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# Acceptance, efficacy, and safety of COVID-19 vaccination in older patients with cancer

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#### **Abstract**

Purpose: The COVID-19 vaccination campaign began in December 2020, in France, and primarily targeted the eldest people. Our study aimed to determine the level of acceptance of vaccination in a population of older patients with cancer. Methods: From January 2021, we offered vaccination with the BNT162b2 COVID-19 vaccine to all patients 70 years and older, addressed to our geriatric oncology center in Marseille University Hospital (AP-HM) for geriatric assessment before initiation of an oncological treatment. Objectives were to evaluate acceptance rate of COVID-19 vaccination, and to assess vaccine safety, reactogenicity, and efficacy two months after the first dose.

Results: Between January 18, 2021 and May 7, 2021, 150 older patients with cancer were offered vaccination after a geriatric assessment. The majority were men (61.3%), with a mean age of 81 years. The two most frequent primary tumors were digestive (29.4%) and thoracic (18%). The vaccine acceptance rate was 82.6% and the complete vaccination rate (2 doses) reached 75.3%. Among the vaccinated patients, 15.9% reported mild side effects after the first dose and 23.4% after the second dose, mostly arm pain and fatigue. COVID-19 cases were observed in 5.1% of vaccinated patients compared with 16.7% in unvaccinated patients. Of the 22 vaccinated patients who agreed to have their serum tested, 15 had antibodies against the spike protein at day 21 after the first dose.

Conclusion: Our study showed a high acceptance rate of COVID-19 vaccination, with good tolerance in this frail population. These results highlight the benefits of organizing vaccination campaigns at the very beginning of oncological management in older patients.

# **Clinical Trial Registration**

This study was registered the 23th May, 2019 in ClinicalTrials.gov (NCT03960593).

# **Key words**

COVID-19, Aged, Vaccination, Drug-Related Side Effects and Adverse Reactions, Medical Oncology, Geriatric assessment

#### **Abbreviations**

APHM: Assistance Publique des Hôpitaux de Marseille; COVID-19: Coronavirus disease 2019; ESMO: European Society of Medical Oncology; SIOG: International Society of Geriatric Oncology; SoFOG: French-Speaking Society of Geriatric Oncology; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2; CGA: Comprehensive Geriatric Assessment; CMR: Comprehensive Medication Reconciliation; IgG: Immunoglobuline G; ELISA: enzyme-linked immunoassay; BMI: Body Mass Index; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; TUG: Timed Up and Go test; OLBT: One Leg Balance Test; ECOG-PS: Eastern Cooperative Oncology Group-Performance status; NA: Not Applicable

#### Introduction

Older frail people are more susceptible to severe forms of Coronavirus 19 disease (COVID-19) than the rest of the population; the infection rate is higher and outcomes poorer, in particular for those with comorbidities such as hypertension, diabetes, cancer, or cardiological and respiratory diseases [1,2]. In patients with cancer, COVID-19 has negative consequences on treatment delays and increases the mortality rate [3–5]. In this context, the COVID-19 vaccination

campaign that began in France on December 27, 2020, primarily targeted the eldest people and then patients being treated for cancer [6,7]. The European Society of Medical Oncology (ESMO), the International Society of Geriatric Oncology (SIOG), and the French-Speaking Society of Geriatric Oncology (SoFOG) rapidly recommended COVID-19 vaccination in patients and older patients treated for cancer [8–10]. The particular severity of COVID-19 in frail older patients and patients with cancer has led to the inclusion of these populations in clinical trials in which they are usually poorly represented [11].

In addition to its effectiveness, one of the other major challenges of vaccination is its acceptance by the population. The first data on vaccination in cancer patients stated a low acceptation rate [12,13] and at best, a mild intention rate for the COVID-19 vaccine [14,15]. The very first data available on the intended acceptance of COVID 19 vaccination in French patients with cancer showed that only half patients intended to be vaccinated as soon as the vaccine was available [12]. Given the polemic surrounding COVID-19 vaccine, especially in the beginning of the vaccination campaign, and the observed worse outcomes in COVID-19 among older patients or cancer patients, older cancer patients' COVID-19 vaccination acceptance was and still is, crucial to limit adverse outcomes for this frail population.

However, the efficacy of vaccines in older patients is still unclear because of immunosenescence, including the reduction of both qualitative and quantitative aspects of the immune system available to respond to a vaccine [13,14]. A study on BNT162b2, a lipid nanoparticle-formulated, nucleoside-modified RNA COVID-19 vaccine, showed 95% efficacy seven days after the second dose in a population including 42% of older adults and 3.7% of adults with cancer [15]. In patients treated with anti-cancer agents, this vaccine could interfere with cancer treatment through a molecular phenomenon known as the permeation and retention effect [16]. Moreover, patients treated with immunotherapy could, in theory, display an exaggerated inflammatory immune response after vaccination. Despite this, vaccination appears to be the main tool to prevent severe outcomes and hospital admissions due to COVID-19.

From January 2021, we offered COVID-19 vaccination to all patients over 70 years old with cancer attending the geriatric oncology center for geriatric advice before initiation of oncological treatment. The main objective was to evaluate the acceptance of COVID-19 vaccination by older patients with cancer. The secondary objective concerned vaccine safety, reactogenicity, and efficacy in the two months following the first dose.

## Materials and methods

Study Design and Participants

This research is a study focused on vaccination prescription before oncological treatment, derived from the ongoing prospective observational cohort study "ChimioAge", initiated in January 2017 at Marseille University Hospital (NCT03960593) [17]. The ChimioAge cohort aims to collect geriatric, oncological and drug prescriptions data of all consecutive patients aged 70 years or over with cancer, referred to our geriatric oncology center for geriatric advice before initiation of treatment. All patients benefit from a Comprehensive Geriatric Assessment (CGA) [18] and a Comprehensive Medication Reconciliation (CMR) [19–21].

From January 18, 2021, COVID-19 vaccination prescription was offered to all patients at the time of the CGA. Those who agreed received the BNT162b2 vaccine, which was administered intramuscularly in two doses 21 days apart, as part of the national vaccination campaign. Inclusion in the "vaccine survey" ended on May 7, 2021 (four months), when vaccination prescriptions were available in other centers (pharmacies or office of general practitioners or nurses) and when patients

addressed for CGA were mostly vaccinated. Participants were followed up by telephone 60 days after receiving the first dose of the vaccine. Patients who were already vaccinated with a vaccine other than BNT162b2 were not eligible for the survey.

Geriatricians and pharmacists collected the data. Patients were included in the study after providing their written informed consent. The study protocol was approved by an Ethics Committee (CPP Ouest IV – Nantes registered under number 61/18 3).

#### Data collection

The CGA, including assessment of autonomy, cognitive status, nutritional status, mobility, handgrip strength and polypharmacy (minimum of five prescribed medications) was assessed by both validated psychometric scales and clinical assessment, and has been previously detailed [17]. Information about demographic characteristics and lifestyle (age, gender, accommodations and presence of a caregiver) were also collected. Cancer site and stage, treatment, hospitalizations, and death were obtained from the medical records. Among data directly related to CMR, only side effects of the vaccination collected during the CMR follow-up were analyzed.

Vaccine uptake, side effects, and efficacy

During the geriatric day hospitalization, patients received a CGA conducted by a geriatrician and a CMR conducted by a pharmacist. The CMR was usually conducted prior to the CGA and consisted of an in-depth interview with the patient about the current treatment and any self-medication or dietary supplements taken by the patient. During the vaccination campaign, the geriatricians and the pharmacists acted in synergy to explain the benefits and risks of COVID-19 vaccination. Vaccination was proposed at the end of the CGA, people who agreed received the first dose of the vaccine. Those who refused vaccination were asked about the reasons for not accepting or contraindications. A hospital pharmacist called all the patients included 60 days after administration of the first dose or refusal. The pharmacist collected reactogenicity and safety data from all the vaccinated patients 21 days after the first injection for the first vaccine dose (at the time of the second injection), and 60 days after the first injection for the second vaccine dose (last follow-up). Dates and reasons for hospitalizations, as well as COVID-19 infection dates, were collected from vaccinated and unvaccinated patients.

## Laboratory analyses

Among the vaccinated group, 22 patients agreed to have their serum samples tested for quantitative detection of anti-SARS-Cov-2 spike (S1) IgG antibodies (Euroimmun®, Luebeck, Germany) before the second vaccine dose. All samples with an ELISA ratio  $\geq 0.7$ , neutralizing antibodies against SARS-Cov-2 were detected using a virus neutralization test (VNT100) [22]. Anti-S1IgG was expressed in standardized units (binding antibody units per mL) with a positive threshold of 35.2 BAU/mL.

Statistical analysis

A descriptive analysis was performed for demographic, oncological, geriatric, and treatment characteristics of our population using headcounts and percentages for discrete data, as well as mean values plus or minus the standard error and the interval between the minimum and maximum values for continuous data. A comparative analysis of patients who accepted *versus* those who refused the vaccine was performed. The Chi-squared test was used to analyze discrete data whereas Student's t-test was used to analyze continuous variables. Concerning the serology testing, we compared the positive and negative serology results. All the statistical analyses were performed using SPSS software (version 17.0).

#### Results

Between January 18, 2021 and May 7, 2021, 150 patients with cancer attending the day-care hospital for a CGA were offered vaccination against COVID-19 with the BNT162b2 vaccine and were included in the survey. The study sample consisted of 58 (38.7%) women and 92 (61.3%) men, with a mean age of 81 years (range 70–94). The most frequent primary tumors were digestive (n=44; 29.4%) and thoracic cancers (n=27; 18%). The socio-demographic, oncological, and geriatric characteristics of the patients are detailed in Table 1.

All patients were offered the BNT162b2 vaccine, and all were expected to have their cancer treatment within weeks of vaccination. Sixty two percent (n=93) of the patients agreed to be vaccinated (79 patients (52.7%) accepted right away, 14 patients (9.3%) initially refused but accepted upon reflection)), 20.7% (n=31) were already vaccinated, and 17.3% (n=26) refused. Among those who refused, four were scared of the side effects of the vaccine, seven were against vaccination, ten were undecided at the time of the proposal, four had already been infected with COVID-19, and the last one had an ongoing infection but not COVID-19 (Figure 1). Patients who accepted vaccination and those who refused did not differ in terms of socio-demographic, oncological, and geriatric characteristics (Table 2).

A total of 82 patients out of the 93 who received the first dose returned for the second injection. Few of them (n=13; 15.9%) reported mild side effects after the first vaccine injection, mostly arm pain at the injection site (Table 3). After the second injection, 23.4% of patients (n=18) described side effects, mainly arm pain and fatigue. Taking into account those already vaccinated at the time of the study, the acceptance rate of the vaccine was 82.7% and the complete vaccination rate (two doses) reached 75.3%.

A total of eight COVID-19 cases were identified during follow-up: five (5.2%) cases in the vaccine group and three (18.8%) cases in the non-vaccinated group. Moreover, 16 patients died during follow-up: 14 in the vaccinated group and two in the non-vaccinated group. In the vaccinated group, one death was COVID-19-related (contamination one week after the first vaccine injection, death 40 days later), and 13 were cancer-related. In the non-vaccinated group, the causes of death were unknown for the two patients.

We analyzed responses to mRNA vaccination against COVID-19 among 22 patients, 21 days after the first dose of vaccine. We found specific antibodies to the SARS-CoV-2 spike protein in 15 patients (68.2%). Neutralizing antibodies against SARS-Cov-2 were detected in three patients using VNT100.

The seven patients with a negative serology were more likely to be men, older, with metastatic cancer, and on multiple medications (Table 4).

# Discussion

This single-center study reports acceptance of the COVID-19 vaccine by patients  $\geq$  70 years with cancer before initiation of oncological treatment. In our cohort, 82.7% of patients agreed to be vaccinated against COVID-19 and 75.3% received

the two recommended BNT162b2 vaccine injections. Less than one in four vaccinated patients reported side effects, mainly injection site pain and fatigue. No serious side effects were reported.

Our results show a much higher acceptance rate of vaccination in the older population with cancer than expected given the results of opinion surveys carried out at the end of 2020 in France. A nationwide study showed that only 60% of the population aged over 65 years were considering vaccination against COVID-19 [23]. A cross-sectional survey on acceptance of COVID-19 vaccination among patients with cancer reported that only 53.7% intended to be vaccinated as soon as the vaccine was available. In the latter, the median age was 67 years and 47% of participants were undergoing active treatment against cancer [12]. However, the reported rate of vaccination refusal was similar to that observed in our study (17%) [12].

Moreover, the percentage of people vaccinated (75.3%) was also higher in our study than observed in the French old population at the same date: in France on May 20, 2021, only 54% of people ≥ 70 years had received full vaccination regardless of the vaccine type [24]. Vaccination was proposed by the geriatrician in the context of CGA, with time available to answer any questions the older patients and/or their caregivers had. In addition, and complement the geriatrician efforts, the pharmacists in charge of the CMR were also present to explain to the patients the benefits and risks of vaccination and reassured them on any fears they may have. The combination of geriatric and pharmacological assessment has certainly helped to improve the acceptance rate of the vaccine among hesitant older people, although it is impossible to distinguish the respective impact of the physician and the pharmacist on the elderly person's choice. In addition, patients did not have to wait for an appointment or come back later for their first injection, which was easily accessible on the same day as the CGA. This convenience may have made a big difference for patients who often have limited mobility. We assume that both the time spent on correctly answering all the patients' questions and fears about the efficacy and side effects of the vaccine, as well as the pragmatic approach, were instrumental in increasing the acceptance rate. Of the remaining 26 patients who refused vaccination, five had reasonable reasons (were recently or currently infected with COVID-19). The last twenty-one patients were not vaccinated during the study (even after 60 days of follow-up).

According to our results, 16% and 23% of patients reported mild or moderate side effects after the first and second vaccine injections, respectively, as previously reported in adults aged over 70 years without cancer [25]. In contrast, the frequency of side effects in our study was lower than the 54% reported after the first dose in patients with cancer [26]; this discrepancy may be due to the fact that we proposed vaccination before cancer therapy was initiated, whereas it was done during the oncological treatment in Monin et al. [26]. Despite our cohort being too small to evaluate vaccine efficacy, the proportion of patients who had COVID-19 in the non-vaccinated group was three times higher than in the vaccinated group. In the study by Bernal et al., vaccination with one dose of BNT162b2 in 156 930 older adults was associated with a significant reduction in symptomatic COVID-19 and further protection against severe disease (43% reduced risk of emergency hospital admission and 51% reduced risk of death) [27]. Other studies showed poor efficacy of one dose of the BNT162b2 vaccine in old patients with cancer but a substantial serological response after 2 injections [12,26]. However, the correlation between the serological response to COVID-19 vaccination and clinical protection is still not fully documented [28].

The high frequency of digestive and lung cancers in our study is consistent with our usual activity but can also be explained by a kind of priority given to certain patients by oncologists, whether they are patients at risk because of pre-existing inflammatory lung disease or patients scheduled to receive immunotherapy. [29].

An important limitation of this study is the small number of quantitative detections of the anti-SARS-Cov-2 spike (S1) IgG antibodies made before the second vaccine dose and the lack of testing carried out after the second dose, which prevents us from drawing any conclusions regarding the effectiveness of the vaccine. Moreover, two vaccinated patients and four

non-vaccinated patients were lost to follow-up at the end of the survey, and causes of death were unknown for the two non-vaccinated patients who died during the survey. The implementation of the study at the very beginning of the vaccination campaign and its termination after 60 days due to changes in national vaccination strategies may have also led to an overestimation of vaccine hesitancy in our study. Furthermore, we were not able to follow up on possible changes of mind in people who had refused vaccination, as the oncological follow-up of these patients was carried out in departments geographically distant from ours. In addition, it was a monocentric study including patients with all types of cancers and systemic treatments.

#### Conclusion

Our survey among older patients with cancer showed a high acceptance rate of COVID-19 vaccination in this population, probably linked to the choice of proposing vaccination in the context of the comprehensive geriatric assessment. COVID-19 vaccination carried out before initiation of cancer treatment was better tolerated than previously described and, of those who were fully vaccinated, only 5% were infected with COVID 19 but none developed severe forms. This suggests the possible benefit of not vaccinating at the same time as systemic cancer treatment when possible and organizing vaccination campaigns at the very beginning of oncological management. Larger studies to measure the durability and effectiveness of vaccine protection should be correlated with the BAU/VNT measurements before general rules can be implemented.

**Conflicts of interest:** the authors have no conflicts of interest to declare about this work.

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Availability of data and materials: The data are available from the corresponding author upon reasonable request.

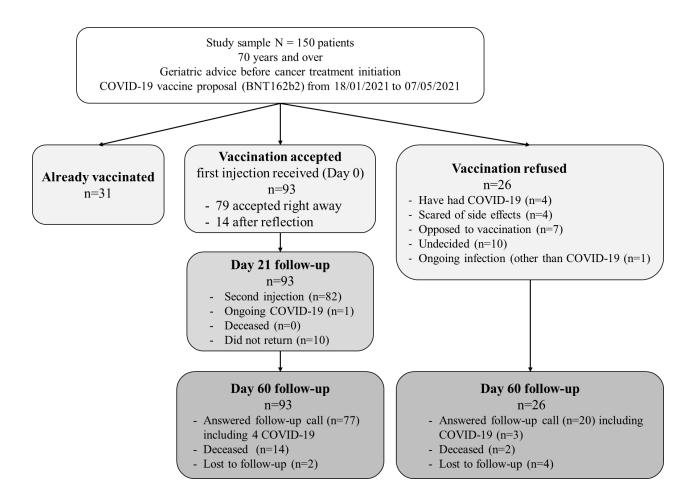


Figure 1: Study Flow Chart

**Table 1:** Characteristics of the population (n=150 old patients with cancer)

	Total population		
Characteristics	N or	% or	
	Mean±SD	[min-max]	
Gender			
	58	38.7	
Women			
Men	92	61.3	
Age	$81\pm0.5$	[70-94]	
70-75	29	19.3	
76-80	45	30.0	
81-85	37	24.7	
> 85	39	26.0	
<b>Accommodation Home</b>	133	88.6	
Care facility	10	2.0	
Nursing home	3	6.7	
Other	4	2.7	
Living alone	33	22.0	
Caregiver present	127	84.7	
Polypharmacy *	96	64.0	
Cognitive impairment (n=149)	65	43.6	
Depression risk	50	33.3	
Malnutrition	60	40.3	
BMI (Kg/cm²)	$25.0\pm0.4$	[16.2-36.8]	
Albumin (g/L)	$38.7 \pm 0.5$	[25.0-65.0]	
Functional status (n=149)		•	
Independent	64	43.0	
Dependent in ADL or IADL	31	20.8	
Dependent in ADL and IADL	54	36.2	
Mobility			
Impaired TUG	104	69.3	
Impaired OLBT	135	90.0	
Impaired gait speed	92	61.7	
Falls in the 3 previous months	20	13.3	
Handgrip strength impairment (n=149)	58	38.9	
G8 impairment	131	87.3	
ECOG-PS (n=149) 0-1	65	43.6	
2-4	84	56.4	
Stage IV (n=148)	56	37.8	
Cancer type			
Digestive	44	29.4	
Thoracic	27	18.0	
Urological	20	13.3	
Prostatic	15	10.0	
Skin	14	9.3	
Head and Neck	12	8.0	
Breast and gynecological	12	8.0	
Hematological	4	2.7	
Other	2	1.3	
Other		1.0	

BMI: Body Mass Index; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; TUG: Timed Up and Go test; OLBT: One Leg Balance Test; ECOG-PS: Eastern Cooperative Oncology Group-Performance status
\*\*at least 5 prescribed medications

**Table 2:** Comparative analysis of geriatric and oncological characteristics between vaccinated and non-vaccinated patients -n=146

Characteristics		Vaccinated (n=124)		Non-vaccinated (n=22)		
		N or % or		N or	% or	<i>p</i> -Value
		Mean±SD	[min-max]	Mean±SD	[min-max]	•
Gender	Women	47	37.9	9	40.9	0.815
	Men	77	62.1	13	59.1	
Age		81±0.5	[70-94]	81±1.4	[70-94]	0.688
8	70-75	24	19.4	4	18.2	0.716
	76-80	37	29.8	6	27.2	
	81-85	32	25.8	4	18.2	
	> 85	31	25.0	8	36.4	
Accommodation Home		111	89.6	18	81.9	0.307
Care	facility	7	5.6	3	13.6	
	ng home	2	1.6	1	4.5	
	Other	4	3.2	_	-	
Living alone		29	23.4	4	18.2	0.784
Caregiver present		104	83.9	19	86.4	1.000
Polypharmacy*		80	64.5	12	54.5	0.473
Cognitive impairment (	n=145)	53	43.1	9	40.9	1.000
Depression risk	(== = == )	42	33.9	5	22.7	0.336
Malnutrition		47	38.2	11	50.0	0.299
	Kg/cm²)	25.3±0.4	[16.2-36.1]	23.3±0.9	[17.1-36.8]	0.044
	in (g/L)	38.8±0.5	[27.0-48.0]	38.1±2.3	[25.0-65.0]	0.761
Functional status	(8/2)	2010=010	[=7.10 .0.0]	2011=2.0	[20.0 00.0]	01701
	pendent	51	41.1	12	54.6	0.456
Dependent in ADL of		28	22.6	3	13.6	******
Dependent in ADL an		45	36.3	7	31.8	
Mobility						
	ed TUG	89	71.8	12	54.5	0.133
Impaired		112	90.3	20	90.9	1.000
Impaired gait speed		77	62.6	13	59.1	0.813
Falls in the past 3		17	13.7	2	9.1	0.739
Handgrip strength						
impairment (n=145)		49	39.8	8	36.4	0.817
G8 impairment		108	87.1	19	86.4	1.000
ECOG-PS (n=145)	0-1	54	43.9	10	45.5	1.000
(n 110)	2-4	69	56.1	12	54.5	1.000
Stage IV (n=144)		47	38.2	6	27.3	0.470
Cancer type		.,	23.2	<u> </u>	25	0.170
D	igestive	35	28.2	8	36.4	0.512
	Thoracic	22	17.7	4	18.2	
	ological	19	15.3	1	4.5	
	Prostatic	11	8.9	3	13.7	
•	Skin	13	10.5	1	4.5	
Head at	nd Neck	8	6.5	4	18.2	
Breast and gynec		11	8.9	1	4.5	
	ological	4	3.2	-	5	
11011101	Other	1	0.8	_		
	Other	1	0.8	-		

BMI: Body Mass Index; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; TUG: Timed Up and Go test; OLBT: One Leg Balance Test; ECOG-PS: Eastern Cooperative Oncology Group-Performance status

\* At least 5 prescribed medications

Table 3: Descriptive analysis of COVID-19 vaccine (BNT162b2) patient-reported side effects

Side effects (SE)*	After first injection (n=82 respondents) *		After second injection (n=77 respondents) **		
	n	%	n	%	
Absence of SE	69	84.0	59	76.6	
Presence of SE	13	15.9	18	23.4	
Local reactivity					
Arm pain	8	9.8	12	15.6	
Rash	2	2.4	-	-	
Systemic reactivity					
Fever	2	2.4	5	6.5	
Asthenia	5	6.1	10	13.0	
Headache	1	1.2	1	1.3	
Other	-	-	1	0.7	

<sup>\*</sup> The 31 patients already vaccinated were excluded from this analysis.

\* Information collected at the time of the second injection (day 21 after the first injection)

\* Information collected at the end of follow-up (day 60 after the first injection)

**Table 4**: Comparative analysis of geriatric and oncological characteristics between vaccinated patients with positive versus negative serology, 21 days after first vaccine injection (n=22)

	Positive serology (n=15)		Negative serology (n=7)		
Characteristics	N or	% or	N or	% or	
	Mean±SD	[min-max]	Mean±SD	[min-max]	
Women	6	40.0	2	28.6	
<b>Age</b> 70-80	7	46.7	2	28.5	
> 80	8	53.3	5	71.4	
Living at home	15	100	6	85.7	
Living alone	2	13.3	3	42.9	
Caregiver present	15	100	5	71.4	
Polypharmacy *	6	40.0	6	85.7	
Cognitive impairment	4	26.7	4	57.1	
Malnutrition	5	33.3	2	28.6	
BMI (Kg/cm²)	$24.3\pm1.3$	[16.5-33.3]	$24.7 \pm 1.5$	[20.1-30.4]	
Albumin (g/L)	41.1±1.1	[34.0-46.0]	37.1±1.7	[28.0-42.0]	
Functional status					
Independent	7	46.7	4	57.1	
Dependent in ADL or IADL	5	33.3	1	14.3	
Dependent in ADL and IADL	3	20.0	2	28.6	
Mobility					
Impaired TUG	12	80.0	5	71.4	
Impaired OLBT	13	86.7	7	100	
Impaired gait speed	10	66.7	4	57.1	
Falls	3	20.0	-	-	
Handgrip strength impairment	4	26.7	1	14.3	
G8 impairment	13	86.7	6	85.7	
<b>ECOG-PS</b> 0-1	8	53.3	4	57.1	
2-4	7	46.7	3	42.9	
Stage IV	4	26.7	3	50.0	
Cancer type					
Digestive	1	6.6	3	43.0	
Thoracic	4	26.7	-	-	
Urological	4	26.7	2	28.5	
Breast and gynecological	3	20.0	-	-	
Other	3	20.0	2	28.5	

BMI: Body Mass Index; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; TUG: Timed Up and Go test; OLBT: One Leg Balance Test; ECOG-PS: Eastern Cooperative Oncology Group-Performance status; NA: Not Applicable \* At least 5 prescribed medications

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