

Looking Beyond Recurrence: Comorbidities in Cancer Survivors

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Cancer recurrence is a very real concern for cancer survivors. Surveillance for recurrence and vigilance for development of new cancers are top priorities during follow-up visits after active treatment ends. However, the cancer survivor also is at risk for the development of comorbid conditions. These conditions, including obesity, diabetes, dyslipidemia, menopause, decreased bone mass, hypertension, and hypothyroidism, are discussed with their relevance for general health and their relationships to disease-specific cancers. All of these conditions should be routinely addressed as part of the patient's survivorship care when appropriate. The oncology nurse is in a prime position to educate survivors about the risks for these conditions, both through evidence-based practice guidelines specific to each condition and also through the use of a treatment summary and care plan. This article discusses these selected comorbidities and offers strategies for nurses to address them with survivors during follow-up visits. Clinical practice guidelines for comorbidities are included, along with oncology implications and relevance for survivors. Recommendations for modifiable risk factors and healthy living also are included, along with Web sites for survivorship care plans.

Thanks to tremendous advances in the treatment of cancer, the number of cancer survivors continues to increase. Oncology nurses and other providers will find themselves faced with a population that is at risk for recurrence and comorbid conditions from the late effects of treatment as well as the natural effects of the aging process.

Nurses should be aware that many survivors may be so focused on recurrence that they risk neglecting other aspects of their health or may not even be cognizant of the fact they may have long-term or late effects from treatment (Hewitt, Greenfield, & Stovall, 2006). In addition, among the population of cancer survivors, those experiencing comorbid conditions report higher rates of disability and overall poorer health status than survivors who do not report comorbidities (Hewitt, Rowland, & Yancik, 2003). Therefore, as more time passes from the

At a Glance

- ◆ For many cancer survivors, the fear of recurrence takes precedence over other health concerns, including comorbidities that can have a more immediate and debilitating outcome.
- ◆ Oncology nurses can help survivors understand and manage comorbid conditions, some of which may be late effects of cancer treatment.
- ◆ A treatment summary and care plan are invaluable tools to help survivors plan for their health care from a holistic perspective.

conclusion of active treatment, the risk for recurrence decreases and the need to focus on other aspects of survivor health should move to the forefront. The purpose of this article is to provide

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oncology nurses and nurse practitioners with a background of some of the comorbidities of concern to adult cancer survivors and strategies to address them. This article will examine guidelines for more common comorbid conditions, such as diabetes mellitus, obesity, dyslipidemia, menopausal symptoms with related osteoporosis, hypothyroidism, and hypertension. Recommendations for nursing interventions, lifestyle changes, and patient education, in conjunction with reviewing survivorship care plans, will be addressed.

Definitions

Who is a cancer survivor? One of the most widely accepted definitions is from the National Coalition for Cancer Survivorship ([NCCS], 2009) which states that survivorship encompasses the time of diagnosis through the balance of life and includes family, friends, and caregivers. Although broad, this definition is particularly appropriate when discussing comorbid conditions because providers must always be aware of the risk. Comorbidities are medical conditions that exist simultaneously but independently with another condition or are two diseases that occur together (Merriam-Webster, n.d.). Hypertension and cancer often coexist and are the most frequently reported comorbid conditions in cancer registries (Jain & Townsend, 2007). Anti-angiogenic agents, such as bevacizumab, sorafenib, and sunitinib, are used for more advanced cancers in active treatment, but they also can exacerbate hypertension (Albini et al., 2010; Yeh & Bickford, 2009). Another example of a treatment-induced comorbidity is the development of diabetes from androgen-deprivation therapy (ADT) for prostate cancer (Smith, 2008). Some comorbidities may be caused by a combination of treatment and age, such as loss of bone density experienced by menopausal breast cancer survivors coupled with the use of aromatase inhibitors (Coleman et al., 2007).

Prevalent Comorbidities

Obesity

Obesity is increasing in prevalence and is associated with higher mortality rates and the risk for many health disorders, including diabetes mellitus, hypertension, dyslipidemia, coronary heart disease, sleep apnea, cancer, osteoarthritis, cholelithiasis, and impaired quality of life (Daniels, 2006; Flegal, Carroll, Ogden, & Curtin, 2010). Obesity also is a concern to cancer survivors. One study of older survivors of breast, colorectal, and prostate cancer found that, among participants, 60% were overweight and 38% were obese at baseline (Mosher et al., 2009). Ballard-Barbash and Swanson (1996) reported increased relative risks for postmenopausal breast cancer and endometrial cancer for patients with increased body mass index (BMI) and who are considered overweight or obese. To assess for a patient being overweight and obese, the National Health and Nutrition Examination Surveys (NHANES) uses BMI because it correlates with the amount of body fat (National Institutes of Health [NIH], 2000). However, it should be noted that it does not measure body fat directly or distinguish lean tissue; therefore, athletes with large muscle mass

may have a BMI that would erroneously identify them as being overweight. For adults aged 20 years or older, overweight is defined as a BMI of 25–29.9 kg/m² and obesity is defined as a BMI of 30 kg/m² or greater (Centers for Disease Control and Prevention [CDC], 2010a, 2010b; Flegal et al., 2010; NIH, 2000) (see Figure 1). Other methods of estimating body fat and body fat distribution include measurements of skin fold thickness, waist circumference, and calculation of waist-to-hip circumference ratios (Daniels, 2006; National Heart, Lung, and Blood Institute [NHLBI], 2010a).

The prevalence of obesity shows significant variation by racial and ethnic groups and age. According to CDC (2010b) estimates, the prevalence of obesity in the United States is high, exceeding 30% in most age and sex groups except for men aged 20–39 years. Among men, age-adjusted obesity prevalence was 32% overall and 37% among non-Hispanic African American men. For women, the age-adjusted prevalence was 36% overall and 50% among non-Hispanic African American women (CDC, 2010b).

In practice, BMI and waist circumference can be measured to assess for obesity and, if BMI is greater than 35 kg/m², measuring waist circumference is unnecessary (NIH, 2000). Central adiposity, defined as waist circumference of greater than 40 inches in men and greater than 35 inches in women, signifies a greater risk for diabetes, heart disease, hypertension, and dyslipidemia. Additional assessment should include age of onset, the level of motivation for losing weight, previous weight loss attempts, dietary patterns, history of exercise, current and past medications, and history of smoking cessation (Bray, 2010; NHLBI, 2010a).

One of the consequences of obesity is atherosclerotic cardiovascular disease, and patients suffering from this disease tend to have a cluster of risk factors that have been identified as metabolic syndrome. Risk factors include increased waist circumference, elevated triglycerides, reduced high-density lipoproteins (HDLs), and elevated blood pressure and blood glucose (Grundey, 2004).

Diabetes

Diabetes is a metabolic disease characterized by hyperglycemia attributable to defects in insulin resistance or action,

Classification for Body Mass Index

- Underweight: less than 18.5 kg/m²
- Normal weight: 18.5–24.9 kg/m²
- Overweight: 25–29.9 kg/m²
- Obesity (class 1): 30–34.9 kg/m²
- Obesity (class 2): 35–39.9 kg/m²
- Extreme obesity (class 3): more than 40 kg/m²

Waist Circumference

- These values signify higher risk for obesity.
 - Men: more than 40 inches
 - Women: more than 35 inches

Note. Measuring waist circumference is not necessary if a person's body mass index is greater than 35 kg/m².

Figure 1. Criteria for Diagnosis of Obesity

Note. From "The Practical Guide: Identification, Evaluation, and Treatment of Overweight Adults," by National Heart, Lung, and Blood Institute, 2010a. Retrieved from www.nhlbi.nih.gov/guidelines/obesity/practgde.htm. Copyright 2010 by the National Institutes of Health. Reprinted with permission.

secretion, or both. Insulin is a hormone that regulates the movement of sugar into cells. Defects include autoimmune destruction of the B-cells of the pancreas or abnormalities in carbohydrate, fat, and protein metabolism with deficient action of insulin on target tissues, therefore leading to deficient insulin or diminished tissue response to insulin at one or more points in the complex pathways of hormone action (American Diabetes Association [ADA], 2010b). The inability to maintain a normal glucose level can lead to long-term damage, dysfunction, and failure of many organ systems, including eyes, kidneys, nerves, heart, and blood (ADA, 2010b). Diabetes used to be classified as insulin-dependent, now called type 1, and noninsulin dependent or adult-onset, now referred to as type 2 (ADA, 2010b; CDC, 2007; Meredith & Horan, 2000). Type 2 diabetes accounts for 90%-95% of people afflicted with the disease (ADA, 2010c; CDC, 2007).

Type 2 diabetes is a combination of resistance-to-insulin action and inadequate compensatory insulin-secretory response. Autoimmune destruction of B-cells does not occur. Patients may be asymptomatic or complain of symptoms such as polyuria, polydipsia, weight loss, polyphagia, and blurred vision. Long-term complications include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of injuries, including foot ulcers and amputations; and cardiovascular, gastrointestinal, and genitourinary symptoms, including sexual dysfunction (ADA, 2010b). Incidence increases with a family history, age (people aged 40 years or older are at higher risk), obesity (particularly with central adiposity), hypertension, and dyslipidemia. Greater prevalence exists in African Americans, Hispanic and Latino Americans, American Indians, Asian Americans, and Native Hawaiians or other Pacific Islanders (American Association of Clinical Endocrinologists [AACE], 2007; CDC, 2007). Type 2 diabetes is linked to poor exercise and dietary habits and can be undetected for 10 years or longer (prediabetes); many patients have established macrovascular and microvascular complications by the time of diagnosis (ADA, 2010b). Periodontal (gum) disease is more common in people with diabetes, particularly if poorly controlled (CDC, 2007).

A diagnosis of diabetes is another strain on cancer survivors' health and may confer a risk for the development of a secondary cancer. Hu et al. (1999), based on data from the Nurses' Health Study, examined the relationship between type 2 diabetes mellitus and the risk of colorectal cancer prospectively in a cohort of 118,403 women, aged 30-55 years, who were without a diagnosis of colorectal cancer at baseline in 1976. Some of these women had type 2 diabetes at baseline and some developed it during the study. Type 1 diabetics were not included. Hu et al. (1999) reported that 892 new cases of colorectal cancer developed in these diabetic women. The relative risks were 1.43 for patients with diabetes with colorectal cancer (95% confidence interval [CI] = 1.1-1.87; $p = 0.009$) and 2.39 for fatal colorectal cancer (95% CI = 1.46-3.92; $p = 0.0005$), thus establishing increased risks for colorectal cancer in women who have diabetes. It should be noted that, although associations have been found between diabetes and breast cancer in postmenopausal women and renal cell and endometrial cancer in obese women, no clear causal connection has been established between diabetes and these cancers (Volkers, 2000).

Symptoms

- Polyuria, polydipsia, and unexplained weight loss coupled with a casual plasma glucose concentration of more than 200 mg/dl
- Fasting plasma glucose concentration of more than 126 mg/dl. Fasting is defined as being at least eight hours in duration.
- Two-hour post-challenge glucose concentration of more than 200 mg/dl during a 75 g oral glucose tolerance test

Note. The American Association of Clinical Endocrinologists does not recommend hemoglobin A1C for diagnosis, but it is used for ongoing management.

Figure 2. Criteria for Diagnosis of Diabetes

Note. From "Diabetes Mellitus Clinical Practice Guidelines Task Force. Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus," by American Association of Clinical Endocrinologists, 2007. Retrieved from www.aace.com/pub/pdf/guidelines/DMGuidelines2007.pdf. Copyright 2007 by the American Association of Clinical Endocrinologists. Adapted with permission.

Diagnostic criteria for diabetes has been updated (see Figure 2). Hemoglobin A1C is a widely used marker that reflects average glucose levels over two to three months, plays a critical role in management of patients with diabetes, and helps evaluate the effectiveness of glycemic management. However, the use of hemoglobin A1C for diagnosis is controversial. The ADA (2010b) recommends the use of hemoglobin A1C for diagnosis with standardization and certification of hemoglobin A1C assays; however, the AACE (2009) recommends using hemoglobin A1C for measurement of achieving control once therapy has been initiated, not for the initial diagnosis. Hemoglobin A1C is valid for the life of the red blood cell. For patients with cancer who may have had a transfusion, it is important to consider that the readings for hemoglobin A1C may not be reflective of the patient's true reading (Oyer, Shah, & Bettenhausen, 2006).

For patients diagnosed with type 2 diabetes, the recommended goal for hemoglobin A1C is below or around 7%. Weight loss is recommended for overweight and obese individuals, regular physical activity of 150 minutes per week, blood pressure less than 130 systolic, diastolic less than 80, low-density lipoprotein (LDL) cholesterol less than 100 mg/dl, HDL greater than 50 mg/dl, and triglycerides less than 150 mg/dl (ADA, 2010c).

A referral to an educator who specializes in diabetes self-management education also is recommended. Diabetes self-management education is the ongoing process of facilitating the knowledge, skill, and ability necessary for patients to manage their own disease. Instructors may be RNs, dietitians, or pharmacologists who are certified in national standards for diabetes self-management (ADA, 2010a; Funnell et al., 2010).

Oncology nurses should be aware of potential issues with medications that may be used to treat diabetes. Metformin's possible side effects include nausea, diarrhea, or vomiting, and may predispose patients with cancer and survivors, who are undergoing active treatment and also taking metformin, to sepsis, dehydration, or hypoxemia (Oyer et al., 2006). Metformin is contraindicated in renal failure and must be stopped for 48 hours for any iodine contrast dye studies and resumed once creatinine is normal (Oyer et al., 2006; UpToDate, 2010). All patients with diabetes who also have hypertension, including cancer survivors,

should be treated with an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker (ARB) (ADA, 2010c) because of their effectiveness in reducing the decline in kidney function compared to other blood pressure-lowering agents.

Dyslipidemia

High cholesterol is a common comorbidity among cancer survivors and may be present prior to diagnosis since one in six Americans has high cholesterol (CDC, 2009). Prostate cancer survivors using ADT are at risk for unfavorable changes in their lipid profile because ADT has been implicated in total cholesterol increase (Saylor, Keating, & Smith, 2009). A study by Van den Belt-Dusebout et al. (2007) found an increased risk for cardiovascular disease among testicular cancer survivors who had been treated with radiation and chemotherapy. Cancer survivors who have been exposed to thoracic radiation also should have routine cholesterol screening as high cholesterol may contribute to the development of cardiovascular disease in this population, even among those who received doses of less than 30 Gy (Darby et al., 2010). High cholesterol, which is defined as a fasting cholesterol level greater than 240 mg/dl, places patients at high risk for heart disease and cardiovascular complications. Well-established general practice guidelines exist for the treatment of high cholesterol that also are applicable to cancer survivors. A diagnosis of hyperlipidemia is first established with the measurement of a fasting lipid panel (National Cholesterol Education Program [NCEP], 2002). LDL cholesterol is highly correlated with coronary heart disease and is considered the first target of therapy (NCEP, 2002). An LDL of 130–159 mg/dl is categorized as borderline high; an LDL of 160 mg/dl or greater is

Total Cholesterol

- Desirable: less than 200 mg/dl
- Borderline high: 200–239 mg/dl
- High: 240 mg/dl or higher

LDL Cholesterol

- Optimal: less than 100 mg/dl
- Near or above optimal: 100–129 mg/dl
- Borderline high: 130–159 mg/dl
- High: 160–189 mg/dl
- Very high: 190 mg/dl or higher

HDL Cholesterol

- Low: less than 40 mg/dl
- High: 60 mg/dl or higher

Triglycerides

- Good: less than 150 mg/dl
- Borderline high: 150–199 mg/dl
- High: 200–499 mg/dl
- Very high: 500 mg/dl or higher

HDL—high-density lipoproteins; LDL—low-density lipoproteins

Figure 3. Criteria for Diagnosis of Dyslipidemia

Note. From “Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III),” by the National Cholesterol Education Program, 2002. Retrieved from www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm. Copyright 2002 by the National Institutes of Health. Reprinted with permission.

Lifestyle Factors

- Patients should maintain a normal body mass index and waist circumference, balancing calorie intake with physical activity.
- Sugar alcohols and non-nutritive sweeteners are safe to consume.
- Daily alcohol intake should be limited to one drink or less for women and two or less for men.
- Engage in moderate-intensity aerobic activity 30 minutes per day at least five times per week. In absence of contradictions, resistance training should take place three times per week.
- Monitor blood pressure levels.
- Manage lipid totals.
- If a smoker, attend a smoking cessation class.
- Have eyes examined annually.
- Schedule at least two dental examinations per year.

Dietary Recommendations

- Choose most of the foods you eat from plant sources.
- Include five or more fruits and vegetables per day and limit salt intake.
- Include breads, cereals that are whole grains, and high fiber. Avoid processed foods.
- Limit red meat, choose lean meat, and include omega-3 fish such as salmon or tuna.
- Choose fat-free (skim), 1% fat, or low-fat dairy products and avoid hydrogenated fats.

Figure 4. Recommendations for a Healthy Lifestyle

Note. Based on information from the American Cancer Society, 2010; American Diabetes Association, 2010a; National Heart, Lung, and Blood Institute, 2010a, 2010b; National Osteoporosis Foundation, 2008.

considered high (NCEP, 2002) (see Figure 3). For patients with borderline high cholesterol and no additional risk factors, therapeutic lifestyle changes (see Figure 4), such as increasing soluble fiber intake to 10–25 g per day and increased physical activity, should be initiated with reassessment of lipid profile after three months (NCEP, 2002). For patients with high LDL cholesterol and additional risk factors, such as hypertension, drug therapy in the form of HMG CoA reductase inhibitors (statins) or bile acid sequestrants can be initiated along with lifestyle changes. Of note, if a patient presents with high triglycerides, the first goal should still be to lower LDL cholesterol. Once that goal is met, the triglyceride level should be lowered to 150 mg/dl or less (NCEP, 2002). Patients should be instructed to take statins in the evening and report any unusual side effects such as muscle pain (i.e., myalgias) at evaluation (NCEP, 2002).

Menopause

Menopause, although a natural transition for all women, may be a concerning comorbidity to cancer survivors because it can be brought on abruptly by therapies used to treat cancer (Boekhout, Beijnen, & Schellens, 2006). The natural transition generally occurs for perimenopause around age 47, with menopause following around age 51 (Weismiller, 2009). Menopause is defined by the World Health Organization (WHO) as the cessation of menstruation for 12 months because of the loss of ovarian follicular activity (Utian, 2004). However, young female cancer survivors who have been treated with cytotoxic chemotherapies or with ovarian suppression modalities may find themselves postmenopausal without the benefit of a gradual transition. Menopause is associated with symptoms

such as hot flashes and vaginal atrophy, which can cause considerable distress.

No clear evidence-based diagnostic criteria exist for menopause. Multiple guidelines are available for the treatment of menopause-related hot flashes; however, many of these recommend hormone replacement therapy, which is contraindicated in patients with a history of or at high risk for breast cancer (AACE, 2006; North American Menopause Society, 2010). Oncology nurses may find better results with first recommending behavioral strategies such as dressing in layers, avoiding alcohol intake, and lowering room temperatures (Boekhout et al., 2006). If additional therapies are needed, trials of nonhormonal-based therapies, such as venlafaxine or gabapentin, could be considered (Loprinzi et al., 2000; Pandya et al., 2005). For the treatment of vaginal epithelial changes, patients should be counseled on the use of over-the-counter vaginal moisturizers or lubricants. Patients who do not find relief or have more severe atrophy may find benefit from a topical estrogen preparation, with the caveat that these preparations may increase serum estradiol to an unacceptably high level for women with estrogen receptor-positive breast cancer or women taking aromatase inhibitors (Ganz, 2005).

Osteoporosis and Osteopenia

Loss of bone density is a common comorbidity among cancer survivors, and the condition could affect both men and women. High-risk groups include breast cancer survivors induced into premature menopause or those taking aromatase inhibitors, prostate cancer survivors using ADT, and bone marrow transplantation survivors who underwent therapy with long-term glucocorticoids (Andriole, 2009; Ganz, 2006, 2009; Gnant et al., 2007; Stein, Ebeling, & Shane, 2007). When clinical suspicion is high for this condition, screening should proceed with a dual-energy x-ray absorptiometry (DEXA) bone density scan (National Osteoporosis Foundation [NOF], 2008). A DEXA scan is a non-invasive test that measures bone density and provides results in terms of T scores, which are comparisons to “young, normal” adults of the same sex (NOF, 2008). Osteopenia is considered a precursor to osteoporosis and is defined as a T score between -1 and -2.5 (Alexander, 2009; NOF, 2008). Osteoporosis is diagnosed at a T score below -2.5 (NOF, 2008). Guidelines have been established by the NOF for medical treatment for osteoporosis (see Figure 5), but the treatment for osteopenia is not well established. To assist with treatment decisions, the WHO developed the Fracture Risk Algorithm (FRAX) (available at www.sheffield.ac.uk/FRAX) that assesses the 10-year hip fracture risk for patients who are medication naïve (NOF, 2008). Limitations exist for the FRAX assessment, and it should be considered one part of the decision-making process when considering medical treatment for osteopenia (Alexander, 2009).

All individuals should be counseled on the importance of a daily intake of calcium, with 1,000 mg per day recommended as the minimum daily requirement. That amount increases to 1,200 mg for individuals older than 50 (National Institutes of Health Office of Dietary Supplements [NIHODS], 2009). Regular weight-bearing exercise, smoking cessation, and reduction of alcohol intake also are important nonpharmacologic measures to prevent additional bone loss (NOF, 2008). Vitamin D has

The World Health Organization has established definitions based on BMD measurement at the spine, hip, or forearm by DEXA devices.

Normal

- BMD is within 1 standard deviation of a young normal adult (T score = -1 or higher)

Low Bone Mass (Osteopenia)

- BMD is 1 and 2.5 standard deviation below that of a young normal adult (T score = -1 to -2.5)

Osteoporosis

- BMD of 2.5 standard deviation or less of a young normal adult (T score = lower than -2.5)

BMD—bone mineral density; DEXA—dual-energy x-ray absorptiometry

Note. Although these definitions are necessary to establish the presence of osteoporosis, they should not be used as the sole determinant of treatment decisions.

Figure 5. Criteria for Diagnosis of Osteoporosis

Note. From “Clinician’s Guide to Prevention and Treatment of Osteoporosis,” by National Osteoporosis Foundation, 2008. Retrieved from www.nof.org/professionals/Clinicians_Guide.htm. Copyright 2008 by National Osteoporosis Foundation. Reprinted with permission.

been established as necessary for calcium absorption and is an important contributor to bone health. Evidence is emerging that many people are at risk for deficiency, regardless of age or health status (Norman, Bouillon, Whiting, Vieth, & Lips, 2007). Prior to recommending supplementation over 400 IU per day, however, a serum vitamin D level should be drawn to establish a person’s need beyond the recommended daily allowance (Goodwin, 2009). Because the majority of osteoporosis-related fractures result from falls, nurses should evaluate risk factors for falls, including a personal history of falls, muscle weakness, gait and balance issues, visual deficits, and dehydration (NOF, 2008).

Women who have been diagnosed with osteoporosis may be treated with oral bisphosphonates or they may benefit from a once-yearly administration of zoledronic acid at 5 mg via IV (NOF, 2008). Use of zoledronic acid has led to a reduction of vertebral fracture by 71% and a reduction in hip fractures by 41% (Black et al., 2007).

Hypothyroidism

Hypothyroidism is another comorbidity of concern to cancer survivors, not only for those treated for primary thyroid cancer, but also for those who have undergone neck surgery or radiation that involves fields above the diaphragm (Bethge, Guggenberger, Bamberg, Kanz, & Bokemeyer, 2000; Miller & Agrawal, 2009). For example, damage to the vascular supply to the thyroid gland can occur during a neck dissection (Miller & Agrawal, 2009) and Hodgkin disease survivors are at an increased risk for thyroid damage from radiation therapy even when the best blocking techniques are used to shield the gland from unnecessary exposure (Bethge et al., 2000). Hypothyroidism is characterized by symptoms such as fatigue, cold intolerance, depression, and memory impairment (AACE, 2002). As these symptoms can appear in other conditions, such as diabetes or depression, the oncology nurse and nurse practitioner must carefully consider hypothyroidism (AACE,

2002). Evaluation of thyroid function is part of the workup for cancer-related fatigue (National Comprehensive Cancer Network [NCCN], 2010). Because thyroid dysfunction can develop several years after active treatment, patients should be screened for signs of hypothyroidism during every long-term follow-up visit (Smith et al., 2009). A diagnosis can be established with testing for thyroid-stimulating hormone (TSH) and free T4 levels (AACE, 2002). An elevated TSH accompanied by a low free T4 level is diagnostic criteria for hypothyroidism (AACE, 2002) (see Figure 6). Although most patients can be managed with Synthroid® (Abbott Laboratories), frequent follow-up is necessary to ensure patients reach proper TSH and free T4 levels. Individuals with preexisting cardiac or endocrine issues, suspicious thyroid physical examination findings, or who are pregnant should be referred to an endocrinologist for consultation and management (AACE, 2002). Nurse practitioners should be aware that Synthroid is one medicine that may need to be ordered as prescribed with no generic substitutions because bioequivalence is questionable (Gibaldi, 2005). Synthroid should be taken on an empty stomach without other medications or calcium-fortified orange juice for optimal absorption (Katzung, 2004).

Hypertension

Hypertension is the most common reason for physician office visits for adults in the United States, and NHANES data report a 29%–31% incidence rate, which increases with age and obesity (NHLBI, 2010b).

Treatment with targeted cancer therapies that block angiogenesis may exacerbate hypertension with acute and long-term effects on the cardiac system (Albini et al., 2010; Yeh & Bickford, 2009). Although survivors may be on active or extended treatment, clinicians who provide care for patients treated with angiogenic inhibitors should be able to identify and address the risk of developing hypertension in addition to managing patients' cancers (Izzedine et al., 2009).

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood

Elevated TSH

- Low free T4 is diagnostic of hypothyroidism.

Normal TSH

- Until late 2002, normal TSH range was 0.5–5.5.
- After 2003, AACE set the normal TSH range at 0.3–3.

Subclinical Hypothyroidism

- Thyroid TSH levels of 4.5–10 mU/L (but normal free T4)

Overt Hypothyroidism

- TSH levels greater than 10 mU/L. These patients should be treated with medication.

AACE—American Association of Clinical Endocrinologists; TSH—thyroid-stimulating hormone

Figure 6. Criteria for Diagnosis of Hypothyroidism

Note. From "Thyroid Task Force. Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hyperthyroidism and Hypothyroidism," by the American Association of Clinical Endocrinologists, 2002. *Endocrine Practice*, 8, p. 464. Copyright 2002 by American Association of Clinical Endocrinologists. Adapted with permission.

Normal

- Systolic: less than 120 mmHg
- Diastolic: less than 80 mmHg

Prehypertension

- Systolic: 120–139 mmHg
- Diastolic: 80–89 mmHg

Stage 1 Hypertension

- Systolic: 140–159 mmHg
- Diastolic: 90–99 mmHg

Stage 2 Hypertension

- Systolic: 160 mmHg or higher
- Diastolic: 100 mmHg or higher

Figure 7. Criteria for Diagnosis of Hypertension

Note. From "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7)," by National Heart, Lung, and Blood Institute, 2010b. Retrieved from www.nhlbi.nih.gov/guidelines/hypertension/index.htm. Copyright 2010 by the National Institutes of Health. Reprinted with permission.

Pressure defines normal, prehypertension, and hypertension stage 1 and 2 (NHLBI, 2010b) (see Figure 7). The benefits of blood pressure control is a 20%–25% reduction in major cardiovascular events (e.g., stroke, heart failure, myocardial infarction) (Domino & Kaplan, 2009), applicable whether patients are younger than 65 or aged 65 and older (Turnbull et al., 2008). Malignant hypertension is associated with diastolic pressure greater than 120 mmHg with retinal hemorrhages, exudates, papilledema, or encephopathy in previously normotensive patients. Hypertensive urgency is defined as diastolic blood pressure greater than 120 mmHg with no symptoms and no evidence of acute end-organ damage (Domino & Kaplan, 2009).

The pathogenesis in essential hypertension is unclear, but may be caused by increased sympathetic neural activity with enhanced beta-adrenergic responsiveness, increased angiotensin II activity, and mineral corticoid excess; family history and genetics; and environment, including sodium intake, alcohol, dyslipidemia, obesity, and drugs (Domino & Kaplan, 2009). Hypertension may be more common in patients with personality traits such as impatience (Domino & Kaplan, 2009). Secondary hypertension may be caused by renal disease, oral contraceptives, chronic nonsteroidal anti-inflammatory drugs, antidepressants, pheochromocytoma, primary hyperaldosteronism, renovascular disease, Cushing syndrome, thyroid disease, or sleep apnea (Domino & Kaplan, 2009). Proper measurement is essential and no difference has been noted if a bare arm or sleeved arm is used (Ma, Sabin, & Dawes, 2008). History and physical, electrocardiogram, complete blood count, urinalysis, routine chemistries (glucose, creatinine, electrolytes), total LDL and HDL cholesterol, triglycerides, and estimation of glomerular filtration rate should be conducted (NHLBI, 2010b).

General recommendations include lifestyle modifications during the first three months and then, if no improvement is noted, treatment with antihypertensive medications should commence. Three main classes of drugs are used for initial monotherapy: thiazide diuretics, long-acting calcium channel blockers, and ACE inhibitors or ARBs. Beta blockers are not used initially unless a specific indication is noted (i.e., a history of myocardial infarction). More than one agent is needed in some cases (e.g., an ACE or ARB with a thiazide diuretic) to obtain blood pressure levels below 140/90 or less than 130/80 if the patients is diabetic or has a history of cardiovascular disease.

Thiazide diuretics may provide a favorable effect on osteoporosis (NHLBI, 2010b).

Evidence-Based Survivorship Care

One of the recommendations from *From Cancer Patient to Cancer Survivor: Lost in Transition* (Hewitt et al., 2006) was for the development and use of evidence-based clinical guidelines for the management of the late effects of cancer and its treatment. Several sources are available for care following cancer treatment, including information from the American Society of Clinical Oncologists, the NCCN, specialty organizations such as the American Urological Association, and long-term follow-up of survivors of hematopoietic stem cell transplantation, which outline prevention and screening organized by time after transplantation (Rizzo et al., 2006). However, most oncology practice guidelines are focused on surveillance for disease recurrence. Guidelines for screening for and managing comorbid conditions may be best found outside the realm of the oncology specialty. For example, Saylor et al. (2009) stated that evidence-based guidelines for prostate cancer survivors on ADT are lacking. However, the authors did include recommendations for screening for bone loss, diabetes, and increased lipids compiled from guidelines published by nationally recognized sources such as the NOF and the American Heart Association.

With the aging of the general population, the risk increases that patients will have cancer and cardiovascular disease; yet another consideration that should be taken into account when developing clinical trials and guidelines (Albini et al., 2010). Web sites for guidelines for the comorbidities that have been discussed are included in Figure 8 and resources for care plans are included in Figure 9. These may serve as a resource for nurses in managing patients or survivors.

Diabetes

American Association of Clinical Endocrinologists
www.aace.com/pub/pdf/guidelines/DMGGuidelines2007.pdf

American Diabetes Association
www.diabetes.org/diabetes-basics/type-2

Dyslipidemia

National Heart, Lung, and Blood Institute
www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm

Hypertension

National Heart, Lung, and Blood Institute
www.nhlbi.nih.gov/guidelines/hypertension/index.htm

Hypothyroidism

American Association of Clinical Endocrinologists
www.aace.com/pub/pdf/guidelines/hypo_hyper.pdf

Menopause

American Association of Clinical Endocrinologists
www.aace.com/pub/pdf/guidelines/menopause.pdf

Obesity

National Heart, Lung, and Blood Institute
www.nhlbi.nih.gov/guidelines/obesity/prctgd_c.pdf

Osteoporosis

National Osteoporosis Foundation
www.nof.org/professionals/clinical-guidelines

Figure 8. Web Sites for Clinical Practice Guidelines

American Society of Clinical Oncologists

www.cancer.net/patient/Survivorship

Journey Forward

<http://journeyforward.org>

Lance Armstrong Foundation and OncoLink

www.livestrongcareplan.org

OncoLink—OncoLife Survivorship Care Plan

www.oncolink.com/oncolife

Figure 9. Resources for Care Plans

Oncology Nurse Role

Being diagnosed with cancer is a life-changing event. Oncology nurses may find that discussions pertaining to a patient's cancer diagnosis are an opportunity for health and well-being education beyond the cancer diagnosis, including the identification of modifiable lifestyle choices that can prevent or lessen the burden of comorbid conditions (Ganz, 2005). Nurses are a trusted resource for patients during their active treatment and can continue that role during a survivor's long-term follow-up care. *From Cancer Patient to Cancer Survivor: Lost in Transition* specifically called on oncology nurses to play a role in survivorship care (Hewitt et al., 2006). Oncology nurses need to understand and consider comorbidities during the acute, extended, and permanent seasons of survival (Mullan, 1985).

Education about comorbid conditions should begin with an assessment of the survivor's readiness to learn, and the oncology nurse may find it necessary to frame the discussion in terms of cancer prevention if the survivor is not ready or willing to discuss health issues aside from recurrence. For example, a breast cancer survivor may be so fixated on surveillance for recurrence that she may not be willing to discuss weight gain. However, to call attention to other factors, nurses could frame the discussion to reflect, for example, the fact that increased weight places survivors at increased risk for recurrence.

A tool that can assist with opening the lines of communication between a nurse and a cancer survivor is a comprehensive treatment summary and care plan (Earle, 2006). The treatment summary portion of the document details the history of the survivor's cancer therapy, including treatment exposures (e.g., chemotherapy, radiation, surgery), dates of treatment, and responses to treatment (Hewitt et al., 2006). The care plan provides a road map for follow-up care that also includes specific recommendations for cancer surveillance, preventive practices, and noncancer health care (Earle, 2006; Hewitt et al., 2006). The survivor should be encouraged to share this important document with his or her primary care provider and other specialists involved in care (Hewitt et al., 2006).

The authors hope this review of comorbidities will strengthen oncology nurses' ability to see the survivor as a whole person beyond the cancer diagnosis, and enable them to encourage cancer survivors to live well.

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