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The Geriatric Impact in the Management of Complex Cancer Patients: A Monocenter Experience

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Abstract

New technologies, aging-related changes, and evolution in patients' needs have led to a new scenario in all oncological fields in front of which we have to move on. Technological progress has made it possible to increase the number of patients treated, including elderly patients and

generally those at higher risk of toxicity. However, this scenario has led to new problems requiring new skills to be addressed. For this reason, Gemelli-ART (Advanced Radiation Therapy) of Fondazione Policlinico Universitario A. Gemelli IRCCS – Rome, Italy, started a collaboration with a team of geriatricians trained in geriatric oncology to manage the growing number of elderly patients and to deal with treatment-related toxicity and supportive care to complete planned treatment. This study evaluates the impact of geriatric oncology intervention performed by a geriatrician with particular expertise in managing complex cancer patients admitted to an Oncology Unit. The number of complex patients admitted to the Radiation Oncology Unit raised from 90 in 2016 to 226 in 2018 (+151.1%). 63.4% of complex patients underwent treatment, with a curative goal in 43.7% of cases. Among all admitted patients, the treatment discontinuation rate was 14%. The treatment discontinuation rate was 5.5% in patients over 80 years old with planned admission, versus 27.0% in patients admitted from the emergency room. Our data suggest that geriatric expertise in an Oncology Unit helps personalize patients' treatment and allows for treating an increasing number of complex patients. Identifying frail and complex patients is essential to manage these situations effectively and efficiently, optimize healthcare resources, avoid over and under-treatment, and provide the best care.

Keywords
Geriatric oncology; older cancer patients; co-management; supportive care

1. Introduction

Aging is one of the most significant risk factors for cancer [1]. The incidence of new cancer diagnoses occurs mainly in the older population. Approximately 60% of all cancers and 70% of cancer mortality occur in people over 65. Due to the population aging, new cancer cases are expected to double by 2035 and reach 14 million among older adults [2].

Population aging leads to fundamental changes in cancer patients; this scenario requires an appropriate and tailored approach to older patients. Early cancer diagnosis, new therapies, and supportive care have turned many cancers into chronic diseases, among other health conditions that elderly patients may experience. Coexisting health conditions can complicate treatments and management of older adults with cancer. Older patients and especially older cancer patients are often complex, and managing this complexity in fast and busy clinics such as oncology settings becomes increasing challenging.

Complex patients are defined by the Agency for Healthcare and Quality (AHRQ) as persons with two or more chronic conditions where each condition may influence the care of the other state (National Quality Forum. Multiple Chronic Conditions (MCC) Measurement Framework. Washington, D.C.; 2012) [3].

Complex patients with multiple chronic conditions have increased medical costs, a higher number of preventable complications, higher rates of avoidable hospitalizations, and decreased quality of life [4, 5].

The complexity of older people makes it necessary to follow the patient throughout his or her journey and to personalize treatments to reduce toxicity and optimize efficacy. To date, the management of complex patients is often fragmented into multiple specialist consultations with consequent dangerous loss of data and treatment discontinuity. This model attempts to create a multidisciplinary system of care, which could be extremely exhausting and expensive for the patient and his or her family and compromise patient care. Lack of interaction among consulting specialists can result in contradictory messages, the risk of drug interactions, and aggravation of a problem while trying to solve another [6].

Cancer patients are often complex for pre-existing comorbidities, frailty status, treatment-related toxicities, multiple disabling symptoms, or financial toxicities. Moreover, accelerated aging seems to affect cancer patients: an emerging concept in oncology is that chemotherapy causes premature or accelerated aging in adult and childhood survivors [7]. Aging and chemotherapy-related side effects have several common biomarkers, including telomere shortening, decreased maximal oxygen consumption, and increased levels of inflammatory cytokines [8, 9]. Therefore, these patients can be considered "geriatric" in some ways, and a geriatric co-management could be useful for them [10]. In cancer patients, regardless of age, disease and past and ongoing treatments, together with related toxicities and organ dysfunctions, can make them complex to manage, especially in the presence of an acute event that leads to treatment discontinuation and the need for hospitalization.

In many settings, geriatric co-management has become an excellent method to assure specialized treatments with a holistic approach and benefits on length of stay, complication rates, and mortality [11, 12]. The geriatric approach has been validated and is highly recommended in oncology by international societies [13, 14], and geriatric co-management is starting to take hold in several cancer centers [15, 16]. One of the most significant challenges for geriatricians in this field is distinguishing between fit patients who may benefit from standard treatment, vulnerable patients who benefit from personalized treatment, and unfit or frail patients who should be directed to the best supportive care only. Survival and reduction in cancer symptoms should be carefully weighed against chemotherapy-related toxicity and loss of independence.

In 2016, a geriatrician specialized in geriatric oncology started working in the Radiation Oncology Department at Fondazione Policlinico Agostino Gemelli Hospital. Our study observed how the direct oncogeriatric approach and geriatric skills in an oncology unit changed how complex patients were managed and treated.

2. Materials and Methods

In 2016, the Gemelli-ART (Advanced Radiation Therapy) Centre of Fondazione Policlinico Universitario "A. Gemelli" IRCCS in Rome hired an onco-geriatrician to co-management the complex patient in the Radiation Oncology Unit. Before 2016 the ward was run by radiation oncologists who could consult with a general geriatrician when needed. From 2016 the oncogeriatrician took part in all patient's clinical pathways, from clinical assessment to better support treatment choice, supportive care and management of treatment complications, to follow-up. These activities were made possible through a dedicated outpatient clinic for patients selected by the radiation oncologist, admission in the Radiation Oncology ward, and involvement in tumor boards. In particular, the Radiation Oncology ward was dedicated to and focused on managing cancer-related complications

and treatment toxicities and managing treatments in frail and vulnerable patients through supportive care.

We analyzed data from the first three years of this co-management, from 2016 to 2018, evaluating the impact of co-management in taking care of complex patients admitted to the Radiation Oncology unit. Subsequent data were not collected due to the pandemic's impact on healthcare systems. We conducted a retrospective study, analyzing data of patients admitted to the Radiation Oncology ward during the defined period.

All the complex patients admitted to the Radiation Oncology ward from 2016 to 2018 were included. Patients were defined as complex when one or both occur: 1) age ≥80; 2) patients admitted from the emergency department for intercurrent acute disease or severe toxicities related to oncology treatment, regardless of age. Complex patients (according to the MCC definition) [3] were defined as individuals older than 80 years old with multimorbidity, polypharmacotherapy, or frailty status above oncologic disease [17]. In addition, we defined complex patients admitted from the emergency department, regardless of age, because of the admission reason, a sudden illness requiring emergency hospitalization in a patient already suffering from cancer.

Data collected for all patients were diagnosed at admission, length of stay, cancer type and ongoing treatment (classified as palliative or curative), and treatment interruption (any temporary suspension was not considered).

Our study aimed to evaluate the impact of geriatric co-management of complex patients admitted to an oncological unit. The primary outcomes were reduced length of stay and the number of complex patients admitted to the unit.

We developed a database matching the management data of the Fondazione Policlinico Universitario A. Gemelli IRCCS computer system (SI) and the clinical data extracted by SPEED RO – KBMS (Knowledge-Based Medical Software), an Italian management software specialized for the radiation oncologists' needs, which archives patient's clinical history and management of Radiation Oncology Department.

Categorical variables were compared to Pearson's Chi-square test, and the column proportion between groups was compared according to the Z-test.

3. Results

2949 patients were admitted between 2016 and 2018 from the Radiation Oncology Unit; 456 (15.5%) were complex patients [Table 1].

Table 1 Complex patients in the Radiation Oncology Unit.

COMPLEX PATIENTS IN THE RADIATION ONCOLOGY UNIT	Total	2016	2017	2018
Complex patients (n)	456(100%)	90	140	226
Male (n)	187(41%)	43	54	90
Female (n)	269(59%)	52	86	131
Mean age (years)	60.3	59	60	62
Planned admission of patients over 80 y (n)	264	63	78	123
ED unplanned admission (n)	192	30	64	98
Hospital length of stay (days)				

- total hospital admission average	-	5.6	5.5	5.5
- ED unplanned admission average	-	20.6	17.2	13.2

We observed an annual increase in the number of older patients. The number of 65 years old patients discharged increased with a percentage growth of +28.7% in 2017 and +46.7% in 2018. The number of patients over 70 years old arises with a growth of +41.4% in 2017 and +72.3% in 2018. The number of patients over 80 years old increased with +23.8% in 2017 and +95% in 2018.

Considering complex patients admitted to the ward, the number raised from 90 in 2016 to 226 in 2018 (+151.1%). The admissions from the emergency department to the Radiation Oncology ward rose from 30 in 2016 to 98 in 2018 (+226.6%) [Figure 1].

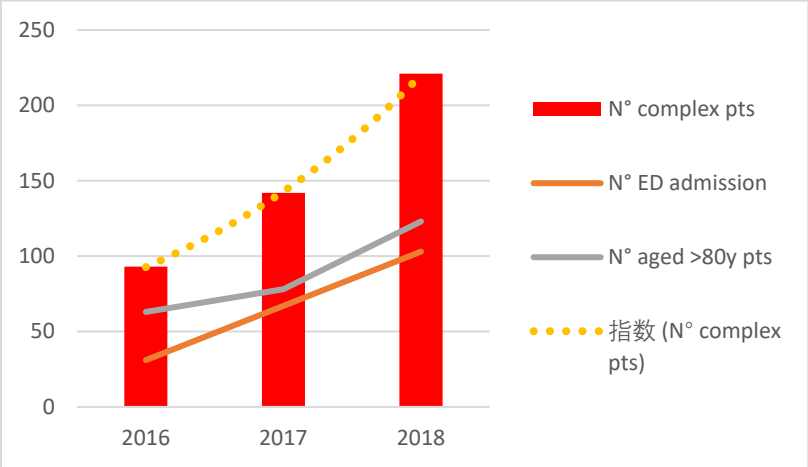

Figure 1 Complex patients in a Radiation Oncology Unit.

Despite the increase in complex patient admissions, the average hospital length of stay for the entire ward remained unchanged: 5.6 days in 2016, 5.5 days in 2017 and 2018. Meanwhile, the average length of stay of patients from the emergency department decreased significantly: 20.6 days in 2016 to 13.2 days in 2018 (almost 36% less) [Table 2].

Table 2 Hospital length of stay (number of days).

	2016	**2017**	**2018**	**p-value**
Overall (n = 2895)	5.6; SD 15.3	5.5; SD 13.8	5.5; SD 11.2	0.895
OVER 80 y (n = 264)	6.9; SD 6.5	5.8; SD 5.5	5.8; SD 5.7	0.151
ED (n = 192)	20.6; SD 18.1	17.2; SD 11.3	13.2; SD 9.2	<0.001

The most frequent cause of admission for patients coming from the emergency department was pain (29.8%), followed by respiratory failure (15.4%), fever (13.0%), and neurological alterations (9.6%) [Table 3].

Table 3 Admission diagnosis.

ADMISSION DIAGNOSIS			
N° ED unplanned admitted patients	**192 (100%)**	**N° planned patients over 80 y**	**264 (100%)**

Pain	62(32.3%)	Pain	72(27.3%)
Respiratory failure	32(16.7%)	Radiotherapy	56(21.3%)
Fever	27(14.0%)	Radio-chemotherapy	56(21.3%)
Neurological alterations	20(10.4%)	Electrochemotherapy	14(5.3%)
Sepsis	18(9.4%)	Biopsy	8(3.0%)
Anemia	4(2%)	Sepsis	5(1.9%)
Dysphagia	4(2%)	Renal failure	5(1.9%)
Mucositis	4(2%)	Chemoembolization	4(1.5%)
Hydronephrosis	3(1.6%)	Mucositis	3(1.1%)
Others	18(9.4%)	Radio chemoembolization	3(1.1%)
		Respiratory failure	2(0.8%)
		Others (<1%)	36(13.6%)

Pain was the most frequent cause of planned admission in patients over 80 years old (28.2%). The second most frequent access causes were radiotherapy treatment (22%) and concomitant radio-chemotherapy treatment (22.0%). [Table 3] since chemotherapies in patients judged frail are performed as inpatients in our unit.

Data on treatments performed were available for 426 patients out of 456. Between 2016 and 2018, more than 60% of complex patients underwent oncological treatments (radiotherapy alone 50.4%, combined radio chemotherapy 41.5%). The treatment intent was 43.7% curative and 56.3% palliative. Among all complex patients admitted, the treatment interruption rate was 14% (38 patients): among patients admitted from the emergency department, the interruption rate was 27.0%; in the rest of the outpatients over 80 years old, the interruption rate was 5.5% [Table 4].

Table 4 Complex patients treated in the Radiation Oncology Unit.

COMPLEX PATIENTS TREATED IN THE RADIATION ONCOLOGY UNIT		
	N° patients (population)	**%**
Patients undergoing cancer treatment (RT and/or CT)	**270(426)**	**63.4%**
Radiotherapy plus Chemotherapy	112(270)	41.5%
Radiotherapy	136(270)	50.4%
Chemotherapy	22(270)	8.1%
Best supportive care	**156(426)**	**36.6%**
Treatment intent		
- Curative	**118(270)**	**43.7%**
- Palliative	**152(270)**	**56.3%**
Treatment interruption	**38(270)**	**14%**
- Planned admitted patients over 80 y	7(127)	5.5%
- ED Unplanned admitted patients	31(143)	27.0%

The most frequent reasons for treatment interruption were infections (40.8%), pain (17.1%), neurological alterations (10.5%), and respiratory failure (10.5%). Among the 38 patients who early

closed the treatment, 50% (19 patients) were directed to palliative care services, while 25% (9 patients) died during the hospitalization.

No statistically significant difference was found in the interruption rate of older cancer patients in the observation period. Still 2018, after three co-management years, the completed treatment percentage in older cancer patients rose to 97.1%. In emergency department admitted patients we observed a significant reduction in suspension treatment rate, from 48.1% in 2016 to 5.7% in 2018 (p-value < 0.001) with 94.3% of treatment completed [Table 5].

Table 5 Number of patients who continued and who interrupted the treatment.

	2016	**2017**	**2018**	**p-value**
OVER 80 y (n = 127)	N = 25	N = 33	N = 69	
Continue	24(96%)	29(87.9%)	67(97.1%)	0.151
Interrupted	1(4.0%)	4(12.1%)	2(2.9%)	
ED (n = 143)	N = 27	N = 46	N = 70	
Continue	14(51.9%)	32(69.6%)	66(94.3%)	<0.001
Interrupted	13(48.1%)	14(30.4%)	4(5.7%)	

4. Discussion

The constant and active presence of a geriatrician specialized in geriatric oncology increased and optimized the management of complex and frail patients with cancer.

As it has been shown, the presence of a geriatrician with expertise in geriatric oncology increased the number of older cancer patients managed in the unit each year; the number of patients admitted from the emergency department raised too, which indicates that the oncology unit could manage its patients without the need to use other wards less specialized in cancer treatment (i.e., geriatric or internal medicine unit). The management of a patient in the belonging unit, supported by a physician specialized in managing complexity in cancer patients, permitted the realization of an excellent multidisciplinary and multidimensional care pathway that allowed the patient to continue treatment. Furthermore, this approach improved hospitalization management by reducing length of stay with benefits on hospital costs and patient outcomes such as the risk of hospital-acquired infections and disability [18, 19]. In particular the length of stay of patients from the emergency department was reduced from 20.6 days to 13.2 days in 3 years (almost 36% less; p-value < 0.001) [Table 2].

We also observed that pain was the most frequent symptom of admission for our complex patients. Pain in cancer patients has a prevalence of 15% to 80% and is often undertreated [20]. Cancer pain is multifactorial and needs to be optimally treated to maintain a good quality of life and treatment compliance. Pain management in older and complex patients must consider multiple factors [21] that could be followed in co-management between oncologists and geriatricians.

Our study shows how geriatric co-management can be the key tool to address the modern era of oncology. Oncologists and radiation oncologists must update on new specialized therapies and innovative treatments yearly. Alongside new therapies that prolong life expectancy with cancer, older patients become complex with aging and comorbidity. Oncologists face challenging patients with various concomitant clinical conditions and symptoms, whose integration and cumulative effects result in varying degrees of functional impairment, cognitive deficit, nutritional problems,

and geriatric syndromes. Cancer is often one of several coexisting chronic medical conditions for older patients: 80% of older adults with cancer present two or more different diseases, and one out of four cancer survivors aged 65 to 74 years have more than five comorbidities [22].

The National Institute of Aging described this phenomenon as a "silver tsunami" for which we are unprepared [23]. This change is one the most crucial cause of hospital collapse risk as declared in the Royal College of Physicians report "Hospital on edge? The time for action" which addressed all the main issues and problems of the 20^{Th-} century of medicine as the primary solution to this problem.

Treatment choice among these patients is complex due to significant heterogeneity in physiological reserves, comorbidities, and functional capacity. Older and oldest-old patients are less likely to receive treatments than younger patients [24]. A CGA run by a geriatrician could correctly assess frailty, and predict the severity of treatment, related side effects, and risk of death. In geriatrics, physical performance is strictly related to frailty [25]. Patients with cancer often present a material weakness that can threaten everyday activities [26]. In older cancer patients, low gait speed is associated with mortality and disability [25]. The pharmacological treatment of these complex patients poses a challenge due to the many drugs prescribed and the high risk of adverse drug reactions [27]. Drug-related diseases cause 3-5% of all hospital admissions in Western countries, accounting for 5-10% of hospital costs and substantially increasing morbidity and mortality [28]. The frequency and severity of adverse drug reactions appear to be higher in clinically complex patients [29].

The psychological and social experience of cancer differs for young and older adults. Roles, responsibilities, and support systems change with aging [30]. Lack of social networks and family support may dramatically influence the choice of oncological treatment. Moreover, the financial burden is widespread in older cancer patients and can lower adherence to cancer treatments, shorter survival, poorer prognosis, and greater risk of recurrence [31].

5. Conclusions

Many aspects must be considered in managing complex or frail cancer patients, but above all, we wish for an evolution of cooperation among geriatricians and oncologists. The results of this study highlighted how parallel multidisciplinary management of the elderly cancer patient allows, on the one hand, an entry to treatment for a more significant number of patients (through careful selection) and a tailor-made treatment. On the other hand, a more precise evaluation and management of treatment-related toxicities allows for reducing the interruptions of treatment, reducing the length of hospital stay, and improving patients' quality of life. Modern geriatrics rests its foundations on the knowledge of frailty and complexity. Identifying frail and complex patients is essential to treat these patients most effectively and efficiently, optimize health economic resources, avoid over and under-treatment, and offer the best supportive care.

All the literature data show how that geriatric assessment, in all its forms (screening or comprehensive testing or consultations with geriatricians), improves outcomes related to older cancer patients. There are no studies related to patient co-management. The increasing complexity of patients raises the need for constant intervention not limited to simply framing the patient before treatment. The purpose of our study was to evaluate cost and benefit the constant intervention of an oncological geriatrician within the oncology team and the combined management of treatments.

Author Contributions

Conceptualization and design of the work: AB, BDC, GFC. Methodology and data curation: AB, ERV, BDC, DF, FP. Writing-original draft preparation: AB, BDC, DF. Writing-review and editing: ERV, LT, MAG, SB, VV, FL, GFC. Supervision: GFC, VV, FL. The final paper has been seen and approved by all the authors.

Competing Interests

No conflict of interest to declare.

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