Original Article

Quality of Life Assessment and Outcome of Palliative Care

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Abstract

*Quality of life (QoL) assessment is crucial for the evaluation of palliative care outcome. In this paper, our methodological approach was based on the creation of summary measures. Fifty-eight Palliative Care Units (PCUs) in Italy participated in the study. Each PCU randomly selected patients to be 'evaluated' among the consecutively 'registered' patients. At baseline (first visit) and each week the patient was asked to fill in a QoL questionnaire, the Therapy Impact Questionnaire (TIQ). Short-survivors (<7 days) were not included in the QoL study. The random sample of patients (*n = *601) was highly representative of the general patient population cared for by the PCUs in Italy. The median survival was 37.9 days. We collected 3546 TIQ, 71.4 % completed by the patients. A Summary Measure Outcome score was calculated for 409 patients (81% of the patients included in the QoL study). The results of this national study showed that cooperative clinical research in palliative care is possible and QoL measures can be used to assess the outcome.* J Pain Symptom Manage 2001;21: 179–188. *© U.S. Cancer Pain Relief Committee, 2001.*

Key Words

Quality of life, outcome, palliative care

Introduction

In 1994, an Italian Cooperative Research Group on Palliative Medicine was created to describe the process of care of terminal cancer patients in terms of survival and quality of life. This research was considered useful for providing a framework of quality of life indicators on which the evaluation of the palliative care patients would be based in the future.

The study of Quality of Life (QoL) in palliative care is difficult because of the short survival and the poor cognitive condition of terminal patients. The usual QoL definitions and tools are partially applicable in terminal care. Moreover, the patients taken into care by palliative care services represent different populations: short survivors for whom the process of care is mainly aimed at a 'good death,' and medium/

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long survivors, with different illness burden in terms of consciousness, disability or pain.

In recent literature, the practical feasibility of clinical studies in patients treated by palliative care services has been questioned. Nonetheless, there is a quite large consensus that the palliative care process should be evaluated considering several perspectives and methodologies.[1–4]

The difficulty of collecting 'soft' (subjective) data from patients during a QoL study is well known. Missing data due to the patient's condition or a reluctance to cooperate are critical for data analysis and evaluation. The use of a proxy in evaluating QoL is crucial. Although subjective evaluation is the preferred source of information, in rapidly deteriorating patients, the loss of information can be substantial. For this reason, the caregiver rating has been considered useful, at least for some of the QoL components.[5]

Statistical analysis of longitudinal data is today computationally possible and has had important developments,[6] which are especially useful in exploratory statistical data analysis. However, the aim of this research was mainly to facilitate the clinical interpretation of the QoL outcomes. To achieve this, we adopted the approach of summary measures[7] which offers the possibility of clinically significant results and useful and practical tools also for the professional, non-statistical audience. At the same time this approach improves the power of the study and may reduce the impact of missing data. The goal of a summary measure is to embrace in one estimated parameter the variability of the multiple measurements over time.

The design of the summary measure is crucial to understanding this phenomenon and we considered the last part of the patient's life as the most relevant to assess the outcome of the process of care. The global outcome that we suggest in this article weights in particular the distress experienced by patients immediately before death.

In summary, the main aims of this paper are 1) to describe the feasibility of collecting QoL data in a palliative care setting and 2) to suggest practical ways of presenting longitudinal QoL outcomes in a clinically meaningful way.

Methods

The study design has been already presented in detail.[8] Briefly, all the patients from the 58 centers in Italy were enrolled over the period 1 January 1995 to 30 June 1995. Eligible for the study were patients referred for advanced cancer, aged more than 18 years, living in the Palliative Care Unit's (PCU's) catchment area and taken into care by the local PCU. General characteristics of all consecutive patients were registered, but in each PCU a random sample was selected to be followed-up. Before starting enrolment, each PCU selected a sampling ratio of patients to be 'evaluated' among the consecutively 'registered' patients. The aim of the sampling procedure was to obtain a representative sample of the PCU patients, but also keeping at the minimum the workload for the team.[9]

Each 'evaluated' patient was initially clinically assessed by the PCU's Medical Doctor. During the initial assessment, information on patient and family characteristics, socio-economic status, clinical symptoms, and daily living activities (ADL) were collected. At baseline (first visit) and weekly (for patients at home or in hospital/hospice care), or during each visit for outpatients,[8] the patient was asked to fill in a QoL questionnaire, the Therapy Impact Questionnaire (TIQ). The latter has already been validated in previous research[10–12] and is especially designed for palliative care settings.[13–15] If a patient was unable to fill in the TIQ by themselves or to dictate the answers (self-completed questionnaire), the nurse or the doctor was asked to complete it immediately after the visit and to register the reason (proxy-completed questionnaire).

The TIQ is a questionnaire based on four major components of quality of life of oncological patients: physical symptoms resulting from disease or therapies (24 items); functional condition (capacity to work, to enjoy leisure time, to look after oneself: 3 items), concomitant psychological conditions (emotional and cognitive: 6 items), family and social relationships (2 items), and one item for the patient's global judgement of 'not feeling well;' answers are classified as 'not at all,' 'slight,' 'a lot,' 'very much.' A confirmatory factorial analysis was carried out on terminally ill patients.[11] The relationship of the scales emerging from the factor analysis was further investigated to explore possible ways of regrouping similar scales on symptoms and psychological aspects. Two global scales were generated by the authors: the Physical Symptom scale (9 items), based on

global health status, fatigue and gastrointestinal symptoms; and the Therapy Impact Index scale, based on emotional and cognitive status, social interaction, and functional impairment (in total 11 items).[11] Pain was assessed by 1 item. The score for Physical Symptom, Pain, and Therapy Impact Index scales was transformed to include a range from 25 to 100, the maximum corresponding to maximum distress. Designed and validated in Italian in a case series of 1000 palliative care patients,[11] the use of TIQ is today widespread in Italy and also considered acceptable by patients.[13–15] The QoL outcomes presented in this article, if not otherwise specified, are always related to the separate Physical Symptom, Therapy Impact Index, and Pain scores. TIQs with more than 5 items missing and TIQs completed by proxy in patients defined as in a coma were considered invalid for analyses.

The QoL patient follow-up ended 31 August 1995.The living status and permanence in palliative care were assessed until 31 December 1996.

Statistical Analysis

Subjects living less than 7 days after the first visit were not included in this analysis. Other patients were categorized (7 to 20 days; 21+ days) according to the duration of the patient follow-up until death or until the end of the study period.

The QoL data quality and the compliance of the patients with the QoL measurement protocol were assessed. The number of valid TIQs actually compiled by the patient vs. the number of expected forms (observed/expected ratio) was calculated for each week of home care patients ($n = 363$). The index is shown separately for the self-completed and for all the TIQ measurements, by time since enrollment, and the reason of non-compliance was specified.

The exploratory analysis of the longitudinal data collected in the study was done using the Lowess method—locally weighted scatterplot smoothing—which is a smoothing technique available in STATA 6.0.[16] This is considered both robust (it avoids excessive dependence on few observations) and useful for exploring longitudinal data because it tends to follow the observed data.[6] A bandwidth of 80% was chosen, meaning 80% of the data were used in smoothing each point.

In the subsequent analysis, a summary measure was calculated to assess the QoL outcome of each patient. The first visit QoL measure was considered as the baseline and never included in the summary measure. Using a backward approach, the mean of the QoL scores calculated in the last two weeks of life was considered separately to estimate a last score. This score was the only available for short survivors (7 to 20 days).

A second measure was the mean of the QoL scores during the entire palliative care process after the first TIQ (baseline), calculated until the end of follow up (end of the study period) or the two weeks before death (Intermediate score). The global QoL outcome (Summary Measure Outcome) was calculated as the mean of the Intermediate and Last scores. In the absence of one of them, the only one available was assumed as the Summary Measure Outcome.

The Summary Measure Outcome and baseline scores were classified in three groups: Absent or Low distress (score < 50); Medium distress (50–74) and High distress (≥ 75). A Change score was calculated as the difference between the baseline and the second week measure. Positive change means QoL improvement.

Survival analysis was carried out according to the Kaplan Meier method.

Results

Figure 1 shows a flow chart of the patients enrolled in the Italian study on palliative care. Out of the 2,667 eligible patients who have been shown to be a representative sample of the patients cared by PCUs in Italy,[9] 601 patients were randomly selected for further QoL evaluation. Ten patients died before the first medical visit, and 2 were considered ineligible by the medical doctor at the first visit.

The median survival after enrollment in the study was 37.9 days; 15.3% of the patients lived longer than 180 days and 14.3% of patients died within 7 days and were not considered in this paper. In total, we collected 3,546 TIQ, 71.4 % self-completed, from 505 patients, and 304 (8.6%) were considered non-valid.

Table 1 presents the main characteristics of the 505 patients eligible for QoL analysis. The mean age of the patients was 67.8, and 47.3%

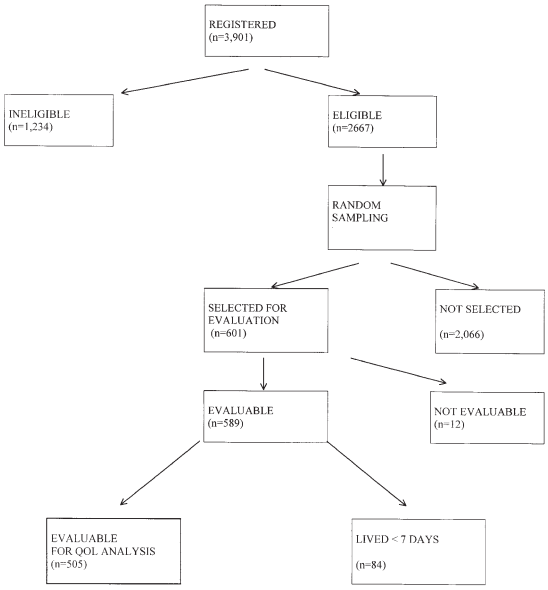


Fig. 1. Flowchart of the Italian National Palliative Care Study patients.

were women. The most common diagnoses were lung-pleura cancer (20.0%) and colon-rectal cancer (13.9%). The baseline TIQ revealed some degree of pain present in 74.2% of the patients. The initial clinical assessment reported incident pain in 38.4%.

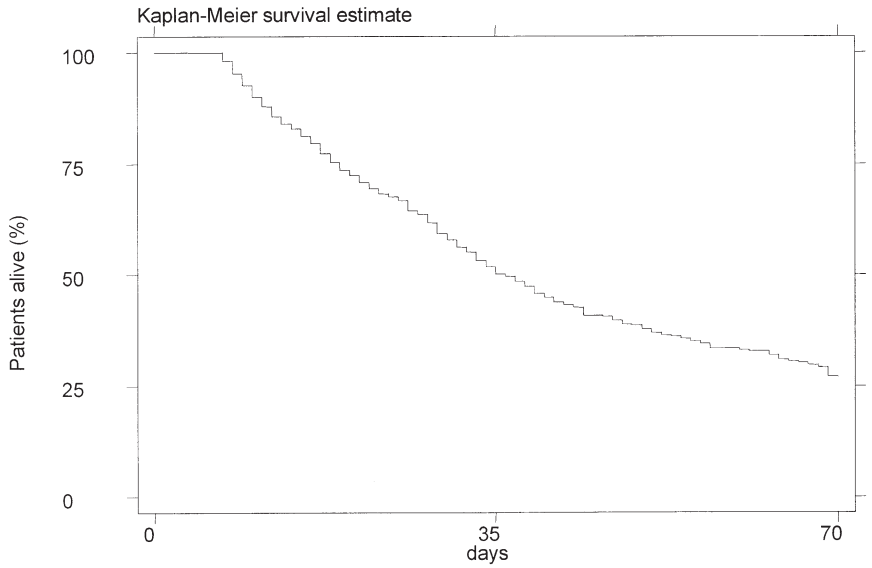
Table 2 shows the Observed /Expected Ratio considering the number of completed and valid TIQs since enrollment for patients cared exclusively at home (n = 363). A higher proportion of patients with severe cognitive/physical impairment (including coma) is evident in the first two weeks after enrollment. The self/expected ratio decreased from 65% to 39%, whereas the decrease in proxy completed TIQs was from 87% to 52%. At 70 days after enrollment, 17% of patients (24% considering the proxy TIQs) had a complete data set (i.e., they completed all the TIQ planned for the period).

The exploratory statistical analysis of the TIQs completed by patients who had died by 31 December 1996 was carried out using the Lowess method. In Figure 2, the Lowess smoothing is shown by time since enrollment and time since death. In the forward approach, the distress improvement of the patients after baseline is evident for the Physical Symptoms and the Pain score. As time elapses the distress worsens (especially if the self-completed + proxy ratings are considered). Looking backwards from

Table 1
Characteristics of the 505 Patients Evaluable for QoL Analysis

	n	(%)
Age mean ± SD	67.8 ± 12.2	
Gender		
Male	266	(52.7)
Female	239	(47.3)
Cancer		
Upper digestive tract	57	(11.3)
Colon—Rectum	70	(13.9)
Pancreas	25	(5.0)
Lung—Pleura	101	(20.0)
Breast	59	(11.7)
Female genitourinary	24	(4.8)
Prostate	28	(5.5)
Bladder	18	(3.6)
Leukemia–Lymphoma	8	(1.6)
Head—Neck	28	(5.5)
Unknown	15	(3.0)
Other cancers	72	(14.3)
Source of referral		
General practitioner	156	(30.9)
Oncologist	68	(13.5)
Other specialists	104	(20.6)
Relatives, friends	70	(13.9)
Others	107	(21.2)
Palliative care follow up (at 31 Dec 1996)		
Followed until death	418	(82.8)
Care discontinued	74	(14.7)
Alive in care	13	(2.6)
All Patients	505	(100.0)

Table 2
Survival and Compliance to the QoL Assessment for Home-Care Patients (n = 363)



Time Since Enrollment (days)	0–6	7–13	14–20	21–27	28–34	35–41	42–48	49–53	54–62	63–70
Observed										
Self-compiled	236	183	159	129	102	86	71	58	57	47
Proxy-compiled	80	67	68	58	48	35	28	20	23	16
Missing										
Severity of cognitive/ physical status[a]	17	19	9	7	13	6	6	7	4	3
Other reason	13	16	6	6	8	2	3	3	1	—
Reason unknown	17	78	85	81	74	75	64	60	47	55
Expected	363	363	327	281	245	204	172	148	132	121
Self/Expected ratio	.65	.50	.49	.46	.42	.42	.41	.39	.43	.39
Self + Proxy/Expected ratio	.87	.69	.69	.66	.61	.59	.58	.53	.61	.52
% complete set of QoL data, self only	65	43	35	31	26	22	20	19	18	17
% complete set of QoL data, self + proxy	87	64	56	49	40	34	30	26	26	24

[a]Including coma.
Note: Patients who survived <7 days are not considered in our analysis.

death, the distress increases steeply getting closer to death both in Physical Symptoms and in the Therapy Impact scores. The Pain score appears to be well controlled and the Lowess smoothing is flat in the last days of life.

Table 3 shows the number of the patients for whom a Summary Measure Outcome was calculated by length of follow up at 31 August 1995. In 77 patients, the outcome was based only on the last two weeks of life (Last score). The intermediate score (Intermediate score) was estimated in 332 patients. Subjects with less than two valid TIQs are considered as missing in the Summary Measure Outcome assessment (n = 96). Globally a Summary Measure Outcome score was calculated for 409 patients (81%).

The estimates of the mean Summary Measure Outcome of the palliative care patients grouped according to the QoL score at baseline (classified as Low, Medium, and High level of distress) are presented in Table 4. Mean and standard errors of the baseline score, the second week, the change between baseline and second week score, and the Summary Measure Outcome are shown respectively for the Physical Symptom, Therapy Impact Index, and the Pain scales. The Physical Symptom and Therapy Impact Index average baseline scores

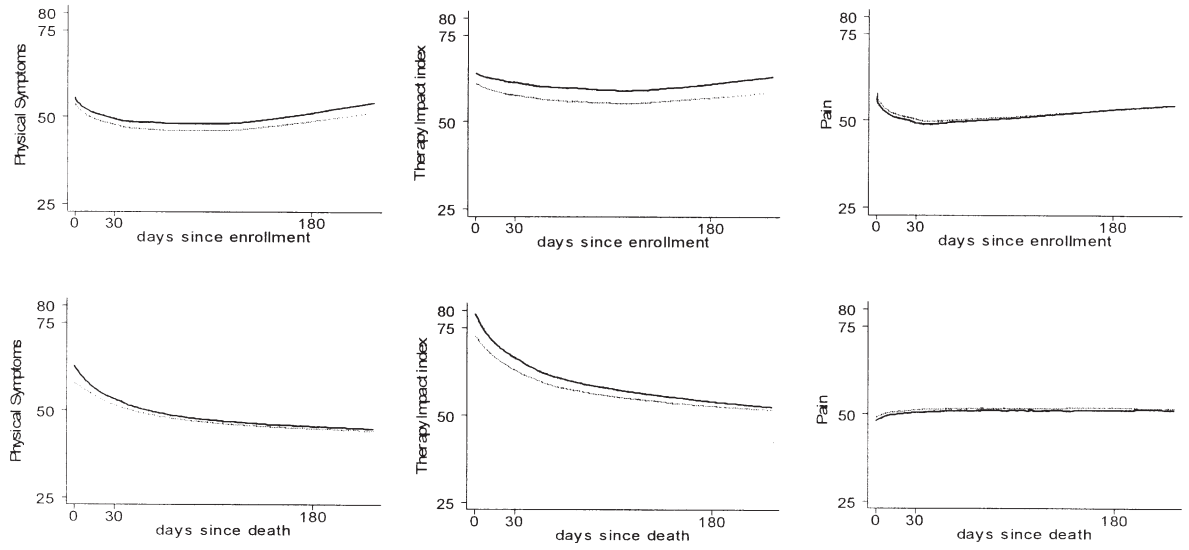


Fig. 2. Quality of life by time since enrollment and by time since death. Lowess smoothing on Physical Symptoms, Therapy Impact Index, and Pain scales: 3014 questionnaires (2257 self compiled). Bold lines are drawn for estimates derived from all valid measures; thin lines are drawn for estimates derived from self compiled TIQ only.

showed a shift towards the mean (worst condition for the low scores, improvement for medium and high scores) and comparable trends in survival, i.e., subjects with high distress at baseline had shorter survival time. On the contrary, on the Pain scale, the Baseline mean score and level of Change were not related to survival time.

Figure 3 presents the proportion of patients classified according to the Summary Measure Outcome category as a function of the baseline condition. Looking at the Physical Symptom scale, patients in the high group at baseline showed a high distress in the Summary Measure Outcome in less than 20% of the cases. Similar results were achieved for pain control: less than 20% of the patients with high distress on the Pain scale at the baseline still had high distress on the Pain scale according to the Summary Measure Outcome. Distress relief was achieved for the Therapy Impact Index less than for the Physical Symptom and Pain scales: almost 80% of the patients with high distress on the Therapy Impact Index scale at baseline remained at a high level of distress on that dimension. This effect is not surprising, considering that the Therapy Impact Index has functional and cognitive status components. The results were very comparable to those obtained using the self-completed TIQs only.

Table 3
Presence of Intermediate and Last 15 Days of Life Scores and Summary Measure Outcome, by Length of Follow-Up

	Length of follow-up, *n* (%)		
	≤20 days	>20 days	total
Intermediate score only	8 (6.2)	126 (33.5)	134 (26.5)
Last score only	62 (48.1)	15 (4.0)	77 (15.2)
Intermediate and last scores	1 (0.7)	197 (52.4)	198 (39.3)
Summary Measure Outcome	71 (55.0)	338 (89.9)	409 (81.0)
Missing Summary Measure Outcome	58 (45.0)	38 (10.1)	96 (19.0)
Total	129 (100)	376 (100)	505 (100)

Note: Summary Measure Outcome is missing when there are <2 valid TIQ.

Table 4
Mean and Standard Error (SE) of Baseline, 2nd Week, Change, and Summary Measure Outcome Scores

	Baseline	2° Week	Change	Summary Measure Outcome Alive or Withdrawal at 08/31/95	Summary Measure Outcome Dead at 08/31/95	Median Survival at 12/31/96
Physical symptoms						
Baseline						
Low (<50)	39.5	41.9	−2.2	41.5	49.9	73
n = 187	(0.5)	(0.9)	(0.8)	(1.1)	(1.1)	
Medium (50–74)	61.1	55.4	5.5	49.4	58.9	43
n = 193	(0.5)	(1.0)	(0.9)	(1.5)	(1.0)	
High (75–100)	82.6	64.2	18.4	62.2	61.9	37
n = 29	(1.0)	(3.6)	(3.6)	(5.9)	(3.5)	
						log rank test chi2 (2d.f.) 23.19 $P < .0001$
Therapy Impact Index						
Baseline						
Low (<50)	32.1	40.5	−8.2	40.1	55.0	79
n = 141	(0.5)	(1.3)	(1.3)	(1.8)	(1.7)	
Medium (50–74)	63.5	61.0	2.6	54.0	69.4	55
n = 157	(0.6)	(1.2)	(1.2)	(2.0)	(1.1)	
High (75–100)	83.3	79.1	4.3	72.5	79.7	38
n = 111	(0.6)	(1.1)	(1.0)	(3.1)	(1.1)	
						log rank test chi2 (2d.f.) 21.91 $P < .0001$
Pain						
Baseline						
Low (<50)	25.0	33.2	−8.2	39.4	36.5	44
n = 82	(0.0)	(1.5)	(1.5)	(2.3)	(2.0)	
Medium (50–74)	50.0	46.9	3.1	48.4	47.0	56
n = 166	(0.0)	(1.3)	(1.3)	(2.1)	(1.3)	
High (75–100)	80.0	57.8	22.4	53.5	55.1	64
n = 161	(0.8)	(1.4)	(1.6)	(2.2)	(1.5)	
						log rank test chi2 (2d.f.) 2.02 $P < .3649$

Note: Positive change means QoL improvement; change is calculated as the difference between baseline and the second week score.

Discussion

The probability of success of a study like this was very low, due to the number of centers involved and the difficult task of collecting routine QoL data. To overcome these potential pitfalls, we adopted three practical strategies. We chose to differentiate subpopulations within the palliative care patients according to survival time; we considered the ratings of proxies useful; and finally we designed a Summary Measure to summarize the most relevant information about the patient QoL outcome.

In this article, we considered only patients who had a survival time long enough for the evaluation of the palliative care intervention in terms of QoL. Patients with short survival received palliative care only aimed at a 'good death.' The latter is a construct that quality of life instruments, like TIQ, are not designed to evaluate. Specific instruments should be implemented to study the very last period of life. Within the study, in fact, a specific questionnaire with this aim was tested.[17]

The collection of self-completed questionnaires was critical also for the subpopulation selected in our study. Nonetheless, it is extremely difficult to achieve a better compliance in the real world of clinical care[5] and the findings seem quite good given the complexity of our study. Furthermore, the exploratory longitudinal statistical analysis did not show substantial differences in the pattern of QoL when only self-completed TIQs were used.

The Summary Measure approach allowed for a reduction of the influence of missing data and an improvement in the clinical interpretation of the data. As Matthews et al have shown,[7] the Summary Measure approach does not solve

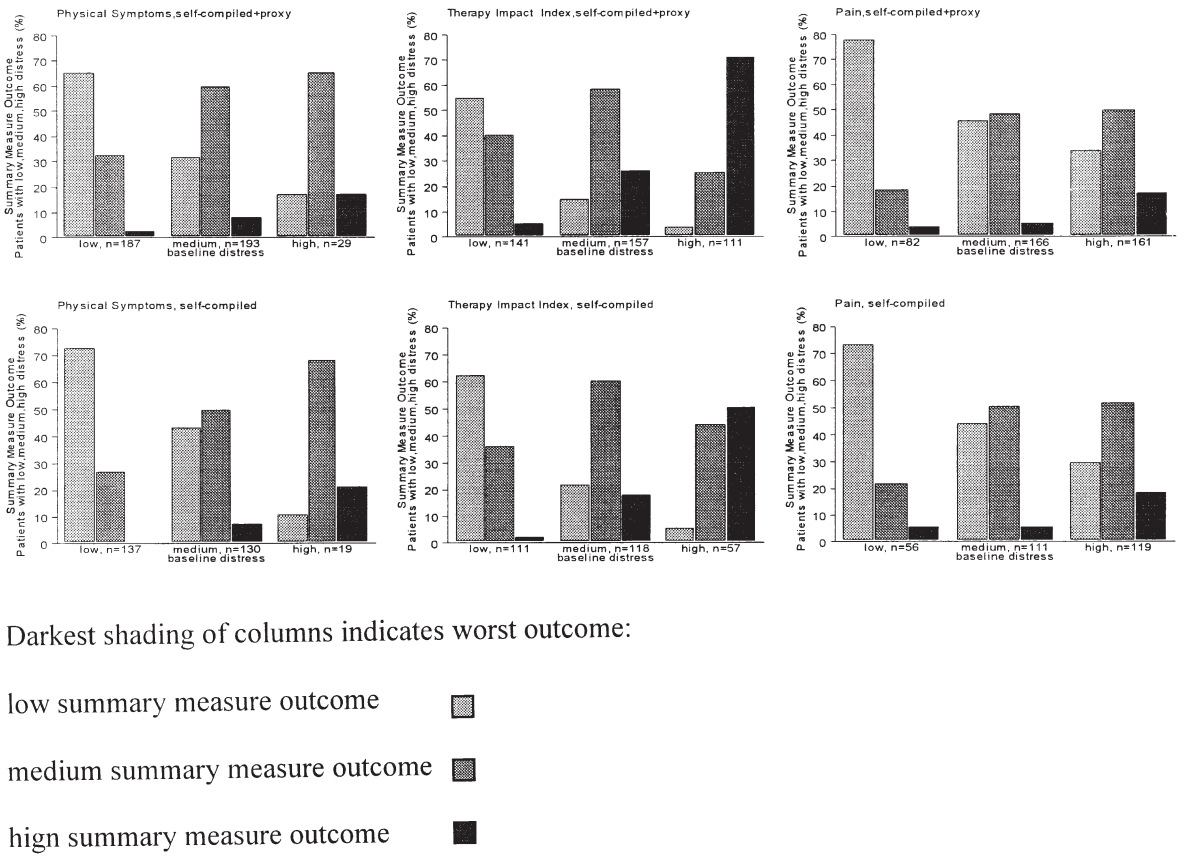


Fig. 3. Summary Measure Outcome on Physical Symptoms, Therapy Impact Index, and Pain scales by low, medium, high baseline distress. Self-compiled + proxy ratings (n = 409) and self-compiled ratings only (n = 286). Darkest shading of columns indicates worst outcome.

the problems present in a study, but nevertheless is valuable for extracting useful information from the data.

The Summary Measure we selected to show the QoL outcome of the palliative care patients was discussed by the working group and considered as a useful way to represent the conditions of the patients over time. The QoL on the last two weeks (Last score) was weighted separately considering this evaluation as especially relevant for the global outcome assessment. Nonetheless, we think that the palliative care process should achieve good results over all the entire care period, which had a median value of 37.9 days in our sample.

The exploratory longitudinal data analysis by the Lowess method suggests that the summary measure we chose corresponds to the QoL pattern over time. Using the backward approach from the moment of death, the trend of the QoL increases faster in the last period of life. This finding is observable for the Physical Symptom and Therapy Impact Index scales and not for the Pain scale. This result is consistent with the description we obtained through the Summary Measures.

Dying during the study period is a strong indicator of patients who entered the palliative care intervention in very poor health conditions. We expected and observed a worst QoL outcome for patients like these.

The observed result showed a reduction of the Pain score in the last weeks of life and may be attributable either to effective pain control by drugs or to under-reporting of pain in the last period of life by the patient or the proxy.

This study is an observational, clinical study and aimed to describe the relationship between the condition at baseline and the outcome. Nothing can be said about the efficacy of the palliative care intervention in the absence of an adequate epidemiological design

comparing the treated with the control patients. In observational studies, continuous variables are possibly biased by the so-called regression to the mean effect. Subjects with high scores at the baseline might have positive changes, (which means improvement) between baseline and second week score only for this reason. This effect is possibly working also in our data, where the average distress score regresses towards the mean when the outcome is compared with the baseline. Only a randomized clinical trial could respond to the question of efficacy of the palliative care intervention, but we consider the design of this study a first step for future implementation of randomized clinical research in this field.

In conclusion, this study showed that clinical and QoL research is possible in palliative care, but it can be done only in very selected categories of patients and has many methodological limitations. The definition of different subpopulations of patients is important because different tools should be used. For this reason we dropped short survivors from this study. An assessment of the process of dying should be especially designed for patients with brief survivals, considering that the usual QoL instruments are not very informative about the last hours of life.

The terminal care process is difficult to evaluate and a is challenge for clinical research. Results cannot be considered the 'truth,' but a contribution to understanding. Case studies, qualitative research, and observational and experimental research should be considered together as different types of knowledge to the interpretative activity of researchers and the clinical community. The a priori knowledge of the methodological limitations of clinical research should facilitate its use for understanding practice in palliative care. Future development of this research would address the possibility of experimental evaluations of interventions among terminal patients.

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