

# Management Patterns of the Older Population with Cancer during The Early State Of Alarm In the Valencian Autonomous Community: The GIDO GERICOV-2020 PROJECT

**Keywords:** Cancer; Neoplastic disease; Covid-19; Immunocompromised

## Abstract

In the current care scenario of the COVID-19 pandemic, older oncology patients are especially vulnerable and find themselves facing a double threat. On the one hand, the risk of contracting an infection that we still know little about facilitated by immunosuppression and potentially aggravated by the antineoplastic treatment toxicity, comorbidities, and the cancer severity [1]. On the other, the neoplastic disease itself, along with the risk of losing an opportunity because of the reduction of medical cancer care, due to the limitation or re-allocation of resources [2]. Therefore, one priority aspect is establishing the individual risk associated with the neoplasm and the treatment, in the context of each type of oncological patient [3]. Although cancer is assumed to be an adverse prognostic factor in patients with COVID-19 and in older persons, there is still uncertainty and a lack of robust evidence. Recommendations have surged concerning therapeutic decisions in oncology patients, and the records of cancer patients with COVID. Nevertheless, the real impact of therapeutic decisions in clinical practice remains unknown, especially in the older patient group as well as the evolution of this population group.

To increase the available evidence in the current pandemic, we aimed to retrospectively record the management of patients 70 years and older with cancer who received care in the Medical Oncology services of the hospitals belonging to the GIDO group during the early pandemic.

## Objective

To increase knowledge regarding this population, we planned to retrospectively analyse patients with cancer aged 70 year or older that had been assessed in the Medical Oncology service of the Hospitals belonging to the GIDO group: Group for Investigation and Divulcation in Oncology.

## Introduction

On 14th March 2020, a state of alarm was declared in Spain [4]. A COVID-19 infection is a threat for oncology patients, immunocompromised by definition, owing to their neoplasia and the treatments administered to treat it [5-8]. The risk/benefit balance that is always considered during the treatment of an oncology patient has become exceptionally complex during the COVID-19 pandemic. Both older patients and patients with cancer have a greater risk of infection and mortality due to the COVID-19 infection [9]. During this situation, multitudes of recommendations have arisen, not only how to avoid the infection and for its management, but also in making decisions regarding active treatment in the oncology

population. In general, the recommendations agree in maintaining adjuvant indications despite the threat of COVID-19 infection during treatment [2,8]. The decisions concerning the population with metastases are more contradictory, because while there is a risk of infection, delays in palliative treatment may allow the basal status of the patient to deteriorate and cause a loss of the therapeutic window [2]. Delays should also include the evaluation of the increased risk of admission for the management of palliative symptoms during a situation when available resources are scarce [2,8]. With the arrival of the pandemic, new methods of communication with patients have been implemented, promoting the use of telephone contact and reaching an agreement with patients regarding delays, cancellations, or administration of treatment. In summary, we find ourselves in a challenging situation regarding therapeutic decisions for the oncology patient, proposing how and when to provide cancer treatment during this time [3].

## Materials & Methods

### Study Design & Participants

A retrospective observational study was designed to collect online data from the Medical Oncology service of the hospitals integrated in the GIDO. Patients with outpatient services booked were identified for the period 16th March 2020 to 31st March 2020, including patients that were being followed-up and those that were receiving active treatment. Planned first consults during the data collection



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time period were also included. Patients 70 years or older at the time of inclusion were included.

Data were collected from electronic clinical histories, including demographic and clinical characteristics.

The project objective was to determine the relationship between the older outpatient population with cancer and COVID infection, and, in particular, to describe the management patterns of this population during the first weeks of the state of alarm.

Here, we present the second part of the project, in which we analyse the treatment of the sample population both in terms of follow-up and active treatment.

This study was approved by the Research with Medicines Ethics committee of the University and Polytechnic Hospital La Fe and classified by the Spanish Medicines Agency as an Observational Study No Post-Authorization (NO-EPA, as per the Spanish abbreviation). Informed consent for voluntary participation was requested from the patients, allowing consent to be provided via phone call to avoid hospital contact. The definition of COVID contact or infection was collected from the clinical history.

### Statistical Analysis

For the descriptive analysis, continuous variables were presented as means with standard deviation or medians with the corresponding interquartile range (IQR), depending on which was the most appropriate for each case. Categorical variables were presented as numbers and percentages (%). Potential risk factors and associations with COVID infection were explored using the Cox proportional model with hazard ratio and the corresponding confidence interval (HR 95%CI). All statistical analyses were conducted using SPSS Statistics version 21.0 (IBM: New York, NY). A p-value <0.05 was considered as statistically significant.

### Results

Following the required approvals, 13 Researchers from 9 hospitals in the Valencian Autonomous Community participated (Figure 1). In total, data were analysed for 1127 patients that were included for the period 16 March 2020 to 31 March 2020.

#### Demographic Characteristics

The median age was 76 years (70-94). Patients 80 years and older comprised 26% of the study sample. The gender distribution was even (51% women). Breast cancer predominated (24%), followed by lung cancer (19%), and colon cancer (16%). The demographic characteristics and histological distribution are shown in the Table 1. The majority of the patients (55%, 616) had stage IV at the time of their appointment. 63% of appointments were for treatment administration, and 35% of first appointments (66 total) were also for treatment administration. Appointments were kept for 91% of the patients (1020), and more than half were face-to-face consults (600, 59%).

#### Demographic Characteristics between Both Types of Populations

The demographic characteristics of both groups are compared in Table 2. Over half (736 patients, 65%) of the patients included were receiving active treatment compared with 35% (391 patients)

**Table 1:** Summary of patient characteristics.

CHARACTERISTIC	PACIENTS (N:1127)
Age (median, extremes)	76 (70-94)
≥ 80 years old	294 (26%)
Female/Male	568 (51%)/559(49%)
Histology	
Breast cancer	278 (24%)
Lung cancer	221 (19%)
Colon cancer	180 (16%)
Rectal cancer	41 (4%)
Prostate cancer	71 (6%)
Bladder cancer	57 (5%)
Pancreatic cancer	44 (4%)
Gastric cancer	33 (3%)
Ovarian cancer	32 (3%)
Liver/Bile ducts	27 (3%)
Melanoma	26 (3%)
Head and neck cancer	24 (2%)
Lymphoma	20 (2%)
Endometrial cancer	17 (1.5%)
Sarcoma	15 (1%)
Kidney cancer	14 (1%)
Neuroendocrine	10 (1%)
Anal cancer	7 (0.6%)
Esophagus cancer	5 (0.4%)
Brain cancer	3 (0.3%)
Cervix cancer	2 (0.2%)
Stage at the visit time	N: 1127
Stage 0	45 (4%)
Stage I	88 (8%)
Stage II	160 (14%)
Stage III	194 (17%)
Stage IV	616 (55%)
Stage IVNED	24 (2%)
Kind of assessment	N: 1127
First visit follow up	43 (4%)
First visit for treatment	23 (2%)
Follow up	352 (31%)
Treatment	713 (63%)
Type of treatment	736
Adjuvant	139 (19%)
Neoadjuvant	45 (6%)
Concurrent	18 (2%)
Metastatic first line	300 (41%)
Metastatic second line	134 (18%)
Metastatic third line	60 (8%)
Other	40 (6%)
Kind of treatment	736
Intravenous chemotherapy	339 (46%)
Oral chemotherapy	82 (11%)
Hormonotherapy	162 (22%)
Immunotherapy	72 (9%)
Tyrosine-Kinase Inhibitor oral	36 (5%)
Other	45 (7%)
Decision related to appointment	N: 1127
Cancelled	57 (5%)
Delayed	50 (4%)
Done	1020 (91%)
Type of contact	N: 1020
Face-to-face	600 (59%)
Remote (by phone)	420 (41%)

that were being followed-up. Overall, no significant differences were detected between groups for median age (77-76, p=0.157). Although the population 80 years and older were more likely to be found in the follow-up group (p=0.045). In terms of histological subtype, more patients with breast cancer and lung cancer were receiving active treatment compared to a larger number of patients with colon cancer who were being followed-up (p=0.0001). More patients receiving active treatment had stage IV (70% versus 26%, p=0.0001). More first

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assessments for follow-up than for treatment were conducted (11% vs. 2%,  $p=0.001$ ). More visits were cancelled in the follow-up group than in the active treatment group ( $p=0.0001$ ).

### Management Patterns in the Active Treatment Group

Out of 736 patients receiving active treatment, 139 (19%) were for adjuvant therapy, 18 (2%) concomitant therapy, and 40 (5%) neoadjuvant therapy. The patients with metastatic disease (539, 74%), 300 received first-line treatment, 134 second, and 60 third-line metastatic treatment. In terms of treatment type, 22% (162) were being treated with hormonotherapy, 82 (11%) oral chemotherapy, 71 (10%) immunotherapy, and 339 (46%) with intravenous chemotherapy. Around 5% (36) were receiving oral tyrosine kinase inhibitors.

#### A. Treatment Modification

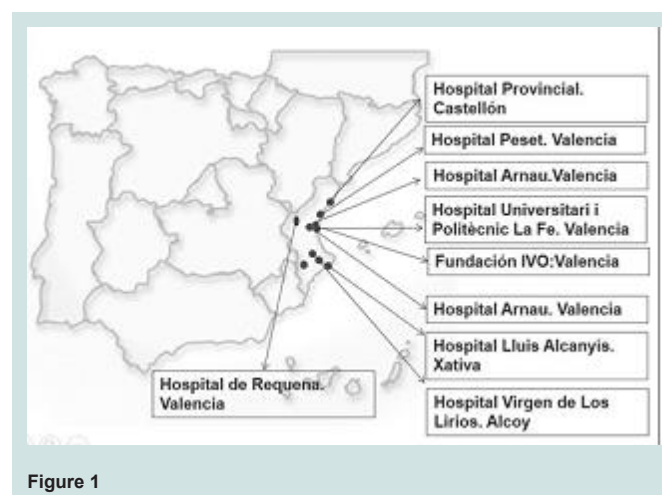
Out of the 736 patients in active treatment, the treatment regimen was modified in 190 (26%) cases. Of these 190 cases, 82 cases had treatment cancelled (43%), 19 had a reduction in dose (10%), and 89 cases had treatment administration delayed (47%). In total, the administration of treatment was suspended in 11% of the patients included in this study, delayed in 12%, and a dose reduction in 3% (Figure 2). In the cases whose treatment was suspended (82), in

**Table 2:** Comparison between patients groups (follow up versus treatment).

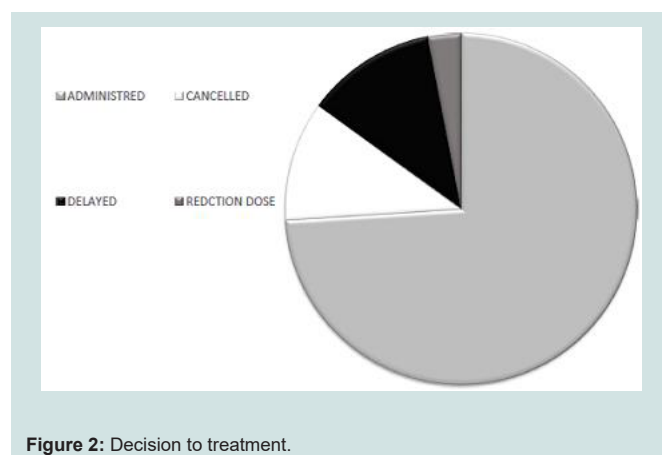
Characteristic	Follow up (n: 391) (35%)	Treatment (n:736) 65%	p
Age (median, extremes)	77 (70-91)	76 (70-94)	0.157
≥80 years old	115 (30%)	179 (24%)	0.046
Male/Female	198(50%)/193(50%)	361(49%)/375(51%)	0.661
Histology			
Breast	68 (77%)	208 (28%)	0.0001
Lung	70 (18%)	151 (20%)	
Colon	86 (23%)	94 (12%)	
Stage 0	33 (9%)	12 (1%)	0.0001
Stage I	48 (12%)	40 (5%)	
Stage II	98 (25%)	62 (9%)	
Stage III	94 (24%)	100 (14%)	
Stage IV	100 (26%)	510 (70%)	
Stage IVNED	12 (4%)	12 (1%)	
First appointment	43 (11%)	22 (3%)	0.0001
Decision			0.0001
Cancelled	33 (9%)	24 (3%)	
Delayed	23 (6%)	27 (3%)	
Done	335 (85%)	685 (94%)	
Cancelled tests			0.0001
Yes	80 (20%)	67 (9%)	
No	311 (80%)	669 (91%)	
Geriatric assessment			0.001
Si	51 (13%)	154 (21%)	
No	340 (87%)	582 (79%)	
Result of GA			0.001
Fit	19 (37%)	86 (56%)	
Vulnerable	10 (20%)	55 (35%)	
Frail	22 (43%)	15 (9%)	
Last follow up			0.0001
Alive without cancer	250 (63.7%)	152 (20.8%)	
Alive with cancer	115 (30%)	544 (74%)	
Dead without cancer	0	0	
Dead with cancer	22 (6%)	37 (5%)	
Dead by COVID-19	1 (0.3%)	1 (0.1%)	
Dead other reasons	0	1 (0.1%)	

**Table 3:** Reason for cancelling treatment.

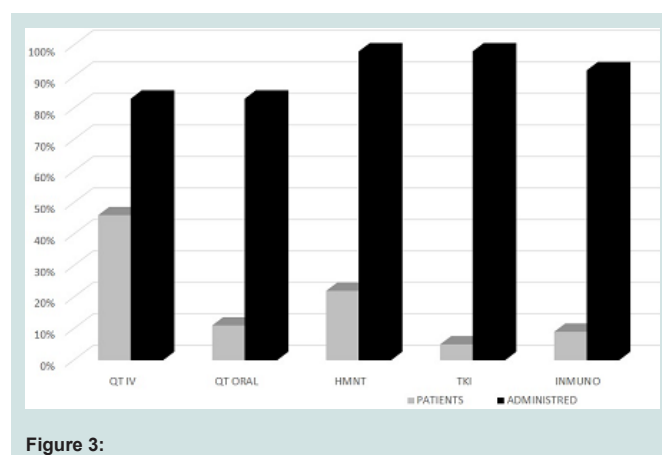
Reason For Cancelling Treatment	N: 82 (11%)
Physician's decision	44 (53%)
Toxicity	14 (17%)
Progression	11 (14%)
Patient's decision	11 (14%)
COVID infection	2 (2%)



**Figure 1**



**Figure 2:** Decision to treatment.



**Figure 3:**

53% this decision was made by the physician; in 17% of cases due to toxicity, 14% due to progression, and in 14% this decision was the patients. In 2 cases (2%), treatment was suspended due to COVID-19 infection (Table 3). The probability of suspending treatment did not correspond with older age, or with being older or younger than 80 years, nor gender, nor the planned appointment date. No correlation was found with histological subtype. It was correlated with stage, with treatment suspended in the patient group with stage IV ( $p=0.001$ ). More treatment was cancelled among patients with metastatic disease who were receiving second or third-line treatment ( $p=0.001$ ). In terms of type of treatment administered, treatment was continued in 98% of patients receiving hormone therapy, 83% of intravenous chemotherapy, 92% of immunotherapy, and 83% of oral chemotherapy (Figure 3).

#### B. Type of appointment

In the group of patients receiving active treatment, 25 appointments were cancelled (3%), 27 (4%) were delayed, and the appointment was maintained in 93% of cases (684). 500 in-person appointments were conducted, and 27% (184) were conducted via telephone. The probability that an appointment was cancelled correlated with histology (more appointments were cancelled among those with breast or colon cancer), with stage (more appointments were cancelled or delayed among patients with stage IV). No significant correlation was found with treatment indication (adjuvant, stage IV, etc.). More visits were cancelled for first-line metastatic treatment ( $p=0.0001$ ), (not with age, no with those older than 80 years, nor gender, nor appointment date, appointments were not cancelled for hormone therapy, intravenous chemotherapy, immunotherapy, nor oral chemotherapy).

The use of telephone contact was related with older age ( $p=0.0001$ ). In terms of telephone contact, 47% was in those older than 80 years vs. 26% in those younger than 80 years ( $p=0.0001$ ). Telephone contact also predominated among women (38%) vs. 23% ( $p=0.001$ ). A significant correlation was also observed for its use among patients with breast cancer (46% of contact via telephone was for patients with breast cancer). No correlation was found with appointment date. More telephone contact was used in the initial stages of hormone therapy treatment, but no telephone contact was used in the population treated with intravenous or oral chemotherapy, or immunotherapy.

#### C. Cancellation of complementary tests

In 67 cases, complementary tests were cancelled during the period analysed (9%). In more than half the cases (39, 58%), the test cancelled was a CT scan. In 2 cases elective surgery was cancelled, as well as 16 analytical tests, and 7 mammograms.

The cancellation of tests was not correlated with age or gender. More exploration tests were cancelled among patients with breast and lung cancer. Although no statistically significant relationship was detected, more tests were cancelled during the early days of the state of alarm declaration. More tests were cancelled among patients with advanced stages ( $p=0.005$ ), and patients receiving intravenous chemotherapy ( $p=0.023$ ).

#### D. Geriatric assessment

In the group receiving active treatment, a geriatric assessment

had been conducted at some point in 154 patients (21%). 14 cases were frail (9%), 54 pre-frail (35%), and 86 robust (56%).

#### Situation at the Final Evaluation

At the final study evaluation, one patient had died due to COVID (0.1%), 37 had died due to cancer (5%), and 1 had died due to other causes (0.1%). 544 were still alive with neoplastic disease (74%), and 152 alive without neoplastic disease (20.8%).

#### Characteristics of the Follow-Up Population

##### A. Type of appointment:

Of the 391 patients receiving follow-up care, 32 appointments (8%) were cancelled, 23 (6%) were delayed, and the appointments remained the same for 86% (336 patients). Telephone consults were conducted for 238 cases compared to 98 in-person appointments for those in follow-up care (71% vs. 29%). There were no differences for in-person appointment or telephone appointment based on age; however, telephone appointments were more frequent for women (76% of telephone appointments among females vs. 63% in males,  $p=0.04$ ). In terms of histology, telephone check-ups were more frequent in those with breast cancer (79% vs. 21%), followed by colon cancer (65%), and lung (60%) ( $p=0.006$ ). In-person or telephone appointments varied during the initial days of the state of alarm (Figure). In-person or telephone contact was not affected by stage at the time of follow-up.

Appointment cancellation was not correlated with age or gender. Cancellation was also not correlated with histology: colon cancer (14%,  $p=0.003$ ) vs. breast (3%) or lung (7%). More appointments were cancelled in stage II during follow-up care (Figure,  $p=0.002$ , 17% vs. 8% in stage IV).

##### B. Cancellation of complementary tests

In the group receiving follow-up care, tests were cancelled for 80 patients (20%). More tests were cancelled in the group of 80 years or older (25% vs. 18%,  $p=0.095$ ). There were no differences by gender (23% among women vs. 18% among men,  $p=0.176$ ). No differences were observed according to histology (23% breast, 23%, colon, 20% lung). More tests were cancelled for patients with stage II (25%) than for those with stage IV (18%) ( $p=0.03$ ).

##### C. Geriatric assessment

In the group of patients receiving follow-up care, 50 patients (13%) had undergone geriatric assessment: 14 cases were frail (42%), 10 pre-frail (20%), and 19 robust (38%). In terms of conducting a geriatric assessment, there were no differences for age; however, more geriatric assessments were conducted among males ( $p=0.003$ ) (7% vs. 18%), more among patients with lung cancer ( $p=0.0001$ ) (27%) and colon cancer (14%).

##### D. The situation at the final evaluation

At the time of the final evaluation, in the group receiving follow-up care, 1 patient had died due to COVID (0.3%), 22 had died due to cancer (6%), 115 were still alive with cancer (30%), and 250 were still alive and cancer-free (63.7%).

#### Discussion

On the 14th of March 2020, a state of alarm was declared in



Spain [4]. Older persons, with co-morbidities, such as cancer, were considered especially susceptible to suffering from the infection and its effects, with a higher probability of a fatal outcome than for other populations, given their immunosuppressed state, both due to the neoplasm and the treatment [1,2,10]. Given the potential infection risk that hospitals and medical centres supposed, many scientific associations released management recommendations for patients with cancer, in particular, focusing on avoiding frequenting hospitals [5-7]. Despite this, the majority of societies and cooperative groups did not initially include recommendations for the management of the older population group. In fact, French authorities proposed an age limit of 60 years for postponing cancer treatments, irrespective of whether the indication was curative or palliative [13-15]. Initially, only an opinion article published in the *Journal of Geriatric Oncology* was available [1], which suggested that older patients with cancer should not be systematically excluded from active treatment. Subsequently, the International Society of Geriatric Oncology (SIOG) declared that chronological age was not an exclusion criterion for treatment in this population and published their management recommendations [2]. Therefore, older patients with cancer found themselves in a situation at risk of being excluded from diagnostic, treatment, and follow-up processes to protect their health during the pandemic. Nevertheless, early on during the pandemic, no recommendations existed in our environment, and therefore each centre, service, and physician had to make decisions based on their own criteria, which changed depending on the progression of the infection. Neither has the actual management of older patients with cancer been published retrospectively, at least in our environment.

We present the first study with data of older patients with cancer in eight hospitals of the Valencian Autonomous community, which collates the management patterns of this population. The management of 1127 patients 70 years or older with cancer, seen between 16th of March 2020 and 31st March 2020, are presented. This manuscript deals with an older population, with 26% over 80 years of age (currently considered “the oldest old”) [11]. The data analysis demonstrates that oncogeriatrics is a reality, with an elevated number of older patients evaluated in consults during this period, also bearing in mind that the week of the 16th of March was a week of bank holidays in many places. We were unable to compare the percentage of the older population with adults due to a lack of records. The most frequent cancer types were breast, lung, and colon, more than half (55%) had stage IV, and 63% were receiving active treatment. Despite the adversity of the situation, active treatment was maintained in 74% of patients, cancelled in 11%, delayed in 12%, and modified in 5%. The probability of cancelling treatment was related with cancer type (breast and colon) and with stage IV. Very few appointments were cancelled, and a third of them were via telephone (older patients with breast cancer and oral treatment). The cancellation of exploratory tests in the treatment group was low (<10%). However, on the patient group receiving follow-up care, the majority of the appointments were changed to telephone consults (women with breast cancer) and more exploratory tests were cancelled (20%). None of these actions appeared to be correlated with an increased or decreased risk of COVID-19 infection.

The evidence extrapolated from the collected data suggests that the administration of active treatment was safe during the first weeks

of the state of alarm. The number of cancelled treatments was low, and especially correlated with indications for palliative treatment. In terms of follow-up care, the majority of consults were remote. Consults were prioritised, with first visits maintained as well as those consults in particular with pathologies that were not able to be delayed or those whose treatment intent was palliative-curative. Telephone consults were promoted, when appropriate, to avoid patients coming to the hospital and increasing their risk of infection. In terms of treatments, different modifications were made to minimize the risk of infection.

The pandemic and state of alarm has raised the need for rapid adaptation to oncology care. Despite the many recommendations aimed at minimising patient's attendance in the hospital, antineoplastic treatment should not be delayed [10]. The general perspective in the various clinics was quite homogenous for the older patient population with cancer, with few cancellations and treatment delays. Although our data may be biased owing to the initial low detection of asymptomatic cases, and because the participating hospitals were not the most affected by COVID infection in our environment. The oncology services that included cases did not cancel or shut down their service, and were therefore able to continue providing care, and in general, maintained their care provision. In contrast, our data showed that consults were suspended in palliative and advanced cases, where the benefit in this population is not clearly demonstrated. Chronological age is not a good parameter to base a decision for cancelling or not a consult or oncological treatments that have been demonstrated as beneficial in this population [2]. The approach via geriatric or frailty assessment may assist in the assessment of global health status in these patients and help to personalise therapeutic plans, although in our environment geriatric assessments are not widely used. Although oncogeriatrics is a reality, our data show relatively low use of the geriatric assessment in the management of this population (26%). Given the scarce number of assessments, no significant relationships were able to be established.

In conclusion, during the first weeks of the pandemic and state of alarm, in 8 medical oncology services of the Valencian Autonomous Community, provision of care was able to be maintained for patients receiving active treatment, and the majority of those receiving follow-up care had their appointments changed to remote telephone consults. Specific types of patients (breast cancer, hormonal treatment, colon cancer receiving follow-up care) appear to have an ideal profile for reducing the load of in-person appointments and promoting remote consults as an alternative.

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