

Predictive Factors of Functional Improvement After Palliative Rehabilitation in Patients with Advanced Cancer

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Research Article

Keywords: Advanced cancer, Palliative care, Rehabilitation, Functional status, Quality of life

Posted Date: October 7th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10932703/v1>

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Additional Declarations: No competing interests reported.

Abstract

Purpose

The World Health Organization advocates the development of palliative rehabilitation, aiming to enhance patients' quality of life by optimizing their functional abilities and psychosocial well-being. However, faced with the complex and dynamic nature of cancer, limited criteria are available to help physicians select patients with advanced cancer for palliative rehabilitation programs. The aim of the study was to identify predictive factors of functional improvement after palliative rehabilitation in patients with advanced cancer.

Methods

This retrospective single center study recruited patients with advanced cancer who received palliative rehabilitation. Demographic, clinical, medical, and biological data were recorded at the start of palliative rehabilitation. Functional improvement was defined as a 10% increase in the Palliative Performance Scale score at the end of palliative rehabilitation. Of the 40 patients included, 16 had functional improvement.

Results

Univariate logistic regression analysis identified two significant variables: C-reactive protein and Pronopall survival prognosis score. Functional improvement was observed in 83.3% of patients who had no chemotherapy or radiotherapy and in 66.7% of patients who had no unplanned hospitalizations in the past 12 months.

Conclusion

C-reactive protein and Pronopall score were predictive factors of functional improvement in patients with advanced cancer and could be used to select patients for palliative rehabilitation programs.

INTRODUCTION

The number of patients living with advanced cancer has increased worldwide [1]. This increase could be explained by several factors, including earlier detection of cancer, increased exposure to risk factors, population growth and aging [2]. Despite scientific progress, some patients experience a decline in their functional abilities, which negatively affects their quality of life [3] and that of their families. In addition to physical suffering, functional impairment is often associated with significant psychosocial morbidity [4]. This situation raises significant challenges medically, socially, and economically [5]. The concept of total pain [6] includes four dimensions (physical, psychological, social, and spiritual) that coexist in the patient's overall well-being. It is essential to find solutions that enhance the quality of life of patients with advanced cancer and also reduce the associated healthcare costs.

In 2023, the World Health Organization (WHO) [7] advocated the development of palliative rehabilitation. The aim of palliative rehabilitation is to improve the quality of life of patients with incurable chronic diseases by optimizing their functional abilities, alleviating symptoms, preventing complications related to immobility, and boosting psychosocial well-being. Palliative rehabilitation aims to help patients remain as active and independent as possible in their daily activities. A personalized care approach is provided by a multidisciplinary team that proposes various physical and/or cognitive activities, strategies for compensating and adapting to deficiencies, dietary advice, as well as psychosocial and medical care. Several studies have demonstrated that physical activity provides numerous benefits in the context of cancer, including advanced cancer, particularly in improving quality of life [8, 9], preventing physical deconditioning [10], improving treatment tolerance [11], and supporting mental health [12, 13].

However, the complex and dynamic nature of oncological diseases represents a major challenge [7]. As a patient's health deteriorates over time, their personal goals and needs change. Palliative rehabilitation has its limitations, especially when the patient's overall condition is severely compromised. Patients should start palliative rehabilitation as early as possible. Yet, there are currently limited criteria to help physicians select patients with advanced cancer for palliative rehabilitation programs. A literature review in 2019 [14] established 10 themes for future research, focused on prognosis and predictive factors. Although several predictive survival scores have been developed, such as the Palliative Prognosis Index (PPI) [15], Pronopall score [16], and Palliative Prognostic Score (PaP) [17], limited data are available to help physicians evaluate the ability of a patient to participate in a palliative rehabilitation program.

Functional independence is a key indicator of a patient's health, which reflects a person's ability to remain active and perform daily activities, encompassing physical, psychological, social, spiritual, and intellectual aspects [18]. Functional improvement is the core concept of rehabilitation, aimed at lessening restrictions in activities. Patients' functional abilities have frequently been studied as a risk factor of mortality [19]. A Canadian retrospective study [20] reported that a low Palliative Performance Scale (PPS) [21] score (30%) was associated with a low survival rate (23% at 14 days). The PPS score was also studied by *Downing et al., 2010* [22], who showed that a sudden decline in function on this score was associated with shorter survival. Assessment of functional abilities using the Palliative Performance Scale, which is validated in oncological palliative care and sensitive to clinical changes, provides a comprehensive, simple, and reproducible measure of functional independence by integrating mobility, activity level, care needs, and level of consciousness.

Considering the issues arising in rehabilitation orientation for patient with an advanced cancer – such as delayed or inappropriate rehabilitation – highlighting relevant indicators could help physicians in selecting patients. The aim of this study was to identify predictive factors of functional improvement after palliative rehabilitation in patients with advanced cancer.

MATERIALS AND METHODS

Study design

This was a retrospective, single center observational and analytical study. It was conducted using the medical records of patients with advanced cancer who were hospitalized in the department of Supportive Care Rehabilitation for palliative rehabilitation.

Study population

The study population included patients aged 18 years or more, who had metastatic cancer or who were not eligible for surgery. The presence of cognitive impairment, as documented in the medical records, which prevented the patient from understanding, retaining, and/or following simple instructions was an exclusion criterion. Between January 1, 2023 and May 31, 2024, 143 patients were identified, of whom 50 were excluded for not meeting the inclusion criteria, and 53 were excluded because of missing data.

Data collection

The following data were collected at the start of the palliative rehabilitation program:

- Demographic characteristics: age, sex, body mass index (BMI).
- Clinical characteristics: PPS score (0-100%, with 0% representing the worst performance), self-assessment form Edmonton Symptom Assessment System (ESAS) score (0–10, with 10 representing the worst severity).
- Medical characteristics: primary site of cancer, duration of cancer, number of metastatic sites, number and duration of unplanned hospitalizations in the past 12 months, number of successive therapeutic protocols followed by the patient (including surgery, radiotherapy, immunotherapy, chemotherapy), Pronopall survival prognosis score (0–10, with 10 representing the worst prognosis) [16].
- Biological characteristics: C-reactive protein (CRP), leukocytes, lactate dehydrogenase (LDH), albumin, transthyretin.

PPS score and ESAS score were also collected at the end of the palliative rehabilitation program. These two scores are commonly used in palliative care. The PPS [21] evaluates functional abilities and autonomy, classified into 10 stages, and was assessed by a physician. The ESAS [23] evaluates symptoms commonly found in palliative conditions (pain, fatigue, drowsiness, nausea, anorexia, dyspnea, depression, anxiety, global discomfort), and was assessed by the patient.

Patients reported their personal objectives at the start of the palliative rehabilitation program. At the end of the program, patients assessed their fulfilment of these objectives and the overall benefit of the program on a numerical scale of 10.

Variables

The following variables were evaluated at the start of the rehabilitation program: age, BMI, duration of cancer (in months), number of metastatic sites, number of therapeutic protocols followed, number of unplanned hospitalizations in the past 12 months, total duration of unplanned hospitalizations in the past 12 months (in days), PPS score, Pronopall score, albumin, transthyretin, leukocyte, CRP, and LDH values.

Functional improvement

Functional improvement was defined as an increase of at least 10% in the PPS score at the end of the palliative rehabilitation program. A 10% improvement constitutes the lowest quantifiable change on this scale. In palliative situations, we have opted to regard even slight gains as potentially significant improvements. Data are presented according to the presence of functional improvement or the absence of functional improvement at the end of the program, including patients who died (PPS 0%) or did not complete the program because they were transferred to an acute medical care unit during the program.

Statistical analysis

Data were analysed using SAS software. To determine the factors associated with functional improvement, relevant variables were compared between the two groups (presence of functional improvement versus absence of functional improvement) using univariate logistic regression. Variables with a p-value < 0.15 in univariate analysis were then included in the multivariable logistic regression model. Results are expressed as Odds Ratios (OR) with a 95% confidence interval. All results were considered statistically significant if the p-value was less than 0.05.

Secondary analyses

The mean duration of the palliative rehabilitation program, the mean scores of the overall benefit of the palliative rehabilitation program and of the fulfilment of patients' personal objectives were also analysed. Finally, the ESAS scores at the start of the palliative rehabilitation program were compared with those at the end of the palliative rehabilitation program.

RESULTS

Patients' characteristics

Among the 40 patients included, 14 patients died and 1 patient was transferred to an acute medical care unit before completing the palliative rehabilitation program (Fig. 1). In total, 25 patients completed the program as per the objectives set by the physician.

The characteristics of the patients are presented in Table 1. The mean age of the patients was 70 years. The mean duration of hospitalization was 30 days, with a median duration of 26 days. Lung cancer was

the most represented type of cancer. A low PPS score ($\leq 30\%$) and a high Pronopall score were observed in more patients with no functional improvement. ESAS scores were comparable between the two groups.

Table 1

Characteristics of the population Abbreviations: IQR = interquartile; BMI = body mass index; ESAS = Edmonton Symptom Assessment System.

Sex	Total n = 40	Presence of functional improvement n = 16	Absence of functional improvement n = 24
Women	21 (52.5%)	10 (62.5%)	11 (45.8%)
Men	19 (47.5%)	6 (37.5%)	13 (54.2%)
Age (years): mean [IQR 25–75].	70 [61.5–78]	72.7 [62–84.5]	68.3 [61.5–76]
BMI (kg/m²): mean [IQR 25–75].	23.5 [19.7–26.9]	22.6 [19.8–25.3]	24.1 [19.6–28]
Duration of hospitalization (days): mean [IQR 25–75].	29.9 [17–38.25]	36.5 [21.7–41.2]	25.6 [15–37.7]
Primary site of cancer			
Lung	17 (42.5%)	4 (25%)	13 (54.2%)
Liver	2 (5%)	1 (6.25%)	1 (4.2%)
Intestine	2 (5%)	1 (6.25%)	1 (4.2%)
Stomach	1 (2.5%)	0 (0%)	1 (4.2%)
ENT	2 (5%)	1 (6.25%)	1 (4.2%)
Kidney	2 (5%)	2 (12.5%)	0 (0%)
Bladder	1 (2.5%)	1 (6.25%)	0 (0%)
Prostate	2 (5%)	0 (0%)	2 (8.3%)
Breast	1 (2.5%)	1 (6.25%)	0 (0%)
Skin	3 (7.5%)	1 (6.25%)	2 (8.3%)
Smooth muscle	1 (2.5%)	1 (6.25%)	0 (0%)
Bones	1 (2.5%)	0 (0%)	1 (4.2%)
Haematological	2 (5%)	1 (6.25%)	0 (0%)
Undetermined	2 (5%)	1 (6.25%)	1 (4.2%)
Myeloma	1 (2.5%)	1 (6.25%)	1 (4.2%)

Sex	Total n = 40	Presence of functional improvement n = 16	Absence of functional improvement n = 24
Number of metastatic sites: mean [IQR 25–75]	3.025 [1–5]	2.7 [1–4]	3.3 [2–5]
Duration of cancer (months): average [IQR 25–75].	34.05 [4–54]	25.6 [5.5–29.5]	36.8 [3.5–55]
Number of therapeutic protocols followed: mean [IQR 25–75].	2 [1–2.5]	1.6 [0.5–2]	2.2 [1–3.5]
Pronopall score: mean [IQR 25–75].	5.9 [4–7]	5 [4–7]	6.5 [7–7]
Palliative Performance Scale score			
≤ 30%	4 (10%)	0 (0%)	4 (16.7%)
40–60%	28 (70%)	12 (75%)	16 (66.7%)
70%	8 (20%)	4 (25%)	4 (16.7%)
Initial ESAS score : mean	4.16	4.32	4.05

Analysis of the association between variables and functional improvement

The results of the univariate logistic regression analysis of functional improvement, are summarized in Table 2. Increased CRP was significantly associated with decreased functional improvement (OR = 0.97 [0.95; 0.99] p = 0.0243). A higher Pronopall score was significantly associated with decreased functional improvement (OR = 0.69 [0.49; 0.98] p = 0.0397).

Table 2
Univariate logistic regression of functional improvement

Variables	Univariate analysis		
	OR	95% CI	p-value
Age (n = 40)	1.03	[0.98 ; 1.09]	0.2826
BMI (n = 40)	0.93	[0.81 ; 1.07]	0.3233
Duration of cancer (months) (n = 40)	0.99	[0.97 ; 1.01]	0.3672
Number of metastatic sites (n = 40)	0.86	[0.62 ; 1.18]	0.3440
Number of therapeutic protocols followed (n = 40)	0.83	[0.57 ; 1.21]	0.3293
Number of unplanned hospitalizations in the past 12 months (n = 40)	0.77	[0.48 ; 1.24]	0.2822
Total duration of unplanned hospitalizations in the past 12 months days) (n = 40)	0.98	[0.96 ; 1.00]	0.1351
Palliative Performance Scale score (%) (n = 40)	1.02	[0.97 ; 1.07]	0.4149
Pronopall score (n = 38)	0.69	[0.49 ; 0.98]	0.0397*
CRP (n = 40)	0.97	[0.95 ; 0.99]	0.0243*
Leukocytes (n = 40)	0.88	[0.74 ; 1.05]	0.1666
LDH (n = 38)	0.99	[0.98 ; 1.00]	0.1322
Albumin (n = 40)	1.04	[0.94 ; 1.15]	0.4250
Transthyretin (n = 39)	> 999.999	[0.17 ; > 999.99]	0.1169
<i>*p-value < 0.05. Only the CRP and Pronopall score variables are significantly associated with functional improvement.</i>			
<i>Abbreviations: OR = Odds Ratio; CI 95% = confidence interval; BMI = body mass index; CRP = C-Reactive protein; LDH = Lactate dehydrogenase.</i>			

Among the variables tested in univariate analysis, four factors were retained for multivariable analysis: total duration of unplanned hospitalizations in the past 12 months (in days), Pronopall score, CRP, and LDH. The variables “number of therapeutic protocols followed” and “duration of cancer” were forced into the multivariable model, as these factors are frequently linked to cancer prognosis in clinical practice and may thus serve as confounding factors in the association of the studied variables.

The results of the multivariable logistic regression model are presented in Table 3. They confirm the trends found in the univariate analysis, but no variable was significantly associated with functional improvement.

Table 3
Multivariable logistic regression of functional improvement

Variables	Univariate analysis			Multivariable analysis (n = 38)		
	OR	95% CI	p-value	OR	95% CI	p-value
Total duration of unplanned hospitalizations in the past 12 months (days) (n = 40)	0.98	[0.96 ; 1.00]	0.1351	0.99	[0.96 ; 1.01]	0.3133
Pronopall score (n = 38)	0.69	[0.49 ; 0.98]	0.0397	0.96	[0.55 ; 1.69]	0.8916
CRP (n = 40)	0.97	[0.95 ; 0.99]	0.0243	0.97	[0.94 ; 1.00]	0.0609
LDH (n = 38)	0.99	[0.98 ; 1.00]	0.1322	0.99	[0.98 ; 1.01]	0.4793
Number of therapeutic protocols followed (n = 40)	0.83	[0.57 ; 1.21]	0.3293	0.89	[0.51 ; 1.53]	0.6672
Duration of cancer (months) (n = 40)	0.99	[0.97 ; 1.01]	0.3672	0.98	[0.96 ; 1.01]	0.1349
<i>p-value < 0.05. Among the variables selected for multivariable analysis, none had a significant functional improvement.</i>						
<i>Abbreviations: OR = Odds Ratio; CI 95% = confidence interval; CRP = C-Reactive protein; LDH = Lactate dehydrogenase.</i>						

Table 3
Multivariate logistic regression of functional improvement

Variables	Univariate analysis			Multivariate analysis (n = 38)		
	OR	95% CI	p-value	OR	95% CI	p-value
Total duration of unplanned hospitalizations in the past 12 months (days) (n = 40)	0.98	[0.96 ; 1.00]	0.1351	0.99	[0.96 ; 1.01]	0.3133
Pronopall score (n = 38)	0.69	[0.49 ; 0.98]	0.0397	0.96	[0.55 ; 1.69]	0.8916
CRP (n = 40)	0.97	[0.95 ; 0.99]	0.0243	0.97	[0.94 ; 1.00]	0.0609
LDH (n = 38)	0.99	[0.98 ; 1.00]	0.1322	0.99	[0.98 ; 1.01]	0.4793
Number of therapeutic protocols followed (n = 40)	0.83	[0.57 ; 1.21]	0.3293	0.89	[0.51 ; 1.53]	0.6672
Duration of cancer (months) (n = 40)	0.99	[0.97 ; 1.01]	0.3672	0.98	[0.96 ; 1.01]	0.1349
<i>p-value < 0.05. Among the variables selected for multivariate analysis, none had a significant functional improvement.</i>						
<i>Abbreviations: OR = Odds Ratio; CI 95% = confidence interval; CRP = C-Reactive protein; LDH = Lactate dehydrogenase.</i>						

Functional improvement was observed in 83.3% of patients who had no chemotherapy or radiotherapy and in 66.7% of patients who had no unplanned hospitalizations in the past 12 months.

Self-assessments

Patients' personal objectives at the start of the palliative rehabilitation program are presented in Table 4. Patients could have multiple objectives for the same hospitalization. The most frequently reported objective was independent movement. For patients who completed the program, the mean scores for fulfilling their objectives and for the overall benefit of the palliative rehabilitation program were 6.7/10 and 8/10, respectively.

Table 4
Patients' personal objectives

Personal objectives	n = 52
Independent movement (transfer, walking, wheelchair movement)	18
Autonomy in activities of daily living (washing, dressing, cooking)	5
Get back to your routine, your hobbies	2
Taking charge of your life	1
Improvement of fatigue	3
Improvement of pain	5
Improvement of dyspnea	3
Improvement of diet, reducing anorexia	3
Improvement of balance	2
Improvement of physical performance	8
Reduced feelings of depression	1
Rediscovering the meaning of life	1
Figure	
53 patients excluded because of missing data	
Patients with no functional improvement, PPS < 10%	
(n = 24)	
Including 1 transferred and 14 died	
50 patients excluded:	
• 20 patients were cancer-free	
• 30 patients had cognitive impairment	
Patients considered for inclusion (n = 143)	
Patients with functional improvement: PPS ≥ 10%	
(n = 16)	
Patients included (n = 40)	

For patients who completed the program, the ESAS score at the start of the program was compared with the ESAS score at the end of the program. A global symptom improvement score was calculated by subtracting the number of worsened symptoms from the number of improved symptoms. A majority of

patients reported an improvement in at least three symptoms. No patient had an overall worsening of symptoms.

DISCUSSION

Main findings

In this study, 25 of the 40 patients included completed the palliative rehabilitation program, and 64% of them had a functional improvement of at least 10%. However, 35% of patients died during hospitalization, a larger proportion compared to other studies on palliative rehabilitation [21, 24]. These were patients who needed more palliative care than rehabilitation. These results point to the clinical fragility of this population and reinforce the need to optimize selection of patients with advanced cancer for palliative rehabilitation programs.

Through univariate logistic regression analysis, we showed that CRP and Pronopall score were statistically significant predictive factors of functional improvement in patients with advanced cancer. Although not shown in multivariable analysis, these results support the findings of the few studies associating palliative rehabilitation with predictive factors, in particular CRP. *Chasen et al.*, [24] found that among 116 patients with advanced cancer, those with CRP levels ≤ 10 mg/L were more likely to finish the program (RR = 1.52; $p = 0.029$; 95% CI [0.99; 2.34]). Similarly, *Amano et al.*, [25] demonstrated that an increase in CRP was associated with a decrease in physical and functional performance. As simple and widely used indicators, these two variables may guide physicians in evaluating the suitability of rehabilitation referral.

The other variables tested in the study were not significant. However, some items of the Pronopall score, such as a low number of metastatic sites, a high PPS score, high albumin levels, and low LDH levels, showed a trend towards functional improvement. Individually, these variables were not significant in this study, likely due to insufficient statistical power. Moreover, variables associated with aggressive cancer, such as multiple hospitalizations for acute medical events in the past year, undergoing several therapeutic protocols, and having a recent diagnosis of advanced-stage cancer (within the last 3 months or less), appeared to reduce the likelihood of functional improvement. The effect of repeated hospitalizations on the loss of patient autonomy should not be overlooked. Furthermore, the potential role of prehabilitation, corresponding to a preparatory program aiming to optimize functional performance before an intervention, should be explored, particularly before palliative chemotherapy for newly diagnosed cancers. A study by *Nottelmann et al.*, [26] demonstrated that the quality of life of patients with newly diagnosed advanced cancer (≤ 8 weeks) improved significantly in the group that received rehabilitation alongside cancer treatment, compared to the group receiving only oncological care. In the same study, patients in the rehabilitation group appreciated the systematic consultation with a rehabilitation-palliative care physician.

In addition to functional improvement, the key symptoms impacting quality of life, as assessed by the ESAS questionnaire, showed a general improvement in all patients at the end of hospitalization. Similar results were found by *Feldstain et al.*, [12], with a 16.7% improvement in total ESAS scores between before and after palliative rehabilitation.

The main goal of hospitalization for palliative rehabilitation is to improve a patient's quality of life. Patients' objectives may not always be coherent with the severity of their illness, and it is the physician's responsibility to discuss these objectives with the patient and suggest more achievable objectives. In this study, patients reported achieving a mean of 67% of their initial personal objectives, based on their own assessment. Achieving independence, especially in mobility and daily activities, was the most commonly cited objective. The keywords describing the patients' objectives in our study mostly appear in the "Patient Dignity Inventory." This inventory was developed by a Canadian team to identify the recurring issues for improvement according to patients receiving palliative care. These keywords are also included in the "Distress Thermometer" of the National Comprehensive Cancer Network [27], a self-assessment tool used to screen for problems and distress in cancer patients. Themes concerning balance and physical performance are not included in these two lists. The use of checklists in palliative care [28] can help physicians to guide patients regarding treatment options and the impact of their disease on their daily life [29].

Strengths and limitations

The study has several limitations. First, due to the retrospective design of the study many data were missing, in particular the initial and final PPS, which are essential for statistical analysis. Second, the study was conducted in a single center and may lack external validity. The concept of palliative rehabilitation is relatively new, and there are currently only a few palliative rehabilitation centers in France with multidisciplinary teams.

Third, the study included all types of cancer, which may be a confounding factor. Different cancers have different prognoses, and their severity depends on specific and independent parameters. Lung cancer was the most represented cancer in the study, and it is the most aggressive cancer, with a higher mortality rate than other cancers in France [30] suggesting that more patients are in a palliative stage. Among the patients who died during the study, half were diagnosed with lung cancer. This confounding factor causes considerable statistical variability and reduces the power of the analyses. Despite this lack of power, the significant values identified appear to be quite robust.

Finally, a self-assessment bias cannot be excluded, particularly with the ESAS questionnaire. Indeed, the answers may have been dependent on the patient's psychological state at the time of evaluation, leading them to respond in a way they perceived as socially desirable rather than providing entirely truthful answers. However, given the inherently subjective nature of symptoms such as fatigue, pain, dyspnea, and well-being, their evaluation necessitates a self-administered questionnaire. In contrast, functional performance was assessed using a standardized scoring system with clearly defined criteria, evaluated by the physician to ensure the most objective and accurate analysis possible.

CONCLUSION

This study evaluating palliative rehabilitation in patients with advanced cancer showed that CRP and Pronopall score were predictive factors of functional improvement. Although the connection between functional dependence and poor survival is well established, our findings offer a novel perspective by suggesting that vital prognosis scores may also help predict functional improvement. These preliminary results indicate the potential utility of relevant scores for patient selection. Further validation is needed through larger-scale studies, such as the ongoing multicenter European study [31], led by the INSPIRE consortium.

Abbreviations

CRP	
C-Reactive protein	
ESAS	
Edmonton Symptom Assessment System	
LDH	
Lactate dehydrogenase	
OR	
Odds Ratio	
PPS	
Palliative Performance Scale	
WHO	
World Health Organization	

Declarations

Ethics approval and consent to participate

The data analysis was conducted in compliance with medical ethics, anonymity, and confidentiality. The institutional ethics committee of the Rouen University Hospital "Ethics Committee for Research on Existing Data", in accordance with the Declaration of Helsinki of the World Medical Association, approved the study protocol (n° E2023-67). The study is retrospective in nature and is therefore excluded from the scope of the Jardé Law (n° 2012 – 300 of March 5, 2012), meaning that patient consent was not required.

Consent for publication

Not Applicable.

Competing interests

The authors declare that they have no competing interests.

Patients with no functional improvement, PPS < 10%

(n = 24)

Including 1 transferred and 14 died

50 patients excluded:

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contribution

L.D. prepared figure and tables. L.D. and JB.P. wrote the main manuscript text. All authors reviewed the manuscript.

Acknowledgement

The authors are grateful to assist for statistical analysis and Nikki Sabourin-Gibbs, Rouen University Hospital, for her help in editing the manuscript.

Data Availability

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

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Figures

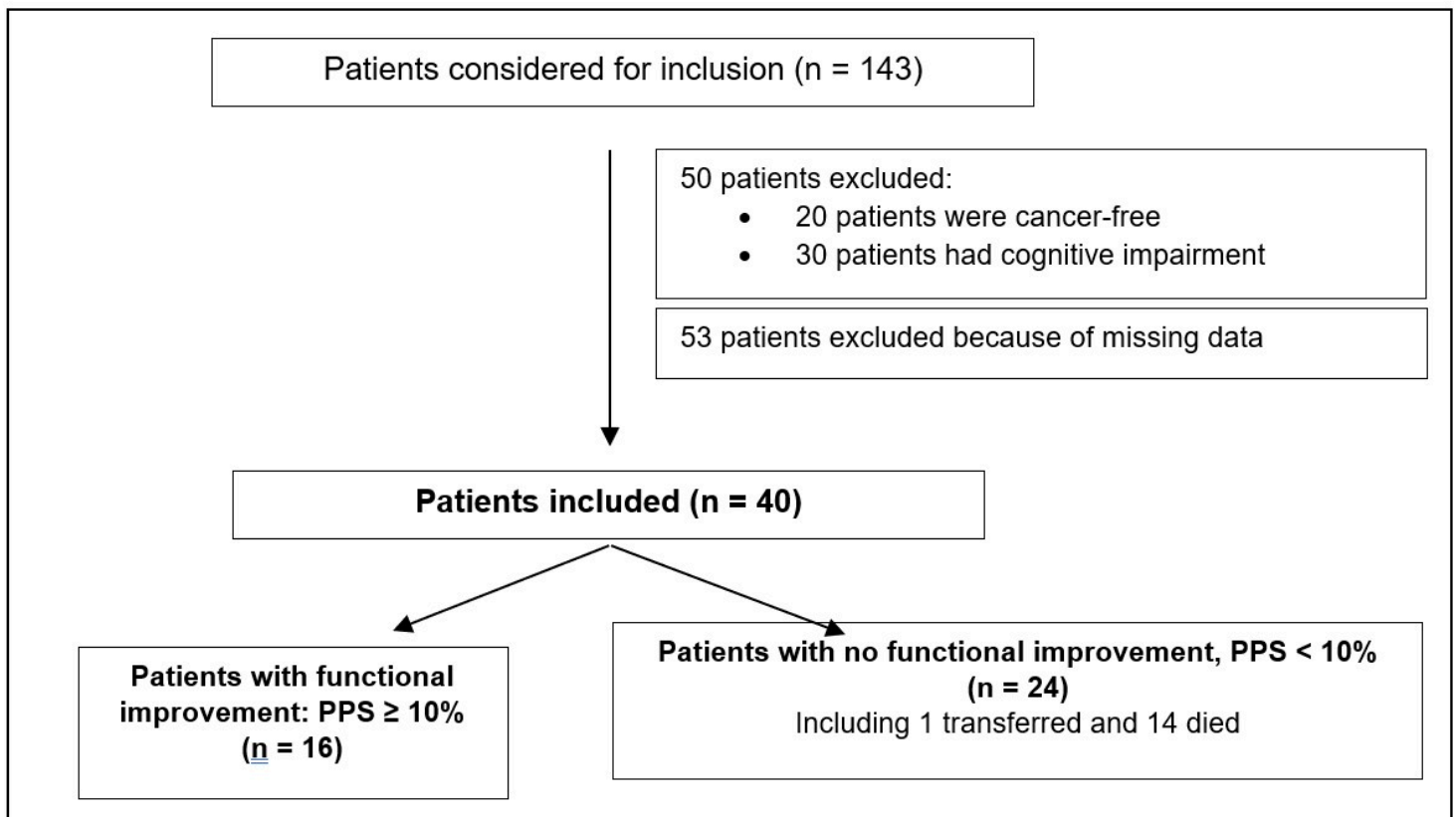


Figure 1

Flow chart

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