

PROGNOSTIC FACTORS IN CANCER PATIENTS WITH PALLIATIVE NEEDS IDENTIFIED BY THE NECPAL CCOMS-ICO® TOOL

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Abstract The early identification of patients with palliative needs has shown benefits in terms of quality of life and treatment goals. No prospective methods have been applied in Argentina to identify palliative needs in cancer patients. The NECPAL tool combines the physician's own insight with objective indicators of disease progression and indicators of chronic advanced conditions. The aim of this study was to identify prognostic factors of mortality in hospitalized and ambulatory patients with cancer and palliative needs according to the NECPAL tool in a University Hospital in Buenos Aires city. Study variables were obtained by interviews with 10 physicians in charge of 317 patients with cancer over a 2-year follow-up period. A total of 183 patients with palliative needs were labelled as NECPAL+. Of these, 137 died after a median 4-month follow-up period. The death rate was 11% patients/month. The mortality was higher in inpatients during the first month ($p < 0.003$). In the multivariate model, the best predictors of mortality combining relevant indicators were: inpatients (HR 1.87; 95% CI 1.24-2.84; $p = 0.003$), initial diagnosis other than breast cancer (HR 2.04; 95% CI 1.23-3.40; $p = 0.006$), metastatic disease (HR 1.67; 95% CI 1.15-2.42; $p = 0.007$), functional deterioration (HR 1.95; 95% CI 1.28-2.97; $p = 0.002$), and malnutrition (HR 1.53; 95% CI 1.04-2.23; $p = 0.029$). The major breakthrough was the systematic prospective identification of palliative needs in cancer patients for the first time in Argentina. The NECPAL tool can improve the prediction of mortality in hospital settings.

Key words: advanced cancer, palliative care, chronic disease, prognosis, mortality

Resumen *Factores pronósticos en pacientes con cáncer y necesidades paliativas identificados con el instrumento NECPAL CCOMS-ICO®.* La identificación temprana de pacientes con necesidades paliativas ha demostrado beneficios en términos de calidad de vida y objetivos de tratamiento. En Argentina no han sido aplicados métodos prospectivos para identificar necesidades paliativas en pacientes con cáncer. El NECPAL CCOMS-ICO® combina la percepción del médico con indicadores objetivos de progresión de enfermedades crónicas avanzadas y es útil para determinar la prevalencia de pacientes con necesidades paliativas en la población general. El objetivo fue identificar factores pronósticos de mortalidad en pacientes internados y ambulatorios con cáncer y necesidades paliativas según NECPAL en un Hospital Universitario de la ciudad de Buenos Aires. Las variables se obtuvieron mediante entrevistas a 10 médicos a cargo de 317 pacientes con cáncer y necesidades paliativas durante dos años de seguimiento. Los predictores de mortalidad en el modelo multivariado fueron: hospitalización (HR 1.87; IC 95% 1.24-2.84; $p = 0.003$), diagnóstico distinto de cáncer de mama (HR 2.04; IC 95% 1.23-3.40; $p = 0.006$), enfermedad metastásica (HR 1.67; IC 95% 1.15-2.42; $p = 0.007$), deterioro funcional (HR 1.95; IC 95% 1.28-2.97; $p = 0.002$) y nutricional (HR 1.53; IC 95% 1.04-2.23; $p = 0.029$). De los 183 pacientes con necesidades paliativas identificados como NECPAL+, 137 murieron en un período medio de 4 meses. La tasa de mortalidad fue 11% por mes. La mortalidad fue mayor ($p < 0.003$) en el primer mes de hospitalización. El mayor logro fue la identificación sistemática y prospectiva, por primera vez en Argentina, de necesidades paliativas en pacientes con cáncer. La herramienta NECPAL puede mejorar la predicción de la mortalidad en entornos hospitalarios.

Palabras clave: cáncer avanzado, cuidados paliativos, enfermedad crónica, pronóstico, mortalidad

Palliative care (PC) has been successfully introduced into the public health system of many countries. The World Health Assembly (WHA) recommends strengthening PC as a part of a comprehensive healthcare approach that encourages all countries to design and implement PC programs in all levels of attention¹. Nevertheless, the development is unequal^{1,2}.

The early identification and the multidimensional assessment of palliative needs have shown clear benefits in terms of symptom control, quality of life, and treatment goals³⁻⁸. Patients who have access to specialized PC have better clinical outcomes with potentially lower treatment costs^{3,9,10}. They also receive less aggressive end of life care and survive longer^{11,12}.

Using the NECPAL CCOMS-ICO® (hereafter NECPAL tool), which has been content-validated in the Catalonian public health system, the prevalence of patients with PC needs was estimated in 1.5% in the general population³. Growing evidence shows that the NECPAL tool is useful to detect individuals with advanced chronic diseases (ACD) and PC needs and that it can be used to determine the prevalence in specific healthcare settings and in the general population^{3,6,8}. The use of a combination of several parameters in the assessment increases its accuracy as a screening tool^{13,14}. The validated NECPAL tool is freely available in Spanish, Catalan and English at http://ico.gencat.cat/en/professionals/serveis_i_programes/observatori_qualy/eines_de_suport/eines/instrument_i_programa/.

Argentina has a medium-high incidence of cancer with over 100 000 new cases per year, in both men and women, and ranks seventh in terms of incidence and third in terms of mortality among countries of the American region¹⁵⁻¹⁷.

Understanding the need of PC is essential for healthcare service planning³. The methods used to estimate PC need in the general population vary according to the different approaches and data sources. In 2016, the National Cancer Institute (Argentina) launched the National PC Program with emphasis on suffering prevention and the improvement of quality of life of cancer patients and their families¹⁸. Nevertheless, it does not establish a method to identify early PC needs in the target population. In the first study carried out with the NECPAL tool in Buenos Aires city, we found that 1 every 3 patients with ACD (cancer or non-cancer) could die within one year and had a clear need for PC. There are no PC public health programs running in the city so far¹⁹. Identifying patients with PC needs and accurately predicting mortality would facilitate a timely and efficient delivery of end of life care.

This study aims to identify prognostic factors of mortality in cancer patients with PC needs in our cultural context using for the first the NECPAL tool, a validated predictive instrument. It is part of the NECPAL Model

Program carried out at the Instituto de Investigaciones Médicas Alfredo Lanari, Universidad de Buenos Aires, and Pallium Latinoamérica.

Materials and methods

A 2-year prospective follow-up study was carried out in 2014-2016. All consecutive inpatients and outpatients ≥ 18 years old with cancer registered in our hospital were included.

The data was gathered by interviews with the medical staff in charge according to the NECPAL tool Manual for Databases²⁰. This tool provides both quantitative and qualitative evaluations. It offers a multifactorial, non-dichotomous assessment process that combines subjective perception (the surprise question [SQ]: Would you be surprised if this patient dies in the next year?) with other parameters, including the request (and need) for PC, the assessment of disease severity and progression, geriatric syndromes, psychosocial factors, and comorbidities (Charlson comorbidity index), as well as the use of health resources. It also includes specific indicators for selected illnesses (Table 1)²⁰. Patients considered NECPAL positive (+) are SQ+ patients who also fulfill at least one of the other parameters of the tool.

Socio-demographic and medical data were collected from medical records. Variables assessed were age, sex, patient's condition as inpatient or outpatient, diagnosis, nutritional status, performance status (Palliative Performance Scale), presence of metastases, specialty of the attending physician (oncologist, urologist, gynecologist, internist, oncohematologist, PC specialist) and date and time of the first visit to the PC ward.

The variables were obtained by interviews with the 10 physicians in charge (69 individual interviews) and by reviewing the clinical records. One evaluator conducted all staff interviews. The patients, identified only by their physicians, were stratified according to four levels of disease: Level 0 cancer (n:317); Level 1 cancer with ACD (n:226); Level 2 cancer with SQ+ (n:183); Level 3 NECPAL+ cancer with SQ+ and at least one indicator listed in Table 1 (n:183). All NECPAL+ patients were followed for 2 years since first detected as such.

Data were anonymized and collected in a digital database. A descriptive analysis was conducted on the demographic and clinical parameters of patients NECPAL+. Continuous variables were expressed as mean values \pm standard deviation and median and range according to distribution.

Survival Kaplan-Meier curves were generated from the date of the patient's identification as NECPAL+ to her/his date of death or last control (2 years). The Log Rank test was used to compare the different groups according to age, gender, primary diagnosis (breast cancer versus other tumors), and patient's condition as inpatient or outpatient. Nutritional status and Palliative Performance Scale or the presence of vital organ metastases and hazard ratios were calculated with the Cox's proportional hazard model. A multivariate model was built to explore the best predictors of mortality, using the variables that stood out as significant in the univariate analysis with the Cox's proportional hazard model. A $p < 0.05$ value was considered significant. The study was approved by the Ethics Committees of the institutions involved in the NECPAL Program, Instituto A. Lanari and Instituto Pallium Latinoamérica.

The statistical analysis was carried out by the Statistical Package for Social Science (IBM-SPSS 22 version (SPSS Inc. Chicago, IL)) program and by Stata V12.

TABLE 1.– The NECPAL CCOMS-ICO® tool: general indicators of severity and progression and disease-specific indicators

The NECPAL tool indicators	
Choice, request or need of Palliative Approach	Has the patient or the main caregiver requested palliative/comfort treatments exclusively or suggests limitation of therapeutic effort? Do healthcare professionals consider that the patient requires palliative care or palliative treatment at this moment?
Functional markers	Serious established functional dependence (Barthel Score < 20) Loss of two or more ADLs even though there is adequate therapeutic intervention or clinical perception of functional decline (sustained, intense/severe, progressive, irreversible) not related to concurrent conditions
Nutritional markers	Serum albumin < 2.5 g/dl, not related to acute episodes of unbalance Weight loss >10% or clinical perception of nutritional decline (sustained, intense/severe, progressive, irreversible) not related to concurrent conditions
Emotional	Presence of emotional distress with psychological symptoms (sustained, intense/severe, progressive) not related to acute concurrent conditions
Geriatric syndromes in the last 6 months	Persistent pressure ulcers (stages III-IV), recurrent infections (> 1), delirium, persistent dysphagia, falls (> 2)
Comorbidity	Charlson Index (> 2)
Additional factors on use of resources	Two or more urgent (unplanned) hospital (or skilled nursing facilities) admissions due to chronic disease in the last year. Need of complex/intense continuing care, either at an institution or at home
Cancer (1 single criterion)	Confirmed diagnosis of metastatic cancer who present low response or contraindication of specific treatment, progressive outbreak during treatment or metastatic affection of vital organs Significant functional deterioration (palliative performance status < 50%) Persistent, troublesome symptoms, despite optimal treatment of underlying condition(s)
Chronic pulmonary disease (≥ 2 criteria)	Breathlessness at rest or on minimal exertion between exacerbations. Difficult physical or psychological symptoms despite optimal tolerated therapy. FEV1 < 30% or criteria of restricted severe deficit: FVC < 40%/DLCO < 40%. Accomplishment of oxygen therapy at home criteria. Recurrent hospital admissions (> 3 admissions in 12 months due to exacerbations)
Chronic heart disease (≥ 2 criteria)	Heart failure NYHA stage III or IV, severe valve disease or inoperable coronary artery disease. Shortness of breath at rest or minimal exertion. Difficult physical or psychological symptoms despite optimal tolerated therapy. Ejection fraction severely affected (< 30%) or severe pulmonary hypertension (> 60 mm Hg). Renal failure (GFR < 30 L/min). Repeated hospital admissions with symptoms of heart failure/ischemic heart disease (> 3 in the last year)
Serious chronic liver disease (1 single criterion)	Advanced cirrhosis: stage Child C, MELD-Na Score > 30 or with one or more of the following medical complications: diuretic-resistant ascites, hepatorenal syndrome or upper gastrointestinal bleeding due to portal hypertension with failed response to treatment. Hepatocellular carcinoma: present, in stage C or D (BCLC)
Serious chronic renal disease (1 single criterion)	Serious renal failures (GFR < 15) in patients to whom substitutive treatment or transplant is contraindicated
Chronic neurological diseases (1): CVA (1 single criterion)	During acute and subacute phases (< 3 months post stroke): persistent vegetative or minimal conscious state > 3 days. During the chronic phase (> 3 months post stroke): repeated medical complications (aspiration pneumonia, pyelonephritis, recurrent febrile episodes, pressure ulcers stages 3-4 or dementia with severe criteria post stroke)
Chronic neurological diseases (2): MND, multiple sclerosis and Parkinson (≥ 2 criteria)	Progressive deterioration in physical and/or cognitive function despite optimal therapy. Complex and difficult symptoms. Speech problems with increasing difficulty communicating. Progressive dysphagia Recurrent aspiration pneumonia, breathless or respiratory failure
Dementia (≥ 2 criteria)	Severity criteria: GDS/FAST 6c or more. Progression criteria: loss of two or more ADLs in the last 6 months, despite adequate therapeutic intervention or difficulty swallowing, or denial to eat, in patients who will not receive enteral or parenteral nutrition. Use of resources criteria: multiple admissions (> 3 in 12 months, due to concurrent processes-aspiration pneumonia, pyelonephritis, sepsis, etc.- that cause functional and/or cognitive decline)

ADL: activities of daily living; BCLC: Barcelona clinic liver cancer; CVA: cerebrovascular accident; DLCO: diffusing capacity of the lung for carbon monoxide; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; GFR: glomerular filtration rate; NYHA: New York Heart Association; MND: motor neuron disease; GDS/FAST: Global Deterioration Scale/Functional Assessment

Results

A total of 317 cancer patients were evaluated; 246 (77.6%) were ambulatory at the time of identification and 211 (66.6%) were women. The median age was 77 years (range 21-99). Table 2 describes the 183 patients identified as NECPAL+ (Level 3).

During the follow-up period, 137 NECPAL+ patients died. The median follow-up period was 4 months for the entire sample but for the 46 patients who did not die, the median follow-up period was 17 months (range 9-23). No patient reached a 24 month follow-up. Figure 1 shows survival curves for the 137 NECPAL+ dead patients: Figure 1a shows the cumulative survival of the entire study population. The overall death rate was 11% patients/month (median 4 months). No significant differences were

found in mortality between men and women or between the different age groups (< 75 vs. ≥ 75 years old). In turn, a significantly higher mortality was found during the first month of follow-up for patients who were hospitalized at the moment of identification as NECPAL+ (Fig. 1b). Significant differences were also found when comparing breast vs. other cancers (Fig. 1c), presence vs. absence of metastasis in vital organ (Fig. 1d), presence vs. absence of nutritional decay (Fig. 1e), and *Palliative Performance* values > 50 vs. ≤ 50 (Fig. 1f). Table 3 shows frequencies of patients with increasing numbers of death risk indicators at the beginning of follow-up.

A preliminary multivariate model was built using these significant variables in a binomial codification (individuals exposed and not exposed to these conditions) (Table 4). Figure 2 shows survival of NECPAL+ patients with differ-

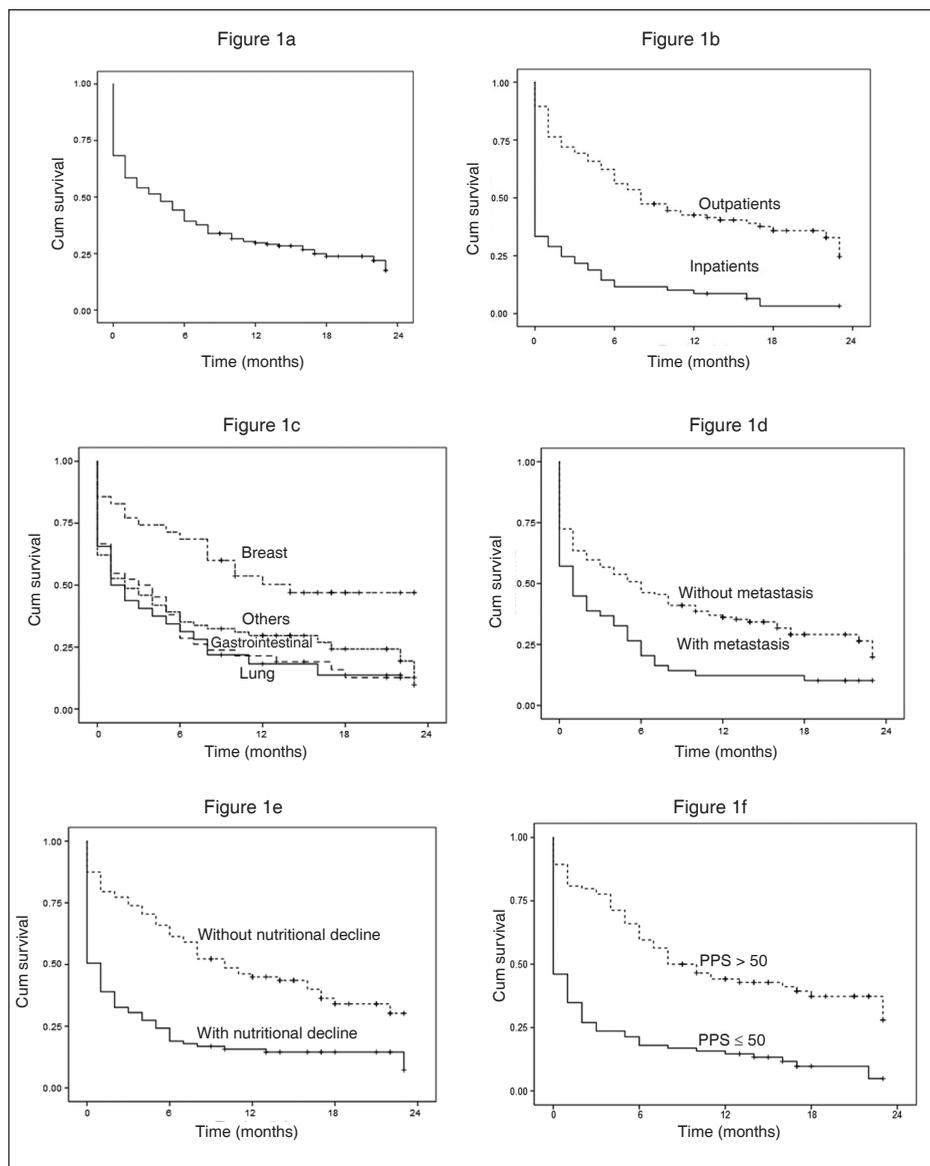
TABLE 2.– Characteristics of 183 NECPAL + patients

		n	%
Sex	Female	111	60.7
Age (years)	Median (range)	77	(21-99)
Primary tumor diagnosis	Breast	35	19.1
	Lung	32	17.5
	Digestive	42	23.0
	Other	74	40.4
Palliative approach	Patient's choice/ request	70	38.3
	Patient's family choice/ request	93	50.8
	Needs agreed by patient, family and physician	169	92.3
Indicators of disease severity and progression	Nutritional indicators	101	55.2
	Functional indicators	127	69.4
	Geriatric syndrome	21	11.5
	Emotional distress	113	61.7
	Charlson's Index median (range)	8	(2-16)
Specific indicators of severe disease	Oncologic disease*	174	95.1
	Respiratory disease	4	2.2
	Cardiac disease	5	2.7
	Neurologic disease	3	1.6
	Severe hepatic disease	3	1.6
	Renal disease	1	0.5
	Dementia	5	2.7
Specific criteria for cancer disease**	Confirmed diagnosis of Stage IV (metastatic), or, in some cases, stage III cancer plus the presence of:	168	91.8
	– Minimum response or contraindication for specific treatment	106	57.9
	– Disease progression during the course of treatment	39	21.3
	– Vital organ metastasis	49	26.7
	– Significant functional decay (PPS ≤ 50%)	89	48.6
– Symptom relapse or poor symptom control despite optimization of specific treatment	56	30.6	

PPS: Palliative Performance Scale

*Patients with advanced cancer disease

**Sum does not equal total because of patients with more than one positive criterion



PPS: Palliative Performance Scale
 Fig. 1.– Kaplan-Meier survival curves with significant differences between groups. 1a: NECPAL+ patients overall survival function. 1b: Survival function in NECPAL+ patients according to inpatient or outpatient condition. 1c: Survival function in NECPAL+ patients with breast cancer and with other types of cancer as primary tumor diagnosis. 1d: Survival function in NECPAL+ patients with vital organ metastasis. 1e: Survival function in NECPAL+ patients with nutritional decline. 1f: Survival function in NECPAL+ patients and significant functional decay (PPS)

ent prognostic indicators. Patients who were hospitalized, whose primary cancer localization was other than breast, who had metastatic disease, functional decline (assessed with the Palliative Performance Scale), or nutritional decline showed a considerable lower survival rate.

Discussion

We present results of a systematic study on death prognosis factors of cancer patients with palliative needs

carried out in Argentina. Both, prognosis and palliative needs, are central aspects of end of life care because they play a central role in care decision making in line with patients' values, preferences and aims^{14, 21}. The major breakthrough was the successful use of a direct prospective method of systematic risk assessment in cancer patients with palliative care needs, aimed to improve the prediction of mortality in hospital settings. The consequences of not identifying these two aspects on time may lead to inadequate symptom control, inappropriate

use of health resources and the absence of planning for decision making^{3,21}.

The NECPAL tool resulted useful in our university hospital setting for the identification of prognostic factors

TABLE 3.– Frequencies of patients with increasing numbers of death risk indicators at the beginning of the study

N° of indicators	N° of patients	%
0	11	6.0
1	47	25.7
2	36	19.7
3	43	23.5
4	28	15.3
5	18	9.8

and mortality risk factors in coincidence with results published by Spanish authors^{13, 14}. It was useful to describe the survival rate after 12- and 24-month follow-up because the 12-month period is exactly the NECPAL tool's point of interest, endorsing the conceptual approach of typical trajectories of decline in ACD (Fig. 3)^{3, 8, 21, 22}.

The presence of ACD has the largest impact on life expectancy and quality of life, especially in elderly people²³. The percentage of patients with PC needs or NECPAL+ in our study was 57.7%. Additionally, most of them had marked functional decline and malnutrition (Table 2). Similarly, in a university hospital in Catalonia nearly 40% of patients were NECPAL+²⁴. In these patients, the benefits of cancer treatment are very limited due to a reduction of life expectancy and an increase of side-effects complications²⁵. The early identification of patients at high risk of death would allow the implementation of early intervention

TABLE 4.– Preliminary multivariate model with statistically significant indicators

	Exposed	Not exposed	HR (CI95%)	p value	Log-rank test Chi Square
Nutritional decay	95	88	1.53 (1.04-2.23)	0.029	29.465 (p 0.000)
Vital organ metastasis	49	134	1.67 (1.15-2.42)	0.007	11.009 (p 0.001)
PPS ≤50%	89	94	1.95 (1.28-2.97)	0.002	40.817 (p 0.000)
Inpatient	69	114	1.87 (1.24-2.84)	0.003	53.090 (p 0.000)
Non-breast cancer as primary tumor diagnosis	148	35	2.04 (1.23-3.40)	0.006	13.460 (p 0.004)

PPS: Palliative Performance Scale

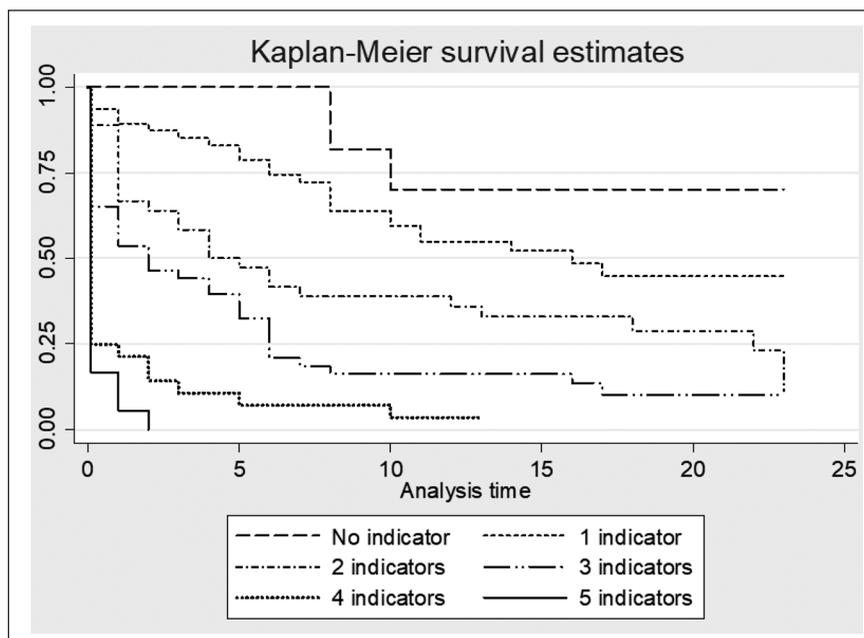


Fig. 2.– Kaplan-Meier survival curves of NECPAL+ patients according to the number of death prognostic indicators (time analysis expressed in months)

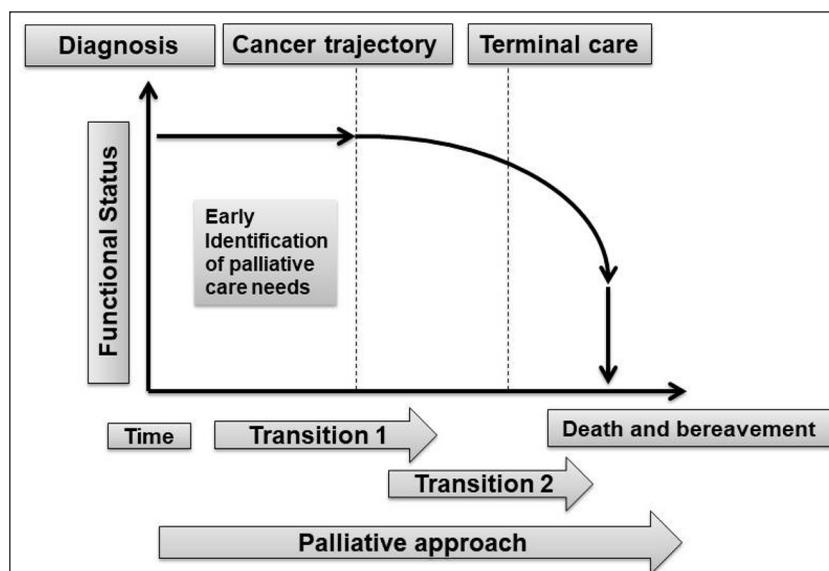


Fig. 3.– Key transitions in cancer end of life trajectory. Trajectories of functional decline at the end of life are quite variable. There are three different clinical trajectories to describe the complex reality of patients at the end of life. The first clinical trajectory, typically associated to cancer, features a stable and/or low decline phase broken up by a severe decline in the last weeks. Asking questions to recognize end of life transitions could be: Transition 1: would my patient benefit from supportive and palliative care? Transition 2: Is my patient reaching the last days of life? Adapted by Tripodoro VA et al from Boyd K, Murray SA^{7, 21}

programs to improve PC²⁶. This is clearly the best choice for patients at high risk of treatment complications and for whom life expectancy without cancer is even shorter than life expectancy with cancer²⁵.

Even if nowadays cancer is no longer the deadly disease that it used to be, near one every three individuals in the western world will develop some sort of cancer at some point of his/her life²⁶. According to the WHO's estimations, 80% of the population who died from malignant tumors could had required PC¹. The cancer mortality rate in Argentina is 115.1/100 000 inhabitants; it means 50 000 people dying of cancer are in need of PC¹⁶. Nevertheless, these estimates include only cancer-related mortality and consider only end of life conditions and therefore are underestimating the real need for PC by not including comorbidities^{5, 16, 18, 19}. Because of the prospective design of our study, we could establish the prevalence and timely clinical follow up of cancer patients with PC needs.

The NECPAL tool, including the SQ, was developed for use in a primary care setting^{3, 22, 27-32}. The SQ has also proved to be useful in the hospital setting³³. Furthermore, it is the only tool which takes into account the patient's or his family's expression of PC need, as well as the presence of severe social or emotional distress²⁸.

A total of 81% of our patients were found to have some sort of underlying ACD and 81% of these had a SQ+. The same patients had at least one additional criterion of disease severity and progression and therefore

were considered NECPAL+. In general practice, the SQ predicted a 12-month survival time in cancer patients in stage IV with 69.3% sensitivity and 83.6% specificity^{27, 28}. In the current study, we did not analyze sensitivity and specificity with ROC curves; however, we found 100% correlation between level 2 (SQ+) and level 3 (SQ+ plus one indicator). The SQ has proved to be a predictor of mortality in specific diseases and settings, primarily cancer²⁸. The NECPAL tool, which combines the SQ with additional indicators, can be used to screen patients for early palliative care with a reasonable degree of predictive accuracy. Nevertheless, the coincidence between level 2 and 3 in our setting opens a new research question. Is the SQ by itself, a good predictor of bad prognosis or, the cancer in our patients was not diagnosed timely enough and they were severely affected at first consultation or hospitalization? Additional research is needed to answer this question.

As seen in Table 2, elderly people were the most affected by functional decline, malnutrition, and comorbidity. Compared with the Charlson comorbidity index, the NECPAL tool is a better predictor of mortality at 6 and 24 months³³. In our study, almost half of NECPAL+ patients had a significant functional decline. In NECPAL+ patients, specific treatments have a poor response or are contraindicated. Our very high 2-year mortality (74.8%) with a very short median survival (4 months) shows the severity of the clinical conditions involved. Most probably, this is

not only reflecting the primary cancer condition but also old age and comorbidities (Table 2) in inpatients.

We constructed a predictive model to identify individuals with PC needs for a 24-month period using the multivariate analysis of a combination of relevant indicators, i.e. hospitalization, cancer other than breast as primary diagnosis, metastases, functional decline, and malnutrition. The concurrence of all such indicators correlated strongly with high mortality risk during the first month of follow-up. Regarding NECPAL tool capacity to predict mortality in cancer patients at 12 months, previous reports showed excellent discrimination ability and very good sensitivity and specificity, although this is not the aim of the tool^{14,28,33}.

We should emphasize that our study excluded all cancer patients who did not fulfill the SQ+ criterium. Thus, we were not able to compare mortality risk of SQ+ vs. SQ- patients. However, significant differences in 24-month mortality were indeed observed at among NECPAL+ and NECPAL- patients in a previous study performed in Catalonia²⁸.

The fact that half of the patients in our population died within 4 months suggests that they might not have been detected promptly enough. Some of the patients NECPAL+ in our study had been diagnosed in advanced stages of disease, therefore they obtained no benefit from specific treatment or had no chance to cure. In these cases, the only effective management is high quality PC to improve the quality of their end of life²¹.

In our study, according to NECPAL tool criteria, healthcare professionals considered that 38% of the patients had palliative needs and half of their families requested PC either in an implicit or an explicit manner (Table 2).

The perception of malnutrition was more common in cancer patients (55.2%) than generally perceived in other ACD groups. The impact of nutritional decline as an important end of life marker in cancer patients is also consistent with what is seen in medical literature^{13, 32-36}. Individuals identified by our healthcare professionals as in need of PC had a risk of mortality > 3 times higher than those who were not¹³. Both this relevant relationship and the fact that the best discrimination ability of the model is seen over 12 months, prove the predictability of the monophasic decline pattern typically seen in cancer patients¹³.

End of life care comprises three overlapping phases of disease: from diagnosis to the beginning of supportive care, from this point to the beginning of end of life care, and end of life care until death (Fig. 3)^{9, 21}. During this progression, there are two turning points known as the first and the second transition. These are key moments in which palliative measures can be incorporated to the care plan to avoid disproportionate treatments and reduce unnecessary costs^{9-11, 33, 36-39}. According to their median survival, most of our patients were in the second transition, that is, closer to the end of their life (Fig. 3)^{19, 21}.

In the current study, the criteria for advanced cancer disease were functional decline and contraindication for specific treatment or minimum response to it. The distribution of primary tumor sites in our sample was in line with official statistics at the national level: breast, lung and colorectal localization¹⁶. The presence of metastases in vital organs was infrequent, ~27%. Even bone metastases did not exceed 35%. High short-term mortality was probably caused by comorbidities and frailty syndrome (70% had functional decline).

A potential limitation of this study is that inclusion criteria are based on the subjective clinical judgment of healthcare professionals with different medical specialties. To reduce this bias, all definitions, procedures, and actions were standardized according to the procedure manual of the NECPAL CCOMS-ICO® tool²⁰. Our model for prognostic factors and mortality risk is probably applicable only to our population and its particular characteristics. However, we had already described in a previous study, that two out of three cancer patients affected by advanced disease could die in the next year and had palliative care needs¹⁹.

In conclusion, the NECPAL tool is a valuable instrument that helps physicians to detect cancer patients with palliative needs and bad prognosis. What is more, the SQ+ can be considered a simple tool to determine when it is good to incorporate PC to patient management²¹. The NECPAL tool considers assessment of other variables like hospitalization, malignancy other than breast cancer, metastatic disease, functional decline, and malnutrition, all of which reinforce its value in the assessment of prognosis and mortality risk.

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Conflicts of interest: None to declare

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