

Review Article

Addressing the disparities and the factors related to prolonged inpatient length of stay for solid tumor oncology patients during the COVID-19 pandemic: A narrative review

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Abstract

Solid tumor oncology treatments are primarily performed in the outpatient setting. However, hospitalizations are inevitable due to complications of cancer and treatment-related toxicities. With rising health care spending, the length of hospital stay (LOS) is increasingly considered a proxy for healthcare costs. There are several ongoing efforts to abbreviate the inpatient LOS and ensure a safe and timely discharge to the outpatient setting. In addition to the acute illness and the associated comorbidities, various factors affect the LOS: social determinants of health (SDOH), nutritional status in cancer patients, and end-of-life issues. Furthermore, it is unclear how the institutional policies on social distancing and visitation during the current coronavirus disease (COVID-19) pandemic may impact the LOS. The purpose of this article is to review various factors and barriers that lead to longer LOS for solid tumor patients during the COVID-19 pandemic, and identify the critical areas of quality improvement.

Introduction

Although most solid tumor oncology patient care is delivered in the outpatient setting, hospitalizations are inevitable through the disease course. An estimated 15% of patients enter intensive care units (ICU) [1]. Although hospital LOS varies across geographic locations, and cancer type, several other key factors also play a role. These include barriers related to the social determinants of health (SDOH) (i.e., transportation, housing situation), nutritional factors, the need for inpatient treatments/procedures, coordination of palliative care consults and hospice placement. Historically, hospital facilities and providers have been equipped with a systematic approach to hospital course. However, due to the unprecedented influence of the COVID-19 pandemic, obstacles to caring for oncology inpatients have been growing, and it has been quite challenging for caregivers to work while maintaining social distancing requirements [2,3].

Furthermore, during the pandemic, rapidly evolving institutional policies on visitation restrictions during the hospitalization are prolonging inpatient length of hospital stay (LOS), especially when patients need a suitable rehabilitation facility or a skilled nursing home after discharge [2]. For example, when unable to care for a patient at home, patients' families and their caregivers often opt for a nursing home discharge. However, the accepting facilities may have restricted policies such as only one visitor per day or none, in which case patients remain in the hospital until a suitable facility is found, thus leading to an extended LOS [3]. Other factors contributing to prolonged inpatient LOS include delays in coordinating home health services for patients needing management of surgical drains, colostomy, and catheters (gastrostomy tube, suprapubic catheters, fistula drains), and wound care [4]. The risk of nosocomial spread of COVID and heightened mortality in vulnerable inpatients

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is also of concern in this setting [5]. As inpatient care for critically ill cancer patients is an ever-evolving process due to the complexities of medical issues in cancer patients, effective hospital admission and discharge process must be in place at a systems' level, and timely discharge planning is crucial especially given the current pandemic situation [3,6]. In this narrative review, we will highlight the various factors related to longer LOS and identify the key areas of quality improvement. We will additionally discuss various barriers related to SDOH and their influence on hospital LOS for oncology patients, briefly comment on the impact of the COVID-19 pandemic on LOS, and share our perspectives addressing this unmet need.

Overall hospital length of stay and geographic variations in the U.S.

The average LOS refers to the average number of days patients spend in the hospital [7]. LOS is measured by dividing the total number of days stayed by all inpatients during a year by the number of admissions or discharges, reflecting overall reduced cost for shorter LOS vs. longer inpatient LOS [7,8]. The hospital's length of stay index (LOSi) is an aggregate of the LOS compared to the risk-adjusted predictor [9]. For example, LOSi can be either >1 or <1 , depending on whether the actual LOS is longer or shorter than expected [9].

LOS can also vary across different socio-demographic regions, income status, comorbidities, and patients' underlying medical conditions. In a review by Freeman, et al., a total of 35.7 million hospital stays were documented in the year 2016, contributing to a cost of over \$417 billion, with a mean cost of \$11,700 per stay [10-12]. The authors reported higher rates of hospital stay for the East South Central census division of U.S. (121.3 per 1,000 population), rural areas compared to metropolitan areas with the highest in East South Central division (142.9 per 1,000 population), and among the uninsured ranging from 1.7% in New England to 8.1% of stays in the West South Central division [10]. Geographically, while the West North Central division had the highest rates of hospital stay for children, the East South-Central division had the highest rates of hospital stay for adults. When LOS was evaluated based on income level, patients in the lowest income level had a 20% higher rate of hospital stays compared to their counterparts, with the highest discrepancies being in the New England (133.2 vs. 99.9 per 1,000 population) and South Atlantic regions (129.4 vs. 97.4 per 1,000 population). In their report, Freeman et al. also evaluated the relationship between payer type and LOS. Although the public payers (Medicare and Medicaid) consisted of the main payer types nationally during the hospital stay (62.7%), others included private insurance (30.1%) and uninsured (4.2%), with a variation in LOS for the underinsured in New England (1.7% of stays) compared to (8.1%) in West South Central region. Although the Mountain and Pacific regions had lower LOS regardless of the income

status, nationally, higher LOS reported among the low-income group suggests other barriers to hospital LOS [10].

Hospital length of stay and the financial toxicity for cancer patients in the U.S.

Inpatient LOS also varies by the cancer type [13-15]. Although most oncology care is provided through outpatient settings, LOS varies for patients with various solid tumor malignancies, as reported by Frédéric, et al. [13]. In their analysis, between 2008 and 2018, the average LOS was shorter for breast cancer (2.7-4.8 days) and prostate cancer (3.5-4.5) [13]. Frédéric, et al., and other investigators also reported a longer average LOS for colorectal and lung cancer in the years 2008 to 2013 ((8.1 -7.4 days), and (6.3-5.8 days) respectively) [13-15]. The economic burden of hospitalized patients is higher in oncology patients given the intricacies of the disease and treatment, compared to non-oncology inpatients (controls). Suda, et al. conducted a retrospective case-control study from October 2002 through September 2003, to further explore the cost of LOS, using a medical cost accounting database from a larger tertiary hospital [16]. Compared to controls, cancer patients were older (mean 64.4 years \pm 12.9 vs. 62.4 \pm 16.7), used hospice services frequently (2.8% vs. 0.3%); $p < 0.05$, and had a higher total hospital, medication, and surgery costs ($p < 0.001$) [16].

An additional and unfortunate aspect of caring for these patients is the presence of disparities across the cancer continuum. These include race, socioeconomic status (SES), presence vs. absence of healthcare insurance, and healthcare access, are associated with high costs to inpatient and outpatient cancer care and outcomes. Whittle, et al. evaluated the inpatient LOS and hospitalizations cost among childhood cancer hospitalizations across Medicaid or commercial insurance payer types and reported longer LOS for Medicaid payer type [17]. Hispanic ethnicity was associated with a higher cost of hospitalization regardless of payer, and among the Medicaid populations, the black race was associated with higher costs during the hospitalization, emphasizing the need for further evaluation and intervention [17]. These studies reflect additional hospital costs and financial strain on patients from low socioeconomic communities.

Social Determinants of Health (SDOH) and the impact on LOS

Neighborhood factors. Although less commonly addressed at the health systems' level, the barriers and factors related to SDOH play a significant role in an individual's overall wellbeing in the outpatient setting and inpatient LOS [18,19]. A strain on factors related to SDOH, i.e., financial resources, optimal housing situation, neighborhood factors, food insecurity, transportation, limitations on physical activity level, lead to delays in timely screening and diagnosis; these barriers also lead to delayed medical appointments and treatment [20-23]. There is a paucity of literature evaluating



the role of SDOH in hospital LOS for cancer patients, but multiple investigators explored the general predictors such as neighborhood factors that may influence LOS [24-26]. Ye, et al., analyzed U.S. National data from the 2012 Area Health Recourse files, from over 3,148 counties, and reported the factors associated with LOS: urban vs. rural areas, poverty rate, presence of health insurance. In their analyses, the authors implied that access to healthcare promotes timely treatments, and the disadvantaged populations have reduced rates of timely care, emergency room visits, including preventive screening [24,25]. After adjusting for other factors, not surprisingly, the presence of health insurance at the hospital bed capacity was found to be the strongest predictor of LOS ($p = 0.002$) [25].

Socioeconomic status. Although not specific to cancer, the impact of SES on the severity of the disease and the risk of ICU treatment was reported by Bein, et al. [26]. The investigators examined SES related to disease severity at admission, duration of mechanical ventilation, and LOS at an academic tertiary care center in Germany. Patients with low SES had a higher risk of ICU admission (≥ 5 days, multivariate-adjusted OR 1.99, 95% CI 1.06-3.74; $p = 0.036$), and the authors concluded that SES is inversely related to hospitalization and LOS [26]. Additional studies of this nature are invaluable in cancer care.

Behavioral and sociocultural factors. Behavioral factors such as smoking also impacted the hospital LOS [27]. Sari, et al. evaluated the effect of smoking on hospitalization costs in lung cancer patients. At a tertiary hospital in Iran, the investigators examined a patient cohort of 415 lung cancer patients and their smoking habits concerning hospital LOS. Compared to nonsmokers, the LOS for current and former smokers was 72% and 31% higher, and so were the hospitalization costs (48% and 35%), respectively [27]. Furthermore, the lack of social connections, housing instability, and psychological impact of quarantine and decreased physical activity during the pandemic has impacted patients' and healthcare providers' mental health [6,28]. While addressing all the barriers related to SDOH will undertake a massive infrastructure and resources, at a systems level, additional emphasis and ongoing patient education and emphasis on physical activity [29], awareness of the benefits of balanced nutrition [30], and minimization of access to alcohol outlets will improve health behaviors will be invaluable in rapid recovery from an illness [31].

Physical activity. Level of activity is essential in the outpatient but also the inpatient setting. Patients' level of activity and postoperative recovery was evaluated by Ahn, et al. in a randomized clinical trial (RCT), evaluating the impact of low to moderate intensity postsurgical exercise on LOS and postoperative recovery for colon cancer patients [32]. In a study cohort of 31 patients, patients were randomized to exercise group vs. usual care. The mean hospital LOS was

7.82 days \pm 1.07 days for the exercise group compared to 9.86 \pm 2.66 days for usual care (mean difference, 2.03 days; 95% CI, 3.47-0.60 days, $p = 0.005$) [32]. To improve the level of physical activity and in preparation for hospital discharge, currently, many institutions involve physical therapy (PT) services throughout the hospitalization. P.T.'s determination of discharge disposition is crucial, as reported by Shoemaker et al. In their retrospective review of 322 patients at a large tertiary hospital, only 2 of 287 patients (0.70%) with at least one inpatient P.T. visit returned to the emergency department after a hospital discharge, suggesting the priority of P.T. assessment in hospital discharge process [33].

Impact of the COVID-19 pandemic on the mental health of patients and providers. In the inpatient setting, providers, are often provided with limited resources to address sociocultural issues. However, during the COVID-19 pandemic, the lack of social connections, housing instability, and quarantine's psychological impact has impacted both patients and healthcare providers' mental health [6,28]. Providers experience increased stress around the risk of contracting the virus and spreading it to family members, as well as the increased burden of inpatient care [6]. A review of quarantine and isolation's psychological impact found that patients and providers experienced similar mental health consequences during periods of quarantine, such as depression, anxiety, distress, and insomnia [6]. While this area remains unexplored, taken together, addressing mental health issues in a systematic method will ensure an easier outpatient transition and prevent readmissions in our patients.

Influence of age, race, gender, and comorbidities in Hospital LOS

Geriatric oncology patients. Disparities related to various demographic factors such as age, race, and comorbidities play a vital role in LOS for hospitalized patients, yet these are somewhat less addressed in the inpatient setting. In addressing the mortality associated with LOS in older adults, Shayne et al. conducted a retrospective study using a university health systemic consortium database that consisted of 386,377 patients ≥ 65 years of age with solid tumors across 133 U.S. academic medical centers from 1995-2003 [34]. Higher mortality was correlated with longer LOS: overall mortality was 7.3% among the older patients, a two-fold increase in death with LOS ≥ 10 days ($p < 0.0001$). The authors reported that 38% of older cancer patients who died in the hospital had curable disease. The malignancies associated with higher inpatient mortality included; central nervous system cancers (OR = 1.81; 95% CI, 1.59-2.07), esophageal (OR = 1.74; 95% CI, 1.54-1.97), and lung cancer (OR = 1.57; 95% CI, 1.43-1.72). While it is unknown that geriatric oncology patients may have their challenges, disparities among older adults from vulnerable communities need additional evaluation and interventions wherever



possible. African American race, Hispanic and Asian race/ethnicity, and male gender were associated with a higher risk of mortality ($p < 0.0001$) [34].

Despite the widespread prevalence of psychiatric disorders in cancer patients and the detrimental effects of depression and coping on survival, these issues are not consistently addressed among older adults with cancer [35]. Existing data suggest psychiatric morbidity like adjustment disorders, mood disorders, anxiety, and delirium correlates with prolonged LOS, thus underscoring the need for early recognition and effective treatment [36]. The psychological wellbeing of the caregivers caring for elderly cancer patients has been addressed in several studies, demonstrating caregiver fatigue, anxiety, and the challenges of the end-of-life decision-making process [37].

Impact of nutritional status and body mass index

Malnutrition in cancer patients. Malnutrition frequently occurs among cancer patients, and it can be a critical factor in discharge planning [38]. In a meta-analysis by Baldwin, et al., the authors examined 13 randomized controlled trials (RCTs) and identified 1,414 patients with cancer who were either malnourished or at risk of malnutrition and receiving oral nutritional support compared with routine care. Although nutritional supplementations showed no significant weight gain or energy intake after adjusting for the primary sources of heterogeneity ([38], nutritional intervention demonstrated benefits in the QOL but did not affect mortality (relative risk = 1.06, 95% CI = 0.92-1.22, $p = 0.43$) [38]. Other ongoing concerns include low caloric intake due to cancer-induced cachexia, swallowing difficulties due to anatomical constraints in the head and neck, and upper G.I. cancers [39,40]. Additionally, cancer therapy-induced toxicities of radiation and chemotherapy such as mucositis and diarrhea are common, leading to nutritional depletion [41,42]. Furthermore, malnutrition is prevalent among the elderly. D'Almeida et al. evaluated the prevalence of malnutrition among hospitalized elderly patients across 44 institutions in Brazil [43]. A Mini Nutritional Assessment -Short Form (MNA-SF) [44] was administered to 3061 older patients within two days of admission. Authors reported the rates of nutritional status and the LOS: 3.4% of patients were malnourished (inpatient LOS, 7.07 ± 7.58 days), 39.3% were at risk for malnutrition (LOS 5.45 ± 10.73), and 27.3% had normal nutritional status (LOS 3.9 ± 5.84).

On the contrary, patients with higher body mass index (BMI) often have issues of airway resistance, restrictive/obstructive ventilatory patterns, hypoxia, and respiratory failure [45]. In this context, worsening of the disease and prolonged LOS is anticipated. These patients need to be closely monitored and work in conjunction with a nutritionist to address the high BMI [46]. Obesity as a risk factor for hospitalization during the COVID-19 pandemic was described by Bellini, et al. Using the Istituto Superiore

di Sanita Tuscany COVID-19 database, the authors conducted an observational study evaluating the role of obesity as a risk factor hospitalization during the COVID-19 pandemic [47]. Of the 4481 subjects included in their cohort (36.9% aged over 70 years), 1907(42.6%) were admitted to the hospital, and the association of obesity higher for hospitalized patients (OR: 2.99 (ci 95% 2.04-4.37)) [47]. Based on the data mentioned earlier, BMI and nutrition status must be addressed in an outpatient setting upon hospital discharge. Optimal nutrients' intake is emphasized for the optimal immune function to protect against viral infections, especially during the COVID-19 pandemic [48]. Nutritional deficiencies are common in cancer patients undergoing chemotherapy and various procedures, and providers should have an open dialogue with patients in addressing these [49].

End of life decisions and trends in aggressive treatments for terminally ill patients

The use of palliative care in outpatient and inpatient settings is crucial in cancer patients [50,51]. Previous studies reported disparities in end-of-life decisions across multiple cancers. Rosenfield, et al. reported disparities in inpatient palliative care use in patients with gynecologic cancers. In a nationwide inpatient sample of 67,947 patients, the authors evaluated the factors associated with the use of inpatient palliative care. While the use of palliative care was increased from 2% to 10% in 2011, in a subset analysis, only 23% of patients who died in the hospital used palliative care. The demographic factors of patients who received palliative care included, older adults (age ≥ 63 median, odds ratio (OR) = 1.52, 95% confidence interval (CI): 1.36-1.70; $p < 0.0001$), and black race (OR = 1.22, CI: 1.08-1.39; $p < 0.01$) [50]. In a separate National Cancer Database (NCDB) study, Islam, et al. analyzed the racial and ethnic disparities in palliative care use among gynecologic patients. The authors reported an overall increase of palliative care use from 2004 (4%) to 2015(13%), non-Hispanic (NH) blacks (aOR: 0.87, 95% CI: 0.78-0.97) and Hispanic patients (aOR: 0.77, 95% CI: 0.66-0.91) were less likely to utilize palliative care compared to NH-White patients [51]. Outcomes of aggressive treatments at the end of life are associated with low quality of life and higher toxicity rates without incremental survival benefit [52-54]. Chemotherapy administration in the last 14 days of life, admission to the intensive care units in the last 30 days of life, and lack of enrollment to hospice care are defined as poor quality of cancer care leading to avoidable extended hospitalizations [55,56]. A continued emphasis on end of life treatment decisions early on in the disease course will avoid toxic treatments and promote a symptom based comfort measures.

Challenges and novel approaches of inpatient care during the COVID-19 pandemic

A novel coronavirus named SARS-CoV-2 of a zoonotic origin emerged in 2019 and the infection called Coronavirus



Diseases 2019 (COVID-19) started spreading worldwide. In March 2020 COVID-19 was classified as a pandemic with rapidly increasing number of cases worldwide. Cancer patients are at a heightened risk of complications with the SARS-CoV-2 infection due to immunosuppression related to underlying cancer and its treatment [57]. While we saw several guidelines put forth by various professional societies, all guidelines had in common a recommendation to defer or delay all non-emergent therapies, restrict visitors and caregivers, pre-treatment COVID testing and significant reduction of face-to-face encounters with patients. The main drivers for these guidelines, especially in the beginning phases of the pandemic put immense pressure on the health care system; with rapid saturation of capacity and limited testing ability, need to preserve personal protective equipment, concerns for potential nosocomial spread of COVID-19, uncertainty of natural history of COVID-19 infection among immune-compromised patients and uncertainty of risk of COVID-19 complications. The aforementioned aspects of evolving strains amidst the pandemic were especially intensified in patients who required chemotherapy. The actual incidence of inpatient transmission of COVID is unknown but the availability of PPE, hospital infection control policies conceivably help further diminish the risk of in-hospital transmission [58-61]. Social distancing, routine masking, PPE use and hand washing are norms in the management of immunocompromised patients even from the pre-COVID-19 era. Additionally, stringent visitation policies were implemented with adaptation of use of technology such as telehealth, virtual platforms for communications with the patients [56,62]. In devising treatment strategies for patients with cancer, state of community spread, hospital infection control policy and personalized risk and benefit assessment proved to be important determinants. Overall, the traditional face to face to patient -physician interactions are changing with increasing use of telehealth, use of artificial intelligence in diagnosis and treatment and home monitoring. Some aspects of digitalized health care delivery are here to stay such as virtual visits for chronic medical conditions could be convenient for patients without compromising the quality of care.

Post-acute sequelae of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (PASC) refers to a constellation of symptoms in survivors of coronavirus disease of 2019 (COVID-19) infections and immunocompromised patients are at high risk for COVID-19 complications [63,64]. Even after recovery from COVID-19, patients continue to experience symptoms such as fatigue, shortness of breath, fevers, gastrointestinal symptoms, anxiety, depression, and "brain fog" which can last several months from the initial infection [65]. While the data on PASC in COVID-19 survivors is still evolving, it is estimated that 32.6 to 87.4% of patients suffer from persistent symptoms following acute infection. Interestingly, patients with non-critical COVID-19 infection

also report symptoms consistent with PASC underscoring the overall impact in the post pandemic phase [66]. A recent longitudinal study reported that a substantial proportion of patients report ongoing symptoms including decline in overall quality of life in the post-acute COVID-19 setting. Also, PASC results in ongoing morbidity, including the inability to return to normal activities, physical and emotional symptoms, and financial loss [67-72]. This results in re-hospitalization in 15% - 20% and death in approximately 10% of cases [65,66,73]. Even after recovery from COVID-19, patients are at risk of secondary infections due to the protracted lymphopenia and immune dysregulation. Hence, overall impact of PASC in COVID-19 survivors are not inconsequential. Thus, as even we enter post COVID state, utilization of health care resources due to hospitalization, need for rehabilitation in addition to outpatient services targeting specifically at PASC will likely be ongoing and merits future studies [66,74].

Conclusion and future directions

Although most oncology care is provided in the outpatient setting, hospitalized patients for various critical illnesses tend to have ongoing complexities leading to extended LOS, and timely evaluation and intervention are critical in quality improvement. Commitment at both health systems and provider level is invaluable in addressing disparities related to SDOH, nutritional factors, facilitation of outpatient vs. inpatient cancer treatments, and end-of-life discussions for cancer patients. While we strive to provide excellent care for our patients, healthcare systems are somewhat less focused on addressing SDOH during hospitalization, given the acuity of patients' medical illnesses. The challenges in addressing these issues were only augmented during the COVID-19 pandemic. Ongoing efforts to address the barriers to SDOH with navigator and community health workers' based care-delivery models will help transition care from an outpatient to inpatient setting and during the follow-up appointments. Providers also need to consider early discharge planning, i.e., home vs. facility discharge, particularly in light of the rapidly evolving social distancing guidelines during the COVID-19 pandemic.

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