



COMMENTARY

Long-COVID and long-term cancer survivorship—Shared lessons and opportunities

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Abstract

As of 2022, close to 90 million persons in the United States, 243 million persons in Europe and 585 million worldwide have been infected with the novel SARS-CoV-2 (COVID-19) virus and survived. Estimates vary but suggest that up to 50% may experience long-term sequelae, termed 'Long-COVID'. While Long-COVID is a new condition, the phenomenon of disabling long-term effects following an illness requiring ongoing surveillance and management is not. In this commentary, we discuss how Long-COVID parallels the experiences of long-term cancer survivors, highlight shared challenges and offer opportunities to improve research and clinical care for both growing populations of patients as well as other long-term chronic, disabling conditions.

KEYWORDS

cancer, cancer survivorship, COVID-19

1 | INTRODUCTION

As of 2022, close to 90 million persons in the United States, 243 million persons in Europe and 585 million worldwide have been infected with the novel SARS-CoV-2 (COVID-19) virus and survived (World Health Organization, 2022). Estimates vary, but studies in the United States and Europe show that up to 53% of these individuals have or are experiencing prolonged and late effects from the acute infection as far as 12 months after the onset of their initial COVID-19 symptoms (Boscolo-Rizzo et al., 2021). The global prevalence of these conditions is estimated to be 43% of patients (Chen et al., 2022). Further, 32.9% of post-COVID-19 patients report fair or poor general health, compared with 25.4% of non-COVID controls (Rogers-Brown et al., 2021). The individuals with post-COVID conditions are commonly referred to as experiencing Long-COVID, long-haul COVID, post-acute COVID-19, long-term effects of COVID, post-COVID condition, or chronic COVID (Centers for Disease Control and Prevention, 2022; Kluge et al., 2022). In this commentary, we will refer to this condition as Long-COVID.

Long-COVID is defined as a condition where individuals experience at least one symptom that develops during or following infection by COVID-19 and which continues for more than 28 days (Nalbandian et al., 2021). Symptoms range from mild to debilitating, with more severe symptoms being directly correlated with greater severity of the infection phase, as measured by number of symptoms present during infection, admission to an intensive care unit or receiving supplemental oxygen (Boscolo-Rizzo et al., 2021; Nalbandian et al., 2021). Even young and previously healthy individuals with mild COVID-19 infection experience Long-COVID symptoms, with about 20% of cases occurring in adults ages 18 to 34 (Tenforde et al., 2020; Vehar et al., 2021). Evidence suggests that children experience long-COVID, in up to 25%, with mood symptoms (16.5%), fatigue (9.7%) and sleep disorders (8.4%) as main clinical manifestations (Lopez-Leon et al., 2022). Up to 44.1% of patients experiencing Long-COVID have reported a decline in quality of life (Nalbandian et al., 2021) that may persist for 2 years following diagnosis as found in a recent European study (Kluge et al., 2022). In an analysis of private healthcare claim records of nearly 2 million COVID-19 patients, 23.2% sought medical

attention for at least one Long-COVID condition 30 days or more after the initial diagnosis (Fair Health, 2021). These numbers indicate that a growing population of individuals will require long-term medical surveillance and care.

While Long-COVID is a new condition, the phenomenon of disabling long-term chronic disease resulting from prior acute and resolved illness, including virus-borne infections such as HIV, Lyme disease, among others requiring ongoing surveillance and management, is not. This phenomenon also parallels the experiences of long-term cancer survivors, whose cancers may be cured or in remission, but have ongoing late and long-term impairments. The number of cancer survivors in the United States is more than 18 million and 12 million in Europe, and these numbers are expected to increase with almost 50% by the year 2030 (European Commission, 2022; Miller et al., 2022). Cancer survivors have high burden of medical and psychosocial impairments, which leads to detriments in quality of life, employment and other outcomes (National Academies of Sciences, Engineering, and Medicine, 2021). Late and long-term effects are particularly prevalent among childhood cancer survivors, whereby 40% experience at least one severe, disabling, life-threatening or fatal chronic health condition at 30 years from diagnosis (Landier et al., 2015). In total, it is estimated that 40% of individuals who have survived cancer experience long-term or late effects from the disease or accompanying treatment regimen (Magasi et al., 2022).

In this commentary, we discuss how Long-COVID parallels the experiences of long-term cancer survivors, highlight shared challenges and offer opportunities to improve research and clinical care for both growing populations of patients as well as other long-term chronic, disabling conditions.

1.1 | Symptoms, conditions and functional impairments

The symptoms reported by patients with Long-COVID have considerable overlap with those experienced by cancer survivors. Figure 1. Fatigue is most prevalent among both long-term cancer survivors and those with Long-COVID (National Academies of Sciences, Engineering, and Medicine, 2021; Vehar et al., 2021). Fatigue among those with Long-COVID is debilitating and interferes with daily activities including work (Davis et al., 2021). Similarly, studies of cancer survivors who were employed at the time of their cancer diagnosis have found that, on average, 27% did not return to work 2–14 years post-diagnosis (de Boer et al., 2020).

Neurologic, cognitive and psychological impairments are also frequent in both groups. Up to 25% of cancer survivors demonstrate cognitive impairment on a neuropsychological exam, (National Academies of Sciences, Engineering, and Medicine, 2021) usually manifesting as lapses in memory, declined speed of processing and deficits in executive functioning. When self-reporting, 81% of patients with Long-COVID reported experiencing cognitive dysfunction with the most common symptom referred to as ‘brain fog’ (Graham et al., 2021). In addition, many patients suffer psychologic and psychiatric impairments, with depression and anxiety being most common (Graham et al., 2021). Sleep disturbances have also been commonly described and are associated with decreased daytime functioning and distress (Graham et al., 2021). These psychologic and psychiatric impairments are characteristic across chronic/long-term illness including cancer, heart disease and diabetes (Turner, 2000). Further, patients with many chronic conditions face uncertainties about

Psychological

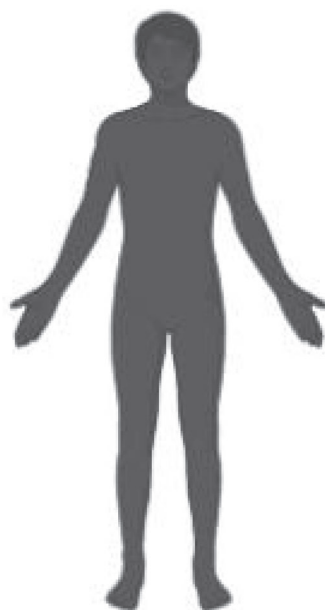
Anxiety
Depression
Fatigue
Post-traumatic stress disorder
Sleep disturbances

Cardiovascular

Arrhythmias
Congestive heart failure
Myocarditis
Vascular/clotting disorders

Pulmonary

Dyspnea
Cough
Lung scarring/fibrosis



Neurologic/Sensory

Cognitive impairment/“brain fog”
Loss of taste and/or smell
Neuropathy
Pain

Musculoskeletal

Muscle weakness
Myalgia, pain
Decrease in bone density
Cachexia

Gastrointestinal

Chronic diarrhea

FIGURE 1 Shared persistent, chronic symptoms/conditions among patients with Long-COVID and long-term cancer survivors. Symptoms may present as single impairments or clusters and may vary in severity across the disease trajectory. Factors including comorbidities, age, gender, and treatment received play a role in the profile of these symptoms in individuals. The list provides examples and is not inclusive of all symptoms/conditions.

prognosis of their illness, as well as severity of symptoms. In all, assessment of individuals' needs, and tailored provision of psychological support, with referral to specialised mental health, as well as financial, vocational and/or other resources, is critical.

While not as prevalent as the psychosocial effects, long-term cancer survivors and patients with Long-COVID experience cardiovascular, pulmonary, sensory and musculoskeletal impairments (Nalbandian et al., 2021; National Academies of Sciences, Engineering, and Medicine, 2021; Vehar et al., 2021). These symptoms and conditions are often accompanied by functional impairments requiring rehabilitation. Symptoms such as nausea and loss of smell or taste among those with Long-COVID can also cause significant impairment to lifestyle and quality of life and may be associated with poor appetite and weight loss. These symptoms are not uncommon among long-term survivors of head and neck cancer (Alfaro et al., 2021).

In both populations, symptoms and impairments may present as single entities or as clusters, can be chronic or transient and may vary in severity across the disease trajectory. When co-occurring, these tend to cause compounded effect on health (Nalbandian et al., 2021). Further, in both Long-COVID and long-term cancer survivors, several factors including comorbidities, age, gender, genetics and treatment received at the time of illness play a role in the development and/or exacerbation of the impairments (National Academies of Sciences, Engineering, and Medicine, 2021; Yong, 2021). As is the case in psychologic impairments where conditions are experienced by those who suffer from other chronic illness, a reference point for management is available (Turner, 2000). Further research into the pathophysiology of symptoms and management efforts will provide greater knowledge for the strategizing of care plans. The shared lessons and collaborative efforts among researchers across Long-COVID and cancer survivorship can advance our understanding and care for these patients as well as others with disabling, chronic conditions.

1.2 | Diagnosis and attribution of symptoms

The identification of patients with long-term, chronic conditions that are linked to a primary disease is challenging. While the diagnosis of cancer is itself not subject to doubt, a direct link between cancer and its treatments with potential symptoms and/or conditions may not be possible. Similarly, in many patients experiencing symptoms suggestive of Long-Covid, a clear causal relationship between infections (e.g., confirmed positive test for the SARS-CoV-2 virus during acute infection) is often lacking (Shah et al., 2021). As the pandemic continues, patients may not pursue testing and/or more currently rely on home testing, thus limiting formal confirmation of disease and its associated impairments. Such difficulty attributing symptoms can lead to frustration by patients and lack of management clarity for health-care professionals. In Long-COVID and cancer survivors, late and long-term associated symptoms and conditions are believed to result from several mechanisms including organ damage incurred from the disease itself and a persistent hyperinflammatory state (Baig, 2020; Nalbandian et al., 2021; National Academies of Sciences, Engineering,

and Medicine, 2021; Raahimi et al., 2021; Sigal, 2021; Yong, 2021). While persistent COVID-19 treatment-related effects are yet unknown, like for cancer therapies, these may be further elucidated over the years to come. In both populations, the development and severity of persistent effects are variable and often unpredictable, thereby requiring a similar approach to research and guidance for identification, diagnosis, management and follow up care of patients.

1.3 | Attention to the patient experience and empowering self-advocacy

Since symptoms in Long-COVID and long-term cancer survivors are variable and direct links to the primary disease are often difficult to make, objective measures alone may not be sufficient. Therefore, clinicians may need to acknowledge and validate patients' symptoms and concerns absence of a clear link. Paralleling the cancer survivorship advocacy movement (Clark & Stovall, 1996), patient advocacy groups for Long-COVID have been newly created and have played important roles in identifying symptoms and influencing research and clinical attention (Nalbandian et al., 2021). Facilitating patient self-management, for both Long-COVID and long-term cancer survivors, can be effective and has become increasingly important in the wake of substantial backlogs in care created by the COVID-19 pandemic (Howell et al., 2021). Moving forward, a similar approach of working closely with patient advocacy groups and returning agency to the patient is an opportunity for advancing long-term health care for both populations.

1.4 | Rehabilitation and secondary/specialty care

For Long-COVID and long-term cancer survivors, rehabilitation is effective in re-establishing patient autonomy and social reintegration, as well as managing long-term impairments. Given the large number of factors playing into the manifestation of multi-system symptoms, it is vital for care teams to be interdisciplinary, and approach care holistically. However, important components of holistic care, most notably, rehabilitation, are not received by many long-term cancer survivors who may benefit from such approaches (Stout et al., 2019; Wade, 2015). More recently, rehabilitation has become increasingly emphasised in cancer survivorship programmes (Stout et al., 2019). For Long-COVID, a focus to develop specialised centres aiming to grow expertise in rehabilitation for Long-COVID patients is suggested (Wade, 2020). As with cancer survivors, to ensure optimal rehabilitation care for patients that need it, early recognition and referral to collaborative, interdisciplinary teams for Long-COVID are recommended (Barker-Davies et al., 2020). For both populations, these teams should include experts in rehabilitation medicine, mental health experts, social workers and financial advisors (Coletta et al., 2020; Greenhalgh et al., 2020). While the potential burden on the rehabilitation system by patients with Long-COVID may further reduce capacity to care for long-term cancer survivors, it is our hope that the expansion of

rehabilitation clinical and research efforts for Long-COVID will result, through collective learning and collaboration, to advances in rehabilitation for cancer survivors.

1.5 | Behavioural strategies and interventions

Pre-morbid lack of physical activity is associated with increased risk for severe COVID-19 (Sallis et al., 2021), likely a result of well-established exercise benefits to the immune system (da Silveira et al., 2020). A recent small randomised controlled trial documented improved symptoms with a 2-week exercise intervention (Mohamed & Alawna, 2021). For patients experiencing conditions of chronic fatigue, personalised managed programmes of exercise may be beneficial but need further studies of validation as exercise has also been demonstrated to cause a relapse in Long-COVID symptoms (Castro-Marrero et al., 2017; Davis et al., 2021). Similarly, a diet characterised by healthy plant-based foods was associated with lower risk and severity of COVID-19 (Merino et al., 2021); obesity is a recognised risk factor for COVID-19 severity. Taken together, exercise and diet are health behaviours that have the potential to alter outcomes of COVID-19 infection. Similar data exist to support the use of exercise and diet to improve symptoms and outcomes for cancer survivors, as noted by well-established guidelines and expert survivorship initiatives from the United States and from European countries including the American College of Sports Medicine, the American Cancer Society, the Netherlands Comprehensive Cancer Organization (IKNL) and the National Cancer Survivorship Initiative in the United Kingdom (Campbell et al., 2019; Netherlands Comprehensive Cancer Organisation, 2011; Richards et al., 2011; Rock et al., 2022). Smoking cessation is critical for both populations. We acknowledge that differences in health behaviours are closely linked to structural inequities and social determinants of health and that to help achieve these goals, focus on equitable access to food, exercise and other resources is needed. These behavioural strategies have positive physical effects but may also have important psychological benefits in that they empower individuals and re-establish their autonomy in managing long-term, chronic conditions.

1.6 | Role of telehealth, models of care and risk stratification

The COVID-19 pandemic has boosted the use of telehealth, as a method of engaging with patients, managing their health and education (Monaghesh & Hajizadeh, 2020). Telehealth can also promote coordination of multidisciplinary teams that are needed to manage the patients with Long-COVID and likewise allow for education of health-care professionals regarding the consequences of COVID-19 infection and resulting rehabilitation needs. It is important to acknowledge that telehealth may promote disparities; hence, careful utilisation of technology in managing patients is needed. Future research may help elucidate when and how telehealth may be used in assessing and managing patients with Long-COVID and long-term cancer survivors.

Methods to proactively stratify long-term cancer survivors based on risk of late effects, identifying those with existing late effects, and developing personalised risk-stratified plans to prevent and/or mitigate untoward outcomes, has been proposed for decades (Alfano et al., 2019). Yet, research into this area remains elusive. As with cancer long-term cancer survivors, efforts to develop risk-stratified pathways of care may be beneficial. Models of care research in cancer survivorship, including the role of primary and secondary/specialty care, can also inform Long-COVID (Chan et al., 2021). Specifically in cancer rehabilitation, a prospective surveillance for rehabilitation in breast cancer proposes ongoing assessments over time to address long term effects of treatment (Stout et al., 2012). Additional approaches for Long-COVID may include decision support pathways and algorithms, as developed for cancer survivors, to the most appropriate type and setting for rehabilitation care, ranging from acute inpatient rehabilitation through community-based exercise programmes (Covington et al., 2021; Stout et al., 2020).

1.7 | Shared pathophysiology and ‘dual survivors’

A challenge to caring for patients suffering from the late and long-term effects of cancer and COVID-19 is the uncertainty in the aetiology and prognosis of symptoms. Research into the pathophysiology may help inform science in both fields. For example, the role of inflammatory cytokines has been examined in their relation to cognitive impairment in COVID-19 (Remsik et al., 2021) and cancer-related fatigue (Jager et al., 2008). A novel and unique case for shared learning may be found in ‘dual survivors’ or those individuals with history of COVID-19 and cancer. Cancer as a comorbidity substantially increases the risk of hospitalisation and death when compared with cancer-free patients (Carreira et al., 2020). While the risk of poor COVID-19 outcomes among long-term cancer survivors has not been elucidated, the concomitant risk factors due to pre-existing chronic medical conditions related to prior chemotherapy and radiation therapy (e.g., cardiomyopathy, coronary artery disease and pulmonary fibrosis, immunosuppression due to prior bone marrow transplant or splenectomy) are likely to place dual survivors at elevated risk. Interestingly, a recent study of childhood, adolescent and young adult survivors found no increase in risk for COVID-19 and severe complications (Gupta et al., 2022). Identifying and caring for such individuals will likely present further challenges as cancer survivors may also have pre-existing symptoms, such as neuropathy, musculoskeletal deconditioning, among others with resultant functional impairments that put them at higher risk for Long-COVID and related sequelae. Data regarding the risk factors and outcomes of patients with cancer who have been diagnosed with COVID-19 can be further explored in newly developed COVID-19 registries (Desai et al., 2021). Longitudinal studies will need to be conducted in order to advance our knowledge about the pathophysiology, prognosis, health care delivery approaches, including the similarities and differences between cancer survivorship, long-COVID survivorship and other chronic diseases.

2 | CONCLUSION

In summary, all around the world, COVID-19 has led to major changes in our health care systems, has shifted the ways that health care is provided and presents an opportunity to rethink strategies and approaches to caring for patients with chronic, disabling conditions (Box 1). Long-COVID care, as a new phenomenon, can learn from research and practice which has developed over for many decades for long-term cancer survivors—who have been burdened with many similar ongoing symptoms and functional impairments. On the flip side, the tremendous investments made in Long-COVID care and the rapid implementation of telehealth may hold valuable lessons for cancer survivorship research and practice.

BOX 1: OPPORTUNITIES FOR LONG-COVID, CANCER SURVIVORSHIP AND OTHER CHRONIC, DISABLING CONDITIONS.

Long-COVID care, as a new phenomenon, can learn from research and practice, which has developed over for many decades for long-term cancer survivors, as the two populations share similar, ongoing symptoms and functional impairments. Further, due to the significant scientific and financial investments being made in aetiology, treatment and the rapid implementation of telehealth, Long-COVID may bring valuable lessons for cancer survivorship research and practice. These advances can also help advance care for other chronic, disabling conditions. Future steps include the following:

1. Continue research into the pathophysiology of chronic, disabling long-term physical and psychological conditions such as those experienced by cancer survivors and those with Long-COVID.
2. Conduct research and evolve health care delivery to provide the needed primary care, secondary/specialty, rehabilitative and psychological support for patients with existing chronic, disabling conditions.
3. Test and implement models of personalised care, using telehealth if appropriate, taking into account individuals' medical history, comorbidities, functional status and capacity for self-management.
4. Work closely with established and emerging patient advocacy groups to create integrated, holistic care teams that provide targeted and tailored services to patients in need.
5. Facilitate patient self-management and understanding by increasing public awareness of long-term conditions.

CONFLICT OF INTEREST

The authors disclose no conflicts of interest.

DATA AVAILABILITY STATEMENT

Not applicable, no new data was generated.

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