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## The Hidden Morbidity of Cancer:

### Burden in Caregivers of Patients with Brain Metastases

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## INTRODUCTION

Despite remarkable progress in cancer prevention, early detection, and treatment, many people still encounter the catastrophic experience of a cancer diagnosis. After diagnosis, patients and caregivers begin a journey on which they encounter the cognitive, psychosocial, emotional, physical, and practical consequences of the disease and its treatment. Although the diagnosis of cancer, in itself, can lead to significant changes in all aspects of patients' and caregivers' lives, the subsequent diagnosis of brain metastases can be even more devastating. Brain metastasis has an annual incidence estimated between 98,000 and 170,000.<sup>1-3</sup> It can elicit rapid deterioration in quality of life brought on by progressive neurologic deficits, which can be daunting challenges for family caregivers.<sup>4</sup> In addition, median survival between 2 and 25 months despite treatment suggests that brain metastases indicate poor prognosis and are associated with increased mortality and morbidity.<sup>5</sup>

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Recently, novel therapeutic discoveries have been shown to improve survival in a subset of patients; however, for most patients with brain metastases, palliation of symptoms, preservation of function, and maintenance of quality of life (QOL) are still considered to be the primary goals of treatment.<sup>4</sup>

Although there is a wealth of literature on the caregiving challenges associated with cancer, less is written about the caregiving challenges associated with brain metastases. This article describes some of these challenges and identifies implications of these challenges for health care professionals. Given the paucity of caregiving research in brain metastases, the discussion relies heavily on research about caregiving in general, with a particular focus on caregiving for individuals who have diagnoses associated with similar progressive neurologic deficits (eg, dementia).

## CAREGIVING BURDEN AND THE EXPERIENCE OF CARING FOR PERSONS WITH BRAIN METASTASIS

The cancer caregiving experience can be distinguished from caregiving for other chronic conditions by the rapid and unpredictable deterioration of the health of patients with cancer. Cancer is unique in that it can be marked by active disease, followed by prolonged remission that may be abruptly interrupted by recurrence, metastases, or a new primary site. In addition, cancer caregivers report spending more time in caregiving, providing higher acuity care in a shorter time frame, and being predisposed to higher financial burden than caregivers of persons with other diseases.<sup>6</sup>

From the first publications introducing the concept to the current state of the science, caregiver burden remains one of the most commonly studied variables in caregiving research.<sup>7-18</sup> Caregiver burden is defined as the cognitive appraisal of the multidimensional response to demands and their consequences within the context of an evolving caregiving experience.<sup>19,20</sup> The critical attributes of caregiver burden include subjective perception, multidimensional phenomena, dynamic change, and overload.

### Subjective Perception

Consistent with reports that the degree and kind of reaction to the stress produced by environmental demands vary among individuals,<sup>21</sup> studies show that, after controlling for patient characteristics and the type of stressors, perception of caregiver burden varies among individuals.<sup>13,22-25</sup> These findings can be linked to the varied sensitivity and vulnerability of individual caregivers to certain types of experiences and to differences in caregivers' interpretations and reactions.<sup>21</sup>

Research suggests that the dynamics of caregiving may differ by diagnosis but study results are equivocal.<sup>26-28</sup> Studies comparing caregiver burden present divergent findings, including higher caregiver burden in psychiatric illness compared with other chronic medical illness and no differences in caregiver burden for caregivers of older adults with different diagnoses.<sup>29,30</sup> Meanwhile, 2 other studies report few differences in caregiver burden by diagnosis and conclude that caregiver resources, not patient diagnosis or illness severity, are primary correlates of caregiver burden.<sup>31,32</sup>

These studies are relevant to caregiving for persons with brain metastases, suggesting that findings from research on the general caregiving population apply to caregivers of patients with brain metastases. They underscore the importance of individual difference. As Ankri and colleagues<sup>33</sup> noted, even when using valid and reliable measures, a score may not provide complete and accurate assessment because caregivers may be affected by different aspects of burden; although one caregiver may be overwhelmed with the physical demands of caregiving, another may experience emotional stress or feel socially marginalized because of the situation.

### Multidimensional Phenomena

Chou<sup>19</sup> describes multidimensional characteristics of burden in terms of outcomes; that is, caregiver burden can affect the physical, psychological, social, and spiritual domains of the caregiver. In addition, the multidimensional nature of the antecedents of burden have been explored. In cancer, variables that have been shown to affect caregiver burden include caregiver age, gender, relationship to the care recipient, length of time providing care, and care recipient tumor type.<sup>34,35</sup> In community-based caregivers (N = 92), the strongest predictors of caregiver burden were the health-related needs of the care receivers, including their behavioral and mental health problems ( $P = .01$ ). Also, 2 personal resources of caregivers (ie, having less resilience and using negative emotion-focused coping) were significantly, but less strongly, correlated with caregiver burden.<sup>36</sup>

The relationships of variables in caregiving situations to caregiver burden are described in the literature<sup>37,38</sup> for many conditions. These studies provide insight into the complexity of caregiver burden for caregivers of persons with brain metastases, a diagnosis that often implies significant physical and psychosocial burden.

### Dynamic Change

From the time of initial cancer diagnosis throughout the illness trajectory, caregivers face challenges.<sup>39</sup> Caregivers are subject to multiple transitions as they adapt to new demands brought on by disease progression, changes in physical and cognitive function, or acquisition of new debilities. Situations that may contribute significantly to caregiver burden may no longer be as stressful as the caregiver adapts and copes, but stress may increase as new problems or crisis situations arise.<sup>19</sup>

Among caregivers of persons with cancer, Kim and Given<sup>40</sup> reported that QOL varied along the illness trajectory. Caregivers of women with advanced breast cancer were more depressed (30% vs 9%;  $P = .02$ ) and experienced higher levels of burden (mean score, 26.2 vs 19.4;  $P = .02$ ) at the start of the terminal period (n = 84) than at the start of the palliative period (n = 15).<sup>10</sup> However, caregivers of patients with dementia reported fewer differences, with 98.9% reporting problems in the initial stage of dementia, 99.1% within 1 to 4 years, and 98% beyond 4 years ( $\chi^2$  test,  $P > .01$ ),<sup>41</sup> although the types of problems varied based on stage. In later stages, 49.1% experienced more problems in their social networks compared with initial stage (25.6%). Likewise, no significant differences in mental health and health-related QOL, a concept associated with caregiver burden, were found in caregivers of patients with cancer (N = 167) in the palliative and the curative phases,

respectively.<sup>42</sup> In caregivers of persons with a guarded prognosis such as brain metastases, usually identified after a sudden unexpected event (eg, severe headaches, focal weakness, gait disturbances, seizures, nausea and vomiting),<sup>4</sup> the impact of dynamic changes can be profound.

### Overload

Caregivers' responses to the caregiving experience range from low to high stress and result from an imbalance of care demand relative to resources; that is, knowledge or training, personal time, social roles, physical and emotional states, financial resources, and formal care resources.<sup>17,43</sup> Demands may come from patients, other family members, employment, or society, whereas resources may be internal or external.<sup>19</sup> The caregiving experience can create physical and psychological strain over extended periods of time and is usually accompanied by high levels of unpredictability and loss of control.<sup>44</sup> These life stressors and demands increase the risk for caregiver burden by exacerbating role conflict and disruption.

Caregivers are responsible for tasks, from managing household chores and finances to assisting with medical and personal care. For persons with brain metastases, caregivers may have been performing the tasks for some time. Caregivers of persons with brain metastases face plural challenges of living their own lives, in addition to providing physical care and extending emotional support while also coping with the anticipated decline of the patient's health.

These critical attributes, subjective perceptions, multidimensional phenomena, dynamic changes, and overload, experienced in combination, can be stressful to caregivers and can be severe enough to result in serious consequences and outcomes.

## DEMANDS OF CAREGIVING

The caregiver role is associated with many demands. For many, these demands result in caregiving burden (an incongruity between demands and the caregiver's ability to cope) and negative biopsychosocial effects.<sup>45,46</sup> These effects can be classified into primary and secondary caregiving demands, defined as stressors inherent in the caregiving situation and those that come from other areas in the caregiver's life, respectively.

### Primary Demands of Caregiving

Primary demands are dictated by the health-related needs of the care receiver. They include cognitive deficits associated with the diagnosis of brain metastases and the functional impairment observed in patients with cancer (Box 1).

**Neurocognitive impairment of care receivers**—Patients with brain cancers often endure a variety of neurologic, cognitive, and emotional problems that, even with the slightest impairment, can significantly alter QOL.<sup>47</sup> In the past, these problems have not been adequately addressed because of the dismal outcome associated with the diagnosis. However, in the milieu of improved survival with the accompanying neurorehabilitative potential of the patient, recognition of cancer-related and cancer therapy-related neurologic outcomes has recently become an indispensable step that precedes therapy selection.

Assessment and interpretation of neurocognitive function in patients with brain cancer is confounded by multiple variables that include neurotoxic effects of anticancer therapies and supportive care agents and the presence of mood disorders. In clinical trials, neurocognitive function has now been proposed as a secondary end point that can provide significant information otherwise not observed in traditional end points, including overall survival, progression-free survival, and radiographic changes. It is viewed as more than just a surrogate marker of disease response to therapy.<sup>48,49</sup> Neurocognitive assessment includes measures of general intellectual functioning (ie, intelligence quotient [IQ]), language, memory, attention, information processing speed, motor speed and dexterity, and executive functioning. In addition, self-reported measures of mood may be obtained in order to estimate the influence of depression on cognitive performances.<sup>50</sup>

Cognitive deficits create care demands for the caregivers and increase the number of tasks with which the caregiver must render assistance. Cognitive dysfunction was identified as a leading cause of disability and the single greatest cause of burden in patients with primary brain tumors.<sup>35,47</sup> Most patients with brain metastases have some degree of neurocognitive impairment, which may even be more common than functional impairment.<sup>51</sup> Mechanisms of cognitive dysfunction in brain cancers are diverse and may include direct damage caused by cancer, indirect effects of cancer (paraneoplastic syndrome), and effects of cancer treatment on the brain.<sup>51-53</sup> These causes add to preexisting neurologic and psychiatric disorders that alter the patient's cognition and mood.

It is important to highlight findings from studies that distinguish between the characteristics and outcomes of caregivers of individuals who have cognitive symptoms with different causes or whose symptoms occur during different time points during the disease trajectory. One study found that depressive symptoms were more commonly reported by caregivers of patients with dementia compared with caregivers of patients with non-dementia-related cognitive impairment.<sup>54</sup> Another study reported divergence in caregiver burden in patients with amnesic mild cognitive impairment and mild Alzheimer disease, in which burden was more severe in patients with mild Alzheimer disease.<sup>55</sup> These studies highlight the findings that multiple factors contribute to caregiver burden at different stages of the disease.

Many other studies explored the relationship between the patient's cognitive impairment and caregiver burden in a variety of diagnoses. One study reported that caregiver burden is directly associated with an increase in patients' comorbidities, independent of behavioral status, functional status, and cognitive impairment.<sup>56</sup> Compared with functional status, cognitive status is a much stronger predictor of caregiver burden in caregivers of patients with dementia according to a meta-analysis of 228 studies of the relationship between caregiving stressors, caregiver burden, and depression,<sup>57</sup> which was supported by a study in patients with Alzheimer disease.<sup>58</sup>

In a study of burden and depressive symptoms in caregivers of geriatric patients, the care recipients' mental status was almost twice as powerful in predicting caregiver burden as the care recipients' functional status.<sup>59</sup> However, in several studies of the relationship between cognitive abilities of patients with dementia and their caregivers' burden, there were either no or weak relationships between the variables. Findings from one study indicated

that cognitive impairment did not contribute significantly to caregiver burden.<sup>60</sup> However, Etters and colleagues<sup>8</sup> postulated that it may be the patients' behavioral disturbances associated with cognitive impairment that predict caregiving burden rather than the cognitive impairment.

**Functional impairment of care receivers**—Functional status is defined as an individual's ability to perform a task. Patients with brain cancer may not be able to perform activities of daily living because of neurologic disorders such as paralysis, paresis, sensory loss, blindness, decreased level of consciousness, ataxia, and headaches. These problems may be complicated by treatment-related toxicities, comorbidities, and mood disorders.<sup>35</sup>

In caregivers of patients with cancer, care recipients' functional status has been consistently reported as a common predictor of negative caregiver outcomes. However, although caring for someone with functional limitations added to burden, functional status was not as strong a predictor of burden as the care recipients' cognitive and neuropsychiatric status. In 488 family caregivers of patients with diverse diagnoses (eg, cerebrovascular, circulatory, musculoskeletal, or pulmonary disorders; fractures of hip or major limb; and cancer), the care recipient's mental status was almost twice as powerful (standardized path coefficient of  $-0.37$ ) in predicting caregiver burden as was the care recipient's functional status (standardized path coefficient of  $-0.23$ ).<sup>59</sup> Similar outcomes were reported in a study involving caregivers of patients with amyotrophic lateral sclerosis ( $N = 140$ ); behavioral changes had greater impact on caregiver burden (odds ratio of 1.4) than the level and pattern of physical disability.<sup>61</sup>

In oncology caregiving, there is a lack of information on caregiver outcomes when multiple variables (ie, alterations in functional, cognitive, and neuropsychiatric status) are examined together.<sup>62</sup> In a study of 95 caregivers of patients with primary malignant brain tumors, the patient's functional status as measured by activities of daily living (eating, bathing dressing, toileting, walking inside the house, and getting out of bed) and instrumental activities of daily living (transportation, laundry, shopping, housework, meal preparation) affected a subscale of caregiver burden but the patient's cognitive status was not associated with caregiver burden, whereas neuropsychiatric status consistently affected every subscale of caregiver burden. However, the investigators suggested that the lack of a significant relationship between the patient's cognitive status and caregiver burden might have been caused by the lack of an objective measure of cognitive status.<sup>35</sup>

Caregivers are key participants in the care of persons with brain metastases and are compelled to take more important roles compared with many other clinical situations. The additional tasks of managing the functional and cognitive deficits of the patient increase the demands on caregivers who must deal with the changes that accompany a diagnosis that is the most common neurologic complication of cancer.

### Secondary Demands of Caregiving

Family, work, and/or society contribute to the secondary demands on caregivers (Box 2). These demands come from outside the caregiving relationship between patients with metastatic brain tumors and their caregivers.

**Family**—Caregiver burden has been reported to be specifically related to multiple roles assumed by the caregiver. Family roles of caregivers directly affect their ability to take on new responsibilities and adjust to living with constant uncertainty.<sup>63</sup> The presence of young children in the household and single-parent families with a female head of household are some of the family structures that have been reported as significant predictors of caregiver burden.<sup>19</sup>

**Work**—The impact of the caregiver's employment on caregiver burden is not clear. Although it is intuitive that work outside the caregiving relationship is a competing priority for caregivers that adds to perceived caregiver burden, several studies have reported that employment or other roles outside the family may be the key to caregiver well-being.<sup>64</sup> In 205 family caregivers of hospitalized patients with cardiovascular disease who participated in a family intervention trial, time demands (38%) and work adjustments (25%) were among the most commonly reported causes of burden.<sup>65</sup>

In contrast, a cross-sectional household survey conducted among 2458 adult residents having at least 1 close relative with any chronic physical and/or mental illness revealed that employment did not significantly contribute to caregiver burden (67.1% of the 1720 who were employed full time did not perceive burden;  $P = .0747$ ).<sup>66</sup> In another study of caregivers of 7 geographically and institutionally defined cohorts of patients with newly diagnosed colorectal and lung cancer ( $N = 677$ ), 21% ( $n = 142$ ) cared for at least 1 other individual, 49% ( $n = 312$ ) were employed (including two-thirds full time), and 28% ( $n = 86$ ) of the respondents who were working either full or part time reported having difficulty balancing work and caregiving demands. In the same study, 67% ( $n = 453$ ) of caregivers faced at least 1, and 19% ( $n = 131$ ) faced 2 or more, of these additional demands, with 1 in 5 reporting poor to fair health.<sup>17</sup>

**Society**—Several studies confirmed that many family caregivers experience financial difficulties related to lost wages from reduced work hours.<sup>63</sup> However, another study revealed that very few caregivers reported financial burden and even fewer caregivers had to give up employment to continue to care for a family member.<sup>67</sup> The differences were attributed to differing health policies between the countries where the studies were conducted.

Caregivers of persons with brain metastases find themselves in an overwhelming and unpredictable role that is primarily influenced by the patient's cognitive and functional decline and aggravated by household, occupational, or societal demands. The caregiving experience presents a situation in which multiple concurrent stressful demands compete for the caregiver's attention. It is therefore important that caregivers be supported to meet the escalating demands of the caregiving experience with as little impact on their emotional and physical well-being as possible.



## CONSEQUENCES AND OUTCOMES OF CAREGIVER BURDEN

The caregiving experience is commonly perceived as chronically stressful and can lead to negative outcomes. In caregivers of patients with brain metastases, that experience begins with the diagnosis of the primary cancer and is relived on diagnosis of brain metastases.

Although the nature and magnitude of caregiver burden vary in the context of different clinical and medical diagnoses, many studies have established the negative effects associated with caregiving.<sup>13,22,68,69</sup> Although not as well documented, it is equally important to consider the reported positive effects of caregiving,<sup>44,64,70-74</sup> as well as effects not directly related to the caregiver. The indirect effects include clinical outcomes of patients (care recipients), effects on the other members of the household, and impact on the health care system in general (Box 3).

### Consequences to Caregivers

The high incidence of brain metastases resulting from improved therapy for systemic disease is contributing to the increase in the number of cancer caregivers. Historically, caregiving was considered a stressor that leads to implications, usually negative, for the caregivers' well-being. More recently, research in this tradition has evolved from an emphasis on the role-specific negative outcome of burden (eg, caretaker role fatigue, spousal burnout, and role engulfment) to more general well-being considerations, including positive psychological well-being (eg, improved relationships, and improved self-satisfaction, gratification, self-efficacy, and self-respect), negative psychological well-being (eg, depression, anxiety), and physical health and immune functioning.<sup>20,64,75-79</sup>

Results of a systematic review to identify the types of problems and burdens faced by family caregivers of patients with cancer reported that 97 of the 164 research-based studies described the physical, social, and/or emotional problems related to caregiving.<sup>69</sup> Investigators assessing the caregivers of patients with newly diagnosed colorectal and lung cancer (N = 677) reported that the relationship between objective burden and caregiver mental and physical health outcomes varied by caregiver resources. More specifically, caregivers with significant coping, social, and material resources were less likely to have deleterious consequences as a result of caregiving demands, whereas those with few resources were at increased risk.<sup>17</sup> In caregivers of patients with prostate cancer who were to begin radiation therapy (N = 60), 12.2% had clinically meaningful levels of depression, 40.7% anxiety, 15.0% pain, 36.7% sleep disturbance, 33.3% morning fatigue, and 30.0% evening fatigue. In addition, those who were older and who had lower levels of state anxiety and higher levels of depression, morning fatigue, and pain reported significantly poorer functional status ( $R^2 = 38.7\%$ ). Moreover, those who were younger, had more years of education, were working, and had higher levels of depression, morning fatigue, sleep disturbance, and lower levels of evening fatigue reported significantly lower QOL scores ( $R^2 = 70.1\%$ ).<sup>80</sup>

**Physical/physiologic/biological implications to caregivers**—The increase in the length of time providing care and the corresponding burden perceived by family caregivers of patients with brain cancers have negatively affected the physical well-being of

caregivers.<sup>79</sup> Caregivers can develop their own health problems from their caregiving responsibilities (Table 1).

Caregivers are less likely to engage in preventive health activities and have a higher risk of contracting serious illnesses.<sup>81</sup> Approximately 50% of caregivers report at least 1 chronic condition, 20% describe their health as fair or poor, and 17% think that their health has deteriorated as a result of caregiving.<sup>81-83</sup> Older spousal caregivers who reported caregiver stress had a 63% higher mortality than noncaregivers of the same age.<sup>84</sup> In addition, data obtained from salivary biomarkers of caregivers of patients with cancer has shown marked changes in neurohormonal and inflammatory processes within the year of the cancer diagnosis<sup>85</sup> whereas a more recent study found higher levels of proinflammatory cytokines in male caregivers with anxiety, in obese caregivers who reported higher burden from disrupted schedules, and in younger caregivers with low self-esteem.<sup>79</sup>

**Psychological/emotional implications to caregivers**—The confounding problems, including fear, uncertainty, and lack of hope, that accompany the diagnosis of cancer continue to surround patients and caregivers throughout the continuum of care.<sup>39</sup> These psychological responses may be heightened on receiving a diagnosis of brain metastases. On the grounds that cancer caregiving has the features of a chronic stress experience,<sup>44</sup> it can be expected that the most common and severe health effects of caregiving are found within the psychological and emotional domains.

In caregivers of individuals with schizophrenia, the psychological impact of traumatic experiences from the patient's violent behavior was significantly associated with caregiver burden ( $P < .05$ ).<sup>86</sup> A systematic review of 164 research-based studies of family caregivers of patients with cancer identified more than 200 problems and burdens related to caregiving responsibilities, with social and emotional implications as the most frequently studied categories.<sup>69</sup>

The National Alliance for Caregiving<sup>87</sup> reported a link between caregiving and higher rates of insomnia and depression, with rates reported as high as 91% for depression, of which 60% was rated as moderate or severe. In addition, a high prevalence of psychological distress in caregivers has been documented in caregivers of patients with cancer in Italy, where more than half scored positive in screening for mood disorders, more than 10% experienced severe levels of posttraumatic stress disorder, and 37% scored positive for clinically relevant emotional disturbance.<sup>88</sup>

Results from a cross-sectional, descriptive, and correlational study involving 410 caregivers recruited from the community indicate a high level of burden and depression among all caregivers. Significant differences ( $P < .001$ ;  $F = 26.11$ ) between the 3 caregiving groups (Alzheimer disease, cancer, schizophrenia) were detected in terms of burden, with the highest reported for Alzheimer disease caregivers. One-way analysis of variance showed significant differences ( $P = .008$ ;  $F = 4.85$ ) between the 3 caregiving groups in terms of depression, with the highest depression levels being for cancer caregivers.<sup>89</sup>

Caregivers of terminally ill patients with cancer in Taiwan showed the dynamic change and multidimensional attributes that can also be observed with the consequences of caregiver burden. In that study, caregivers' depressive symptoms increased as the patients' deaths approached. Adult children or spousal caregivers experienced more depressive symptoms if they self-identified as lacking social support and confidence in offering substantial assistance for younger terminally ill patients with cancer with higher levels of symptom distress. Likewise, the study reported that caregivers were susceptible to higher levels of depressive symptoms if they were heavily burdened by caregiving; that is, experienced more disruptions in schedules, greater health deterioration, stronger sense of family abandonment, and lower caregiver esteem.<sup>90</sup>

**Social implications to caregivers**—The cancer experience can significantly affect the social well-being of caregivers. For caregivers of patients with brain metastases, the uncertain disease trajectory containing a variety of distressing events presents a unique challenge. Caregivers have trouble balancing their work and family responsibilities and many have to adjust their work schedules, take leaves of absence, or reduce work hours as a result of care responsibilities.<sup>91</sup> Caregivers may have to spend their own money to take care of their sick family members. The average out-of-pocket expense for caregivers in 2007 was \$5531, which is approximately 10% of the annual household income for more than 40% of caregivers in the United States. The cost did not include the loss of salary, benefits, and the reduction in retirement savings and social security benefits.<sup>81</sup>

A 2012 study of caregivers of patients with lung cancer (N = 74) reported that close to three-fourths (74%) had 1 or more adverse economic or social changes, such as disengagement from most of their regular social and leisure activities and hours of work lost caused by the illness.<sup>92</sup> The investigators further reported that 16 was the average number of hours of work lost each week because of the illness (standard deviation, 13; range, 1–50). In addition, 28% of the caregivers (n = 21) reported that their families lost their major source of income or made a major change in plans that included delaying medical care for another family member or altering educational plans (22%) because of the high cost of the illness.<sup>92</sup> Nearly one-fifth (18%) of caregivers reported losing most or all of the family savings and another 18% indicated that a family member made a major life change (eg, quit work) to care for the patient.<sup>92</sup>

In a similar study of 70 caregivers of patients in palliative care, Mazanec and colleagues<sup>93</sup> reported that the overall work productivity loss in their sample was 22.9%, which was slightly higher than the number (20.1%) previously reported by Giovannetti and colleagues.<sup>94</sup> This study also found associations between greater work productivity loss and higher levels of depression and anxiety, and greater perceived caregiver burden related to financial problems, disrupted schedule, and health problems.<sup>93</sup>

### Consequences to Care Receivers

Although most studies on cancer caregiving focus on either patient or caregiver outcomes, addressing each as separate individuals, a few studies explored caregiver-patient dyads and dyadic outcomes.<sup>6</sup> This focus is of particular importance to caregivers of patients with brain

metastases because of the multiple assaults to the physical and mental health of both the patient and the caregiver. Despite their good intentions and hard work, caregivers can place their family members at risk if they lack the knowledge and skills to perform their work or if they engage in harmful behaviors, intentional or unintentional, because of their lack of capacity to provide the level of care that is needed.<sup>95</sup> Studies in noncancer caregiver–care-receiver dyads have documented that depressed caregivers are more likely to engage in neglect or abusive behaviors.<sup>96</sup> In a systematic review of risk factors for elder abuse among community-dwelling elders, caregiver burden was a risk factor in 3 studies of elders requiring assistance with daily activities and in 4 studies of elders with dementia.<sup>97</sup> Studies have also linked cognitive behavioral problems of care receivers with an increased risk for abusive behaviors by the caregivers.<sup>98,99</sup>

The stressful work associated with caregiving can increase the risk of the caregiver engaging in harmful behaviors toward the care recipients. In addition, caregiver burden can affect patient outcomes. The National Alliance for Caregiving reported that one-half of caregivers thought that the decline in their own health compromised their ability to provide care for the care recipient.<sup>81,82</sup>

### **Consequences to the Family**

Cancer significantly affects the entire family and is not an isolated experience for 1 individual.<sup>100</sup> The stress of caring for a relative with cancer can create new conflicts or can bring long-standing unresolved family issues to the surface. Conflicts arise when patients and caregivers avoid discussion of sensitive issues surrounding the cancer diagnosis and its treatments. Barriers to communication and negotiation of family roles hinder the caregivers' and the patients' abilities to support one another, decrease spousal intimacy, or have a detrimental effect on marital and family relationships.<sup>101</sup>

Family caregivers assume more load when they assume the responsibilities of the sick family member in addition to their own. It has been reported that primary caregivers need not only the assistance of family members but their expressed encouragement and appreciation as well.<sup>8</sup> Family conflicts have also been found to be predictors of caregiver depression but, on a positive note, prior good family dynamics have been associated with significantly less caregiver burden.<sup>8</sup> It may be that positive family support can be an important resource to caregivers in mitigating some of their perceived burden.

### **Consequences to the Health Care System**

Brain metastases are 10 times more common than primary brain tumors and have been reported in as many as 40% of patients with systemic cancer.<sup>4,102,103</sup> With the increase in the number of patients with brain metastases comes a corresponding increase in the number of caregivers. Although the role of caregivers has been well recognized, most health care systems have yet to develop a formal process to integrate caregiver health into their structures. Caregiver burden has been associated with the caregiver's own poor health status, a decrease in health maintenance behaviors, and increase in health-risk behaviors and prescription drug use.<sup>81,95</sup> In terms of use of acute care services, investigators studying caregivers of patients with Alzheimer dementia reported that 24% of the caregivers (N =

153) had at least 1 emergency room visit or hospitalization in the 6 months before study enrollment.<sup>104</sup> In addition, caregivers who reported higher levels of burden had a higher Framingham Stroke Risk and an increased all-cause mortality risk.<sup>81</sup>

Family caregivers constitute the foundation of the long-term care system and although many studies have reported on the negative impact of caregiver burden on the health care system, family caregiving can also have a positive impact on health care expenditure. Family caregiving saves billions of dollars that would otherwise be required for long-term hospitalization and care.<sup>19</sup> The Association of American Retired Persons estimated that the economic value of unpaid contributions of family caregivers was approximately \$450 billion in 2009.<sup>105</sup>

**Caregiving at the end of life**—Although a subset of patients benefit from novel treatments, cure remains an unrealistic expectation for most patients with brain metastases.<sup>4</sup> Multiple prognostic models predicting the overall survival of patients with brain metastases reiteratively report a median survival of 2 to 7 months,<sup>106</sup> and, because of this, the diagnosis of metastatic disease is often considered an eligibility criteria for admission to hospice (University of Texas Health Sciences Center San Antonio, [[http://geriatrics.uthscsa.edu/tools/Hospice\\_eligibility\\_card\\_\\_Ross\\_and\\_Sanchez\\_Reilly\\_2008.pdf](http://geriatrics.uthscsa.edu/tools/Hospice_eligibility_card__Ross_and_Sanchez_Reilly_2008.pdf)], Hospice and Palliative Care of Greensboro [<https://www.hospicegso.org/wp-content/uploads/2013/07/AdmissionCriteriaBooklet-8-2013.pdf>], Optum [<https://campaign.optum.com/hospice/clinical-professionals/hospice-eligibility.html>], Hospice of the Valley [<https://www.hov.org/hospice-eligibility-guidelines>]). In contrast with the traditional health care delivery model, which is centered on patients' individual needs, hospice provides support with the patient and the family as the unit of care.<sup>107</sup> However, referral to hospice typically occurs very late in the dying process and whether patients and caregivers receive hospice support depends on many things, including patients', caregivers', and health care providers' preferences for aggressive treatment.<sup>108</sup> Hence, these individuals often deal with end-of-life issues before hospice care is even offered as an option.

When caregivers of patients with brain metastases transition from usual care provided in hospitals and ambulatory care settings to the specialized end-of-life care, they receive minimal preparation and limited information from health care providers.<sup>109,110</sup> The lack of preparation and limited information are reflected in the themes that emerged from a qualitative study exploring caregivers' perspectives in providing end-of-life care. In the study, caregivers described end-of-life care as unpredictable, intense, and complex, but at the same time profoundly moving and affirming.<sup>110</sup>

## IMPLICATIONS FOR PRACTICE

It is worth noting that caregivers have regular interactions with the health care system but may not receive the attention they need.<sup>111</sup> Caregivers who continue to suffer in silence as they juggle the tasks and prioritize the needs of the patients, and those who knowingly suppress their needs so as not to contribute to the guilt or remorse of patients with cancer over being the cause of the burden, can be helped by comprehensive and holistic care provided by those same health care systems. Stakeholders need to develop a plan to

integrate the care of caregivers into formal health care systems in cancer care. Clinicians and researchers need to work together to create an infrastructure for more comprehensive caregiver surveillance at national and/or state levels.

Although routine interactions between patients and providers that are focused on an integrated care is the cornerstone of quality comprehensive care, the well-being assessment of family caregivers is currently not considered standard of care. In the age of precision medicine, the care of the caregiver is several years behind the powerful advances in the diagnosis and treatment of cancer. Clinicians need to identify the factors that cause burden, relationship conflicts in the patient-caregiver dyad and among other members of the household, and financial toxicity in caregivers of patients with cancer. More importantly, clinicians need to provide an individualized plan of care for caregivers, including respite for caregivers, supplemental services, and interventions to reduce burden and improve health.<sup>111</sup>

## SUMMARY

Caregiving is a highly individualized experience, as seen in caregivers of patients with brain metastases. Whether expressed or implied, the responsibilities they take up on assuming the caregiving role place additional demands that the caregivers must adapt to and cope with. Although some demands of caregiving are more likely to increase caregiver burden, every caregiver has a different threshold and the variation in responses are as diverse as the characteristics of caregivers.

What is unique about the features of caregiving in patients with brain metastases that would warrant the development of a program of research that does not duplicate the work already done with other caregiver populations? As described in previous articles, improving long-term survival of patients has corresponded with an increased incidence of brain metastases. This sequence of events in the trajectory of patients with cancer has extended the length of the caregiving experience. In addition, the universal concerns about disease recurrence or progression that are unique to cancer predispose patients and the caregivers to uncertainty and stress. Likewise, the diagnosis of cancer takes the patients and their caregivers through a journey that winds through unique stages: initial diagnosis, treatment, survivorship, recurrence, progression, and end of life. The route that patients with cancer and their caregivers take can put them on a direct path to remission or end of life, but can also maneuver them on a path that circles through these stages. In addition, developments in cancer research have increased the complexity of cancer treatment because new therapies, devices, and clinical trials are now available to patients when, only a years ago, options for further treatment did not exist. All these contribute to the demands placed on the patients and their caregivers.

This article describes the challenges of caregiving in brain metastases. It reviews the critical attributes of caregiver burden: subjective perception, multidimensional phenomena, dynamic change, and overload. These attributes have been examined in many caregiver studies within a variety of diagnoses and health conditions. It also describes the demands of caregiving, classifying them into primary and secondary demands, with primary demands being dictated by direct health-related needs of the care receiver and secondary demands being

determined by factors outside the environment of the caregiver-patient dyad (ie, family, work, and society). In addition, it presents the consequences and outcomes of caregiver burden. Although the article mostly describes the negative consequences of caregiving, it acknowledges the growing body of work highlighting positive outcomes and more general well-being considerations for individuals in the caregiving role.

Caregiver burden is an important component of comprehensive and holistic clinical care. It is a consequence of a process that involves several interrelated conditions within the caregiving experience. As health care providers prepare to care for an aging population, and with advancing age being a known risk factor for cancer, it becomes increasingly important to address the needs of caregivers, in effect the other patients, who are at an increased risk for various psychological, physical, financial, and social problems.

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**Box 1****Primary demands of caregiving****Neurocognitive impairment**

- Patients with brain cancers often endure a variety of neurologic, cognitive, and emotional problems.
- Assessment and interpretation of neurocognitive function in patients with brain cancer is confounded by multiple variables.
- Neurocognitive assessment includes measures of general intellectual functioning (ie, intelligence quotient [IQ]), language, memory, attention, information processing speed, motor speed and dexterity, and executive functioning.
- Cognitive dysfunction has been identified as a leading cause of disability and the single greatest cause of burden in patients with primary brain tumors.
- Mechanisms of cognitive dysfunction in brain cancers are diverse and may include direct damage caused by cancer, indirect effects of cancer (paraneoplastic syndrome), and effects of cancer treatment on the brain.

**Functional impairment**

- Patients with brain cancer may not be able to perform activities of daily living because of neurologic disorders such as paralysis, paresis, sensory loss, blindness, decreased level of consciousness, ataxia, and headaches.
- Care recipients' functional status has been consistently reported as a common predictor of negative caregiver outcomes.
- Functional status was not as strong a predictor of burden as the care recipients' cognitive and neuropsychiatric status.

*Data from Refs.*<sup>35,47,50-53</sup>

**Box 2****Secondary demands of caregiving****Family**

- Family roles of caregivers directly affect their ability to take on new responsibilities and adjust to living with constant uncertainty.

**Work**

- Work outside the caregiving relationship can contribute to either increased caregiver burden or improved caregiver well-being.

**Society**

- Health and labor policies have been shown to differentially affect caregiver financial burden.

*Data from Refs. <sup>63,64,67</sup>*

**Box 3****Consequences and outcomes of caregiver burden****Consequences to caregivers**

- Caregiving research has evolved from an emphasis on the role-specific negative outcome of burden to more general well-being considerations, including positive psychological well-being, negative psychological well-being, and physical health and immune functioning.
- Caregivers can develop their own health problems from their caregiving responsibilities.
- Caregivers have been reported to be less likely to engage in preventive health activities and are at a high risk of contracting serious illnesses.
- Most common and severe health effects of caregiving are found within the psychological and emotional domains.
- Caregivers have to adjust their work schedules, take leaves of absence, or reduce work hours as a result of care responsibilities.
- Caregivers may have to spend their own money to take care of their sick family members.

**Consequences to care receivers**

- Caregivers can place their family members at risk if they lack the knowledge and skills to perform their work or if they engage in harmful behaviors, intentional or unintentional, because of their lack of capacity to provide the level of care that is needed.

**Consequences to the family**

- The stress of caring for a relative with cancer can create new conflicts or can bring long-standing unresolved family issues to the surface.

**Consequences to the health care system**

- Caregiver burden has been associated with the caregiver's own poor health status, a decrease in health maintenance behaviors, and increase in health-risk behaviors and prescription drug use.
- Family caregiving can also have a positive impact on health care expenditure.

*Data from* Refs. 19,20,64,75-79,81,91,95

**KEY POINTS**

- The cancer caregiving experience can be distinguished from caregiving for other chronic conditions by the rapid and unpredictable deterioration of the health of patients with cancer.
- Caregivers of persons with brain metastases find themselves in an overwhelming and unpredictable role that is primarily influenced by the patient's cognitive and functional decline and aggravated by household, occupational, or societal demands.
- Although many studies have established the negative effects associated with caregiving, it is equally important to consider the reported positive effects of caregiving, as well as effects not directly related to caregivers.



**Table 1**

Most common aspects of caregiver health that have deteriorated as a result of caregiving (n = 528)

<b>Symptom</b>	<b>Frequency (%)</b>
Energy and sleep	87
Stress and/or panic attacks	70
Pain, aching	60
Depression	52
Headaches	41
Weight gain/loss	38

*Data from* Evercare in collaboration with National Alliance for Caregiving. Evercare study of caregivers in decline: A close-up look at the health risks of caring for a loved one. Evercare, Minnetonka, MN and NAC, Bethesda, MD; 2006.

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