Clinical Digest

Oncology

Looking for Symptom Clusters

"Patients with cancer experience multiple concurrent symptoms that interact with each other and affect patient outcomes in a different way from that of single symptoms," say authors of a recent study. Study of "symptom clusters" is a new field in oncology and entails clinicians creating symptom management interventions based on holistic, integrative views rather than focusing solely on each individual symptom. Many questions exist regarding symptom clusters (including which symptoms should be included in clusters, cutoff points for symptom severity, and how clusters should be evaluated), with no clear consensus on their answers. Therefore, these authors (from the University of Manchester and the University of Stirling, both in the United Kingdom, and the Karolinska Institute, Stockholm, Sweden) sought to explore the patterns of clusters over time, their stability, the statistical strength of any given cluster, and the experience of patients who reported symptoms in their study.

To explore the development and change of symptom clusters over time, they used a longitudinal design for the study, with a time frame of 12 months from diagnosis. Shortly after cancer was diagnosed, 143 patients, who had breast, gynecologic, prostate, gastrointestinal, lung, or head and neck cancers, were recruited from a large specialist oncology hospital. Using the Memorial Symptom Assessment Scale (MSAS), patients were assessed at baseline (T1), with follow-up assessments conducted on 125 patients at 3 months (T2), on 123 patients at 6 months (T3), and on 113 patients at 12 months (T4) after diagnosis. The timings were selected to coincide with milestones in the disease trajectory, such as the initiation and the completion of treatment.

The researchers identified 6 symptom clusters at T1: a gastrointestinal cluster (symptoms of nausea, vomiting, and feeling bloated); a hand/foot cluster (symptoms of numbness/tingling of hands/feet, swelling in arms/legs); a body image cluster (symptoms of hair loss, skin changes, and a yes response to "I do not like myself"); a respiratory cluster (symptoms of shortness of breath and cough); a nutritional cluster (symptoms of weight loss, difficulty swallowing, and lack of appetite); and an emotional cluster (psychological symptoms including anxiety and depression).

A more complex picture of the clusters emerged at T2. The clusters began to show a different pattern of behavior (even though the T2 clusters were largely the same as at T1 and the core symptoms were the same), with new symptoms "entering the cluster" and reshaping it. The researchers note that symptom clusters are "dynamic constructs" that reflect complex relationships and, as such, need a degree of flexibility and inclusiveness in their definition and constructions.

They suggest defining stable clusters as those that have similar core symptoms across different times and populations. Nausea and vomiting, for example, are present in all the gastrointestinal symptom clusters described in the literature and across times, whereas the cough/breathlessness clusters, the hand/foot clusters, and the body image clusters seem to co-occur across assessment points.

Interestingly, a small fraction of the patients experienced symptom clusters at T3. This is a time, the researchers note, when most patients have completed treatments. At T4, however, at least one-quarter to one-third of patients have a "significant symptom burden." This burden has implications for quality of life, as patients learn to live with their cancer and manage several symptoms that are becoming more chronic.

Generic symptom assessments may significantly underestimate the symptom experience in patients who have multiple symptoms in the same cluster, the researchers caution. They found marked differences (scores up to 75% higher) in the frequency, severity, and distress from symptoms between those patients who experienced all of the symptoms in a cluster compared with the whole sample. It may be more helpful, they suggest, to focus symptom management interventions on those patients who have higher symptom experience scores, rather than on broader groups who have symptoms that are not interrelated.

Source: *J Pain Symptom Manage.* 2010;39(5):847–858.

Cardiovascular Disease

Silent Pulmonary Embolism: Measuring the Real Risk

Silent pulmonary embolism (PE) occurs in as many as one-third of patients with deep venous thrombosis (DVT), say researchers from Michigan State University, East Lansing, and St. Joseph Mercy Oakland, Pontiac, both in Michigan. They arrived at this

estimate, which they say is conservative, after completing a systematic review of findings from 28 published investigations.

The researchers identified and included studies if methods of diagnosing PE were described, if PE was stated to be symptomatic, and if raw data were presented. All of the studies then were stratified into 2 tiers. Tier 1 studies included those in which silent PE was diagnosed on the basis of a high-probability interpretation of the ventilation-perfusion lung scan, using criteria from the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED). Tier 2 studies included those in which silent PE was diagnosed by ventilation-perfusion lung scan, using non-PIOPED criteria.

Silent PE was diagnosed in 1,665 of 5,233 patients (32%) with DVT. Among Tier 1 studies, silent PE was detected in 703 of 2,656 patients (27%). Among Tier 2 studies, silent PE was detected in 962 of 2,577 patients (37%). The prevalence of silent PE in patients with DVT may be even higher than their review suggests, the researchers say, as many of the investigations included in their review used stringent criteria for diagnosing PE.

Silent PE was more common in patients with proximal DVT than in those with distal DVT. The researchers say that silent PE seemed to increase the risk of recurrent PE. Among patients with DVT who had silent PE, 25 of 488 had recurrent PE (5.1%). Among patients who had DVT but did not have silent PE, 7 of 1,093 had recurrent PE (0.6%). However, they have no data on the comparative risks of fatal recurrent PE in patients with silent PE.

The frequency of silent PE in patients with DVT suggests that routine screening might be helpful, the researchers say. Screening for silent PE would give a baseline for comparison with future imaging studies if the patient subsequently became symptomatic and would help prevent a misdiagnosis of failure of therapy.

Source: *Am J Med.* 2010;123(5):426–431. doi:10.1016/j.amjmed.2009.09.037.

ENDOCRINOLOGY

Glycemic Control and Depression in American Indians

In the first large-scale investigation of the relationship between depression and glycemic control in a large cohort of American Indians, researchers from MedStar Research Institute, Hyattsville, Maryland; the University of Colorado, Denver; the University of New Mexico, Albuquerque; the University of Oklahoma, Oklahoma City; and the National Heart, Lung, and Blood Institute, Bethesda, Maryland, found a positive relationship between severity of depression and hemoglobin A_{1c} (HbA_{1c}) levels.

In their cross-sectional analysis, the researchers used the Strong Heart Study (SHS), a longitudinal study of cardiovascular disease in American Indians. The researchers say the SHS provided the opportunity to examine the relationship between depression and glycemic control in a large geographically and age-diverse population (the participants of the study were from 13 American Indian communities in 3 distinct geographic areas and were all aged 15 years or older). For their analysis, the researchers used data collected during the fourth examination of the SHS, which focused on a range of psychosocial characteristics. Of the 3,665 participants of the SHS, 2,832 met inclusion criteria for the researchers' analysis.

Depression was measured by the Center for Epidemiologic Studies of Depression (CES-D) scale, a screening tool designed to measure current level of depressive symptoms and depressive affect. Diabetes was diagnosed using fasting blood glucose measures in accordance with American Diabetes Association criteria. To assess whether diabetes was related to level of depression (none, mild, moderate, or severe), the researchers used an ordered logistic regression model, while multiple logistic regression was used to explore the relationship between HbA_{1c} levels and severe depressive symptoms in participants with diabetes.

The results of the study showed that for every 1-U increase in HbA_{1c} value, the odds of severe depression increased by 22% (odds ratio, 1.22; 95% confidence interval, 1.05–1.42). Those with severe depressive symptoms had HbA_{1c} levels almost a full point higher than those with moderate-to-no depression. Women with diabetes showed higher occurrence of depressive symptoms than women without diabetes. Body mass index also was significantly associated with increased risk for severe depression, although the researchers say the magnitude of this effect was small.

They conclude that individuals with diabetes have higher rates of depression than those without diabetes, which is a finding consistent with other patient populations. They say "this relationship suggests that the interaction between glycemic control and depression may create additional challenges in managing each respective condition."

Source: *J Diabet Comp.* 2010;24(4):217–222. doi:10.1016/j.jdiacomp.2009.03.005.