost?

Design and Participants: Quality of life and economic analyses were conducted in a subset of participants in the Occluded Artery Trial (OAT). OAT subjects (*N* = 2,166) were randomized to PCI versus medical therapy alone for 3–28 days post-myocardial infarction. Eligibility included stable condition and proximal occlusion an infarct-related artery with a large region at risk or an ejection fraction of less than 50%. QOL assessments were conducted at baseline and 4, 12, and 24 months post-randomization. Cardiac physical function was measured with the Duke Activity Status Index and psychological well-being was measured with the Short-Form Mental Health Inventory 5 (MHI-5). Economic analyses, confined to US participants, were estimated for up to 2 years using hospital bills and Medicare fees. Participants (N = 951) had a mean age (±SD) of 59.2 years (±1.1); 22% were female and 17.3% were non-white.

Results: A clinically marginal decrease of 3.4 points was noted in the Duke Activity Status Index for the medically treated versus the PCI group at 4 months (P = .007), with lesser differences at other time points. At 4 months, 16.5% of the medically treated versus 10.3% of the PCI group reported exertional angina (P = .01); corresponding figures for exertional dyspnea were 39.6% versus 32.4% (P = .04), 40.2% versus 30.7% (P = .006), and 35.3% versus 28.5% (P = .05), at 4, 12, and 24 months, respectively. There was no significant difference in psychological well being. The mean 2-year net cost was $7,089 greater per individual in the PCI group (P < .001).

Commentary: Given the incidence of coronary artery disease (CAD) in North America, these results are important. These authors have previously reported no difference in the primary outcome (death, re-infarction, and hospitalization for class IV failure) of the OAT trial at 4 years between these two groups, although angina as a secondary endpoint showed better results in the PCI group initially. In the present study, QOL questionnaires showed statistically insignificant differences at 12 and 24 months in physical function, mental health, angina, and dyspnea, despite significantly increased costs in the PCI group. However, at 4 months the late PCI group had better QOL scores. It would be interesting to know whether the small number of medically treated patients who subsequently had stents inserted fared better over time. Is there a subgroup who would benefit from late PCI (eg, patients with a more limited life expectancy)?

Bottom Line: Medical treatment post MI compared with late PCI saves money with a similar long-term QOL outcome. At 4 months QOL reports after receiving late PCI were better than after receiving medical therapy.

Reviewer: Alan Nixon, MB BCh BAO FAAHPM, Richmond Hospital, Richmond, British Columbia, Canada

Source: Mark DB, Pan W, Clapp-Channing NE, et al. Quality of life after late invasive therapy for occluded arteries. *N Engl J Med*. 2009; 360:774-783. To access the abstract of this article, link to NLM—PubMed here.

Occupational Therapy and Mortality

Effect of Home Intervention for Functional Disabilities on Mortality

Background: Functional disability occurs with age-related chronic illnesses and other debilitating conditions and is associated with increased mortality. Can a home-based intervention that improves function favorably impact mortality?

Design and Participants: This exploratory analysis was conducted of participants in the Advancing Better Living for Elders (ABLE) program, a randomized controlled trial of a home-based occupational (OT) and physical therapy (PT) program versus usual care for cognitively intact, English-speaking community-dwelling elders who reported one or more functional disabilities. Intervention participants received six 90-minute sessions (five were OT and one was PT) and one OT phone contact over 6 months, followed by a 6-month maintenance phase, consisting of three brief OT calls. The control group received a home safety education booklet at 12 months. Mortality risk level was calculated at baseline, using 11 items of a 12-item validated prognostic indicator and categorized as low, moderate, or high. Mortality data were obtained from National Death Index records from 2.5–5.25 years from the beginning of the study. Participants (N = 319) had an average age of 79 years; 82% were female, 62% were living alone, 53% were white, and 46% were African American.

Results: Intervention group participants had superior survival to the control group at 2 years (mortality rate 5.6% vs 13.2%; P = .02). The impact on 2-year mortality was greatest in participants at moderate risk (intervention 3.1% vs control 14.1%; P = .02). Survival advantage, although not statistically significant, continued for up to 3.5 years for the intervention group participants. There was no difference in survival between groups at 4 years.

Commentary: The ABLE intervention trial demonstrates that occupational therapy, with a limited physical therapy component, can improve function, reduce fear of falling, and enhance self-efficacy for cognitively intact but functionally limited older patients. An unanticipated benefit was a reduction in mortality for the subgroup at moderate mortality risk, persistent for 2 years, but not 4 years. Occupational therapy with goal-setting and individualized problem solving was the focus of this intervention and may be of potential benefit to individuals in other populations who are likely to have functional disabilities and an increased mortality risk, such as those receiving palliative care. Although ad hoc analysis for any subgroup should be viewed as exploratory and not generalized to other populations, this innovative intervention deserves further study.

Bottom Line: For cognitively intact elders with moderate mortality risk who have difficulty with activities of daily living, a unique program of problem solving using home-based occupational and physical therapy combined with long-term telephone follow-up may reduce mortality.

Reviewer: Laura C. Hanson, MD MPH, University of North Carolina–Chapel Hill, Chapel Hill, NC

Source: Gitlin LN, Hauck WW, Dennis MP, Winter L, Hodgson N, Schinfeld S. Long-term effect on mortality of a home intervention that reduces functional difficulties in older adults: results from a randomized trial. *J Am Geriatr Soc*. 2009; 57:476-481. To access the abstract of this article, link to NLM—PubMed here.

Pain Acceptance

Acceptance of Pain: A Study in Patients with Advanced Cancer

Background: Many people with cancer experience pain despite analgesic use. Pain acceptance, an acknowledgement of pain without directing all efforts toward controlling pain, and the refocusing of efforts toward living a fulfilling life despite chronic pain, is an important adaptation to refractory pain. Acceptance of chronic nonmalignant pain is associated with reduced levels of pain intensity, psychological distress, and catastrophizing. What factors are associated with acceptance of cancer pain?

Design and Participants: This cross-sectional prevalence study evaluated demographics, disease and treatment, pain, and physical, psychosocial, and relationship correlates of acceptance in cognitively intact outpatients with cancer pain using established, well-validated tools. Pain acceptance was measured with the 20-item Chronic Pain Acceptance Questionnaire

(CPAQ), consisting of two subscales: activity engagement and pain willingness. Activity engagement evaluates the degree to which people with pain participate in life activities despite pain. Pain willingness reflects a willingness to experience pain without controlling it. Higher scores are indicative of greater pain acceptance. Multiple linear regression models, using backward elimination, were performed with each CPAQ subscale. Participants (*N* = 81) had a mean age (± SD) of 55.2 years (±12.7). Sixty-seven percent were married, 67 participants had one or more children, 77% were Caucasian, and 83% spoke English as their primary language. Disease sites were breast (26%), gynecologic/genitourinary (22%), and gastrointestinal (21%).

Results: Individuals who scored high on the pain catastrophizing scale and parents living with children were less accepting of pain. Demographics, age, pain severity and duration, gender, treatment factors, and quality of life did not correlate with pain acceptance.

Commentary: This is the first study to show that psychological well-being is important to the acceptance of pain in cancer. Acceptance may play an important role in living with ongoing disease-related pain and completing life's goals. Acceptance was in related domains and physical functioning, which differ from chronic nonmalignant pain. The inverse relationship of pain acceptance and parenting is unique. In the child-parent relationship we can see that the impairment that pain imposes on individuals with cancer threatens a vital function and social role that provides meaning at the end of life. This study points out the importance of a biopsychosocial approach to pain management in cancer and demonstrates that determinants other than pain severity and opioid receptor agonists are responsible for individual responses to pain.

Bottom Line: Psychological catastrophizing and parenting young children are negative determinants to the acceptance of pain as a daily experience in cancer.

Reviewer: Mellar P. Davis, MD FCCP, The Cleveland Clinic, Cleveland, OH

Source: Gauthier LR, Rodin G, Zimmermann C, et al. Acceptance of pain: a study in patients with advanced cancer. *Pain*. 2009;143:147-154. To access the abstract of this article, link to NLM —PubMed here.

PC-FACS Feedback

We appreciate your feedback. Send your comments to Amy P. Abernethy, MD, FAAHPM, Editor, at amy.abernethy@duke.edu.

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American Academy of Hospice and Palliative Medicine
4700 W. Lake Avenue
Glenview, IL 60025-1485
847/375-4712 847/375-6475 Fax
info@aahpm.org www.aahpm.org

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