Functional Decline in the Older Cancer Patient

Subjects: Oncology

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A decline in functional status, an individual's ability to perform the normal activities required to maintain adequate health and meet basic needs, is part of normal ageing. Functional decline, however, appears to be accelerated in older patients with cancer. Such decline can occur as a result of a cancer itself, cancer treatment-related factors, or a combination of the two. The accelerated decline in function seen in older patients with cancer can be slowed, or even partly mitigated through routine assessments of functional status and timely interventions where appropriate. This is particularly important given the link between functional decline and impaired quality of life, increased mortality, comorbidity burden, and carer dependency.

cancer elderly functional decline functional status frailty ageing

1. Introduction

Functional status captures an individual's ability to perform the normal activities required to maintain adequate health and meet basic needs [1]. A decline in functional status is an inevitable part of normal ageing, with the rate of functional decline steadily increasing over a person's lifespan [2]. This decline, however, is accelerated in individuals with cancer, with this cohort experiencing rapid deterioration following a cancer diagnosis and treatment, compared to their cancer-free counterparts [3]. Not only does functional decline impact quality of life, impairment in functional status can also lead to increased comorbidity burden, greater dependency on carers, institutionalisation, and increased mortality [4][5][6].

With early detection and the use of evidence-based interventions, the risk of functional decline in cancer survivors can be at least partly mitigated. Despite this, assessment of functional status rarely plays a role in the routine clinical care of older patients with cancer, particularly if they are not actively receiving treatment.

2. Assessment of Functional Decline

Functional decline is typically assessed through a direct measure of an individual's capacity to independently fulfil their activities of daily living (ADLs) [1]. ADLs are typically categorised as either basic (tasks required for normal day-to-day functioning), or instrumental (tasks that are not necessarily essential but allow for one to live independently). Basic ADLs include tasks such as ambulation, eating, dressing, toileting, and personal hygiene. Instrumental ADLs are typically more complex and include managing finances, shopping, transportation, home maintenance, communication, and managing medications [7].

It should be noted that frailty, typically defined as a “state of reduced physiologic reserve”, is not synonymous with functional decline, although the two frequently measure domains which overlap [8][9][10]. Frailty is a broader concept than functional decline and measures vulnerability to functional decline as opposed to functional decline itself—its clinical utility therefore lies in its ability to predict susceptibility to disability [11]. While functional decline can be observed through the assessment of ADLs, frailty is often initially clinically silent. Its development can instead be identified through markers such as nutritional status, physical activity, mobility, energy, strength, cognition, mood, and social support. In this regard, the assessment of frailty requires a more comprehensive ‘geriatric assessment’ beyond the assessment of ADLs [8]. The Fried frailty phenotype is typically considered to be the gold-standard definition for the measurement of frailty and defines it as the presence of three or more of the following: unintentional weight loss (at least 10 pounds/4.5 kg in the past year), weakness (grip strength in the lowest quintile adjusted for sex and body mass index), slowness (walking time in the lowest quintile adjusted for sex and height), a low level of physical activity, and self-reported exhaustion [12]. Frailty is certainly seen at greater rates in patients with cancer [13][14][15].

There are several measures of functional status that can be used in older patients with cancer; these tools are summarised in **Table 1**. These include instruments such as the Barthel index, the Eastern Cooperative Oncology Group performance status (ECOG), the Katz index of independence in activities of daily living scale (ADL), the Instrumental Activities of Daily Living Scale (IADL), the Rosow–Breslau health scale, and the Karnofsky performance status scale (KPS) [8][9][10]. Performance status, measured by an assessment of ECOG scores (0–4) is particularly relevant in oncology and is often used to measure suitability for anti-cancer treatment [16]. Physical performance measures such as the Timed Up and Go test (TUG), grip strength, 6-min walk test (6MWT), and gait speed can be used as surrogate markers of functional status as physical strength is often necessary to perform ADLs (e.g., adequate grip strength is required for personal care) although this is not always the case, given that some level of function can be maintained in the presence of poor physical performance [8][9][10][17]. The benefit of physical performance measures, however, lies in their measurement requiring direct observation rather than self-report, providing a more objective measure of a patient’s function.

The comprehensive geriatric assessment (CGA) is a more holistic alternative to the above tools that assesses several domains, including medical conditions, medications, nutritional assessment, cognitive status, mental health, social circumstances, environment, and functional status. Given the variety of domains it assesses, the CGA provides a broader overview of older patients with cancer and captures their susceptibility to further decline, as opposed to solely assessing functional status. The CGA bears particular clinical relevance having been recommended by the American Society of Clinical Oncology (ASCO) for assessing frailty in patients over 65 years of age receiving chemotherapy [8][18]. Other tools that provide a broader assessment of older patients and have been validated in cancer cohorts include the 36-item short form survey (SF-36; a quality-of-life assessment) [19], Geriatric 8 (G8) [20], Vulnerable Elders Survey-13 (VES-13) [20], Fried frailty criteria [21][22], Senior Adult Oncology Program 2 tool [23], Groningen Frailty Indicator (GFI) [21], and Rockwood Clinical Frailty Scale [21]. Of these, Garcia et al. recommend the G8 for screening older patients with cancer, given a high level of evidence supporting its sensitivity and specificity when screening for vulnerabilities [20] although it is noted that this tool is a screening measure that provides a less comprehensive view of a patient’s holistic health and is instead meant to identify

patients who require further assessment using a more detailed tool. The authors recommended the VES-13 as an effective screening alternative in resource-poor settings [20]. The Cancer and Aging Research Group (CARG) also provides an online assessment tool for clinicians that combines the KPS scale, TUG, and Blessed Orientation–Memory–Concentration test (a cognitive function assessment aimed at assessing the contribution of cognitive decline on functional ability) [24]. These geriatric assessments tend to provide not only an indication of declines in ADLs, but also frailty and the susceptibility of a patient to future disability.

Table 1. Tools that can be used to assess functional status in older patients with cancer.

Instrument	Method of Administration	Domains Assessed	Comments
		Functional status	
Barthel Index [25] (Basic ADLs)	Patient-reported or direct observation	Feeding, toileting, bathing, dressing, and undressing, toilet transfers, incontinence, bed transfers, and ambulation	Intended for patients with stroke, neuromuscular disorders, musculoskeletal disorders, and cancer.
Eastern Cooperative Oncology Group Performance Status (ECOG) [26]	Patient-reported	Percentage of day spent ambulatory or in bed	5-point scale, where 0 is “Fully active” and independent and 5 is “Dead”. Commonly used in oncology due to its simplicity [27]. Tends to have minimal direct input from the patient. Noted by the International Society of Geriatric Oncology (SIOG) to be a poor marker of function as functional impairment can occur in the presence of good performance status [28].
Karnofsky Performance Status Scale (KPS) (Both instrumental and	Patient-reported	Activity, work, self-care	10–100-point scale, gold-standard measurement of performance status in cancer. Thorne-modified KPS better suited to community-based and palliative care settings [29], while Australia-modified KPS is better suited to settings with multiple venues

Instrument	Method of Administration	Domains Assessed	Comments
basic ADLs)			of care across both inpatient and outpatient settings [30]. Noted by SIOG to be a poor marker of function as functional impairment can occur in the presence of good performance status [28].
Katz Index of Independence in Activities of Daily Living Scale (ADL) [31] (Basic ADLs)	Patient-reported	Bathing, dressing, toileting, transferring, continence, and feeding	Most commonly used instrument in studies assessing activities of daily living in adults with cancer [32]. Shortened versions are often used due to length: modified Katz-1 assesses dressing, bathing, transferring, eating, and toileting, but does not assess continence; modified Katz-2 assesses the original six domains in the Katz ADL scale, as well as walking across a small room [27].
Lawton Instrumental Activities of Daily Living Scale (IADL) [33]	Patient-reported	Ability to use telephone, shopping, food preparation, housekeeping, laundry, transport, responsibility for medications, and finances	Second-most commonly used instrument used in studies assessing activities of daily living in adults with cancer [32].
Rosow–Breslau Health Scale [33]	Patient-reported	Ability to do heavy housework, walk up and down stairs, and walk half a mile	Simple 3-point scale that can be easily implemented in the clinical setting. Less commonly used in patients with cancer and in oncology research.
Functional Independence Measure (FIM) [34]	Direct observation	Self-care, sphincter control, transfers, locomotion, communication, and social cognition	Used for evaluation in the rehabilitation of patients post-stroke, traumatic brain injury, spinal cord injury, or cancer.

Instrument	Method of Administration	Domains Assessed	Comments
Frail Elderly Functional Assessment Questionnaire (FEFA) [35]	Patient-reported	Mobility, transfers, housework, meal preparation, finances, telephone use, eating, dressing, personal hygiene, and medication management	Older, less-widely used tool. Validated against Katz ADL, IADL, and Barthel Index [36].
Elderly Functional Index (ELFI) [37]	Patient-reported	Physical functioning, role functioning, social functioning, and mobility	Newer tool derived from functional domains of common quality of life instrument European Organisation for Research and Treatment (EORTC) Quality of Life Questionnaire Core-30 (QLQ-C30). Suggested for use as an endpoint of functional status in clinical trials or in clinical practice.
Physical performance measures			
Grip strength	Direct observation	Forearm strength	Requires a dynamometer for testing. Poorer scores are associated with poorer health-related quality of life [38] and increased mortality [39] in patients with cancer.
Gait speed [40]	Direct observation	Walking speed over a short distance, typically 4, 6, 8, or 10 m	Poorer scores are associated with decreased survival outcomes and treatment-related complications in cancer survivors [41]. Requires a stopwatch, although electronic gait mats or automatic timing devices provide more accurate assessments [40].

Instrument	Method of Administration	Domains Assessed	Comments
6-Minute Walk Test (6MWT) [17]	Direct observation	Aerobic capacity and endurance over six minutes of walking	Good measure of cardiorespiratory fitness. Validated for use in patients with cancer [42]. Does not require specialised equipment, but does require a stopwatch and a walkway of known length.
Timed Up and Go Test (TUG) [43]	Direct observation	Gait speed and mobility: measures the time taken to rise from a chair, walk three meters, turn around, walk back to the chair, and sit down while turning 180 degrees	Poorer scores are associated with decreased survival outcomes, treatment-related complications, and functional decline in cancer survivors [41]. Can be used as a substitute measure for gait speed. Does not require specialised equipment.
Short Physical Performance Battery (SPPB) [44]	Direct observation	Lower limb muscle strength, balance, and mobility	Poorer scores are associated with decreased survival outcomes, treatment-related complications, and functional decline in cancer survivors [41]. Can be used as a substitute measure for gait speed. Does not require specialised equipment.
Physical Performance Test (PPT) [45]	Direct observation	Writing, eating, dressing, grip strength, mobility, dexterity, communication, upper limb function, and balance	Requires various household items for assessment. Direct comparison with the KPS scale indicates that the PPT is more accurate in measuring functional status in older patients with cancer [46].

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and transportation. While the studies within the meta-analysis do not make comparisons with cancer-free controls, track changes in function over time, or address whether impairment of ADLs occurred as a result of the cancer and/or cancer treatment, it nonetheless offers a broad picture of disability in the older patient with cancer [32]. Blackwood et al. provides a similar snapshot of functional status in older cancer survivors using the surveillance, epidemiology and end results (SEER) national cancer registry and Medicare Health Outcomes Survey. In those older than 85 years of age, breast and prostate cancers conferred the greatest risk of impaired functional status. Functional impairment typically increased proportionally to stage in breast, colorectal, lung, and prostate cancers. As with the previous study, this analysis did not compare the cancer cohort to a control group; however, it did provide an overview of the varying impact of cancer type and stage on functional status [47].

3.2. Cancer-Related Functional Decline

Several studies do, however, demonstrate longitudinal declines in functional status in older adults. Reeve et al. demonstrated a greater decline in physical function in patients with prostate, breast, bladder, colorectal, kidney, and lung cancers, with the latter showing the greatest deterioration although the study did not adjust for treatment variables [48]. Using a modified Rosow–Breslau questionnaire, Petrick et al. found functional declines in patients with lung, prostate, breast, and colorectal cancer within one year of diagnosis when compared to a cancer-free group. These deficits had not returned to baseline levels after one year in the groups with either lung or colorectal cancer, a finding the authors attribute to either early death due to increased mortality in these cancer types or disease-related declines in physical function [10]. Using the ADL and IADL scales, van Abbema et al. similarly found a cancer diagnosis to be a significant predictor of functional decline. Nearly half (43.6%) of the elderly cancer group showed functional status declines compared to 28.1% of the elderly non-cancer group [49]. These findings have been replicated in patients with lymphoma; La Carpia et al. reported statistically significantly poorer functional status scores in cancer survivors when compared to cancer-free controls [50].

Functional decline in patients with lung cancer is a particularly well-documented phenomenon [51][52]. Granger et al. demonstrated poorer scores in various functional outcomes in patients with non-small cell lung cancer when compared to age-matched cancer-free controls, with cancer being associated with poor 6MWT scores (84% of predicted distance) and quadriceps strength (mean difference 4.8 kg, 95% CI 1.6–8.1) at baseline. The study cohort also performed poorly on the functional components of quality-of-life measurements including the SF-36 and European Organisation for Research and Treatment (EORTC) quality of life questionnaire. Moreover, these patients experienced a regression in self-reported physical activity, the 6MWT (84% of predicted distance to 69%, $p = 0.02$), quadriceps strength (−3.9 kg, 95% CI −5.2, −2.6), and grip strength (−2.7 kg, 95% CI −4.6, −1.4) over the course of six months. The patients with lung cancer also demonstrated below-average baseline results in the 6MWT test and grip strength, suggesting an intrinsic impact of cancer as opposed to cancer treatment [51]. Decoster et al. similarly reported decreases in both ADL and IADL scores in nearly half of a cohort of older patients with newly diagnosed lung cancer after 3 months follow-up [52]. This phenomenon may be at least in part linked to patient physical loss of lung capacity impacting exercise tolerance and by extension, functional capacity. The impact of thoracic radiation is likely to compound this given the link between such radiation and cardiorespiratory function [53][54].

3.3. Cancer Treatment-Related Functional Decline

3.3.1. Systemic Therapy

The impact of several modalities of cancer treatment on functional decline is similarly evident. In older patients receiving first-line chemotherapy, 16.7% experienced functional decline as measured via a comprehensive geriatric assessment pre- and post-treatment [55]. Hurria et al. demonstrated declines in physical function post-adjuvant chemotherapy in older patients with breast cancer. While nearly half had recovered by 12 months, almost one-third had ongoing decline after this period. Factors associated with resilience to functional decline after 12 months

included strong social support and lower nodal burden, while baseline dyspnoea and poor appetite predicted persistent decline. The authors also suggest that early interventions aimed at improving functional status may play a role in a patient's ability to 'bounce back' [56]. Kenis et al. similarly reported functional decline in nearly one-third of older patients receiving chemotherapy for various cancer types [57]. Similar declines can be seen in patients receiving hormonal therapy. Alibhai et al. demonstrated declines in grip strength in patients receiving androgen deprivation therapy for prostate cancer compared to cancer-free controls in a longitudinal assessment with testing at baseline, 3, 6, and 12 months. They also noted decreases in the physical function component of the SF-36 over the course of the study in the cancer group, while they found increases in the control group [58].

3.3.2. Radiotherapy

Radiotherapy appears to have a similar impact on functional status. In their analysis of patients with lung cancer, Decoster et al. reported that radiotherapy was a statistically significant predictor of decline [52]. Ursem et al. corroborated these findings in an analysis of older patients with prostate cancer, demonstrating a decrease in minimum data set ADL score from the beginning of radiation to 3 months after, and then again from 3 months to 6 months post-treatment [59]. Notably, there is a paucity of studies stratifying functional decline outcomes by radiation location or dose. Given the impact of thoracic radiation on cardiorespiratory function [53][54], it may be that functional decline post-radiotherapy varies depending on where radiation is delivered.

3.3.3. Surgery

The impact of surgery on ADL disability post-surgery is less clear. Amemiya et al. reported a transient decrease in functional status at 1-month post-operation for oesophageal or colorectal cancer, with recovery of nearly all patients by 6 months post-operation [60]. van Egmond et al. reports similar findings in a group of oesophageal cancer survivors post-oesophagectomy, with a high number of postoperative complications, but an overall return of functional status to baseline after 3 months [61]. Conversely, Tang et al. demonstrated a functional decline rate of 56–60% amongst 1-year breast cancer survivors post-surgery although this cohort comprised nursing home residents who were likely to have a poorer baseline functional status than the general population [62]. In a similar cohort of nursing home residents, nearly one-quarter of patients had persistent functional decline 1-year post-colectomy for colorectal cancer [63]. Given that patients typically require a reasonable functional baseline to be considered fit for surgery, patients receiving anti-cancer surgery may be inherently less likely to experience further decline post-operatively.

4. Mechanisms Driving Functional Decline

The development of functional decline in patients with cancer is likely multifactorial, with shared risk factors, social factors, comorbidities, tumour-related factors, and treatment all playing a role. In older adults, functional decline is likely to already be occurring as a normal consequence of ageing, irrespective of a cancer diagnosis, with the rate of functional decline generally steepening with increasing age [2]. Buchner et al. describes an accelerated ageing model that can be easily applied to the functional decline seen in older adults with cancer (**Figure 1**). Here,

patients slowly lose function as they age, with poor lifestyle behaviours and acute insults, such as cancer and anti-cancer treatment, accelerating this process. This decline can be tolerated while the patient has 'physiologic reserve', the capability of an individual to tolerate stressors, until they reach a point at which functional disability occurs. This model recognises the slow decline of function over the lifespan and acknowledges that acute insults, such as cancer, are not the sole drivers of functional impairment in older patients with cancer, but instead, accelerate a pre-existing decline.

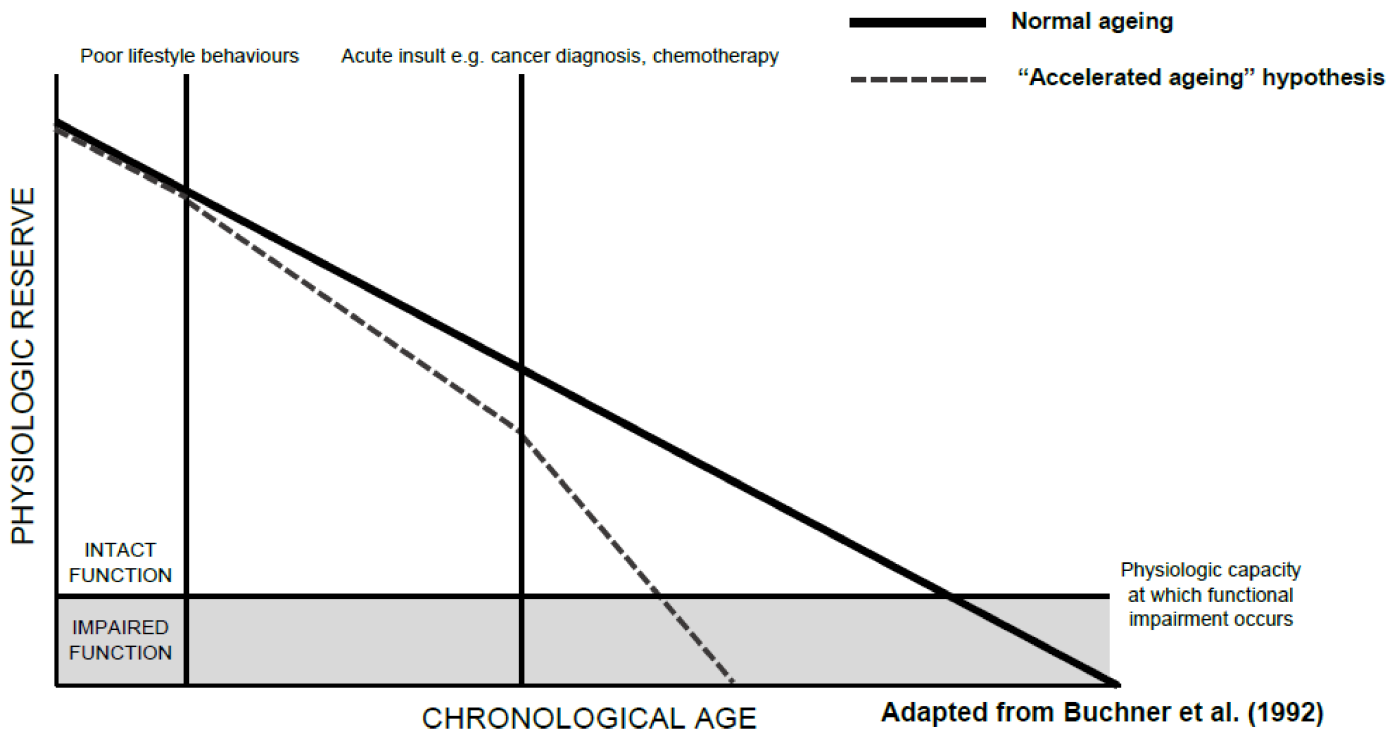

Figure 1. An "Accelerated Ageing" model of functional decline [11].

While some of these represent cancer- and treatment-related factors, the role of shared risk factors in functional decline in older patients with cancer must be acknowledged. For example, smoking is a strong risk factor for lung function decline [64] and has an adverse impact on functional status irrespective of cancer status [65]. Given that smoking is strongly associated with a number of cancer types, with nearly 80% of lung cancers being caused by smoking [66], older patients with cancer with a smoking history may have experienced smoking-related functional decline, regardless of their cancer diagnosis or treatment. These patients may also have concomitant smoking-related lung disease, such as chronic obstructive pulmonary disease, a condition independently linked with poorer functional status [67]. Obesity, another significant risk factor for cancer, particularly in older, post-menopausal women [68], can independently accelerate functional decline [69].

Some of the predictors of functional decline in patients with cancer, both cancer- and non-cancer related, are described in **Table 2**. Note that each factor may not predict functional decline across all cancer types and demographics although many are relevant to the general older cancer-survivor population.

Table 2. Factors that may predict functional decline in older patients with cancer.

Patient Characteristics and Social Factors	Clinical Factors
• Female sex [49] • Older age [49] • Unmarried [56] • Poor financial status [70] • Low educational attainment [10] • Lack of health insurance [62]	• Depression [55] • Poor baseline functional status [55][57][62] • Pre-treatment fatigue [56] • Pre-treatment dyspnoea [56] • Poor nutrition [57] • Polypharmacy [57] • Comorbidities [59] • Cognitive impairment [62] • Obesity [10]
Cancer-related factors	**Treatment-related factors**
• Cancer type (e.g., breast, colorectal, lung) [71] • Stage [71]	• Chemotherapy [55][56][57] • Radiotherapy [52] • Surgical complications [63] • Readmission after surgical hospitalisation [63]

Several tumour-related factors can contribute to functional decline although this varies between cancer types. In patients with primary lung cancer or multiple lung metastases, for example, the replacement of lung volume and subsequent reduction in pulmonary function can adversely impact functional status [72]. Patients with primary or secondary brain malignancies can experience disability in function due to motor or sensory deficits [73]. Similarly, patients with metastatic spinal cord compression are often afflicted by functional deficits [74]. In cancers not impeding on organ structures, tumour-related symptoms such as pain, fatigue, and depressive symptoms are likely to be the primary driving mechanism in functional impairment [75]. This may be particularly common in haematological malignancies, considering the prevalence of anaemia and its subsequent impact on a patient's energy levels [76]. Given that as many as 38% of patients with cancer report moderate-to-severe pain, with fatigue

and depressive symptoms being similarly common, recognising the impact of such symptoms plays an important role in any comprehensive assessment of functional status [77].

Cancer treatment is likely to be the main contributing factor to functional decline in patients with cancer, with exact mechanism varying between treatment modalities. Across all treatment types, fatigue is a common symptom that can result in functional deficits; prevalence estimates of fatigue during treatment can be anywhere from 25% to 99%, with up to one-third experiencing fatigue for as many as 10 years post-cancer diagnosis [78]. Chemotherapy-related toxicity is also incredibly common. Common toxicities, such as nausea and vomiting, diarrhoea, anaemia secondary to myelosuppression, peripheral neuropathy, vestibular dysfunction, weakness, and fatigue, are all likely to be drivers of functional impairment [79][80][81]. Hormonal therapy can have similarly debilitating side effects: In patients receiving androgen deprivation therapy for prostate cancer, for example, weakness and muscle wasting is common [82]. More targeted treatment modalities, such as radiotherapy, are likely to have less impact on functional status than their systemic counterparts. The nature of radiotherapy toxicity is both site- and dose-dependent but can result in complications such as cardiac toxicity limiting exercise tolerance, mucositis impacting personal care and eating, and fatigue that can have a pervasive impact on ADLs, although the latter two tend to be acute and resolve shortly after treatment [83]. Similarly, surgery is less likely to cause persistent functional impairment in older patients with cancer, with most patients returning to baseline functional status within months after an operation [60]. However, patients with post-operative complications and a prolonged length of hospital stay can suffer from accelerated bone loss, malnutrition, cognitive decline, and deconditioning, all factors that can independently contribute to declines in function post-discharge [84].

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