

Integrated Palliative care in Metastatic gastrointestinal Cancer: A Retrospective Experience from a Lead Cancer Centre in Pakistan

Amer Farooqi*, Jamshed Ali, Kashif Sajjad, Sajjad Ullah

SKMCH&RC: Shaukat Khanum Memorial Cancer Hospital and Research Centre, Peshawar, KPK PAKISTAN

Abstract

Background

The goal of palliative care is to alleviate the suffering of patients with advanced cancer, such as through pain management. Multiple randomized controlled trials have supported the early integration of palliative care. Despite the undeniable advantages of early palliative care, most data have come from developed countries. This study offers real-life insights into the integration of palliative care services for patients with advanced gastrointestinal cancer and their impact on quality of life in a developing country.

Materials and Methods

We retrospectively evaluated patients with metastatic gastrointestinal cancer treated at our center from January 2018 to December 2022. The subjects included patients with metastatic gastrointestinal (GI) cancer who received palliative care either within 90 days of diagnosis (early group) or after 90 days (late group). The impact of early versus late integration of palliative care was assessed.

Results

A total of 216 patients were included in the analysis — 123 in the early group and 93 in the late group. While the majority of patients were referred electively to palliative care, emergency referrals were more frequent in the early group (62 total; 40 [64%] in the early group, 22 [36%] in the late group, $p = 0.15$). The number of patients receiving chemotherapy in the last 30 days of life was 39 (early group: 17; late group: 22; $p = 0.06$). On the Edmonton Symptom Assessment Scale (ESAS), symptoms such as pain, nausea, and wellbeing were better controlled in the early group, although the differences were not statistically significant. The disease burden was significantly higher in the early group ($p = 0.01$).

Conclusion

Despite a higher disease burden in the early group, symptom control was comparable between the groups. The greater number of emergency referrals in the early group highlights the role of palliative care during crises and underscores the need for better integration of palliative care services.

Keywords

Palliative Care • Metastasis • Cancer • Pain • End of Life

Introduction

Cancer is a leading cause of death worldwide, responsible for approximately 10 million deaths in 2022 (1). According to Globocan, there were nearly 3 million new cases of colorectal and gastric cancers in 2022 (1). The age-standardized incidence of cancer in Pakistan is 105.6 per 100,000, whereas the mortality is 69.8 (1). The quality-of-life issues in oncology are of paramount importance, as an estimated 39.3% of cancer patients will die from the disease (2).

The concept of palliative care is often unfamiliar in our healthcare setting, where the government is focused on providing life-saving treatments to patients. This is despite international organizations, including the American Society

of Clinical Oncology (ASCO) and the European Society of Medical Oncology (ESMO), advising on the early and ongoing incorporation of palliative care in oncology treatment across the entire cancer journey. Therefore, palliative care is considered an essential pillar of cancer care (3). Pakistan is still facing the challenge of initiating and establishing palliative care services, as recommended by the WHO in 2002. At present in Pakistan, the significant barriers to palliative care are an indifferent government, paucity of medications, and a poorly developed specialty (3). According to one study, the availability of hospice palliative care in Pakistan is one of the lowest per population at 1:157,935 (4).

*Corresponding author: Amer Farooqi
Email: amerrehman964@yahoo.co.uk

In 2020, the age-standardized cancer incidence rate in Pakistan was estimated at 110.4 per 100,000 people/year with approximately 117,149 patients dying of cancer per year (5). Given the poor access to healthcare facilities, an overwhelming majority of cancer patients present late with an advanced stage of cancer, requiring palliation from the get-go.

There is evidence available that the majority of oncologists tend to detach themselves from the patients who are in the final phase of their illness and are dying, due to the feeling of failure, insecurity, and helplessness(6). In comparison to standard care alone, the prompt inclusion of specialised palliative care for patients with advance cancer provides considerable advantage in symptom management, health-related quality of life, and overall survival. The early integration of palliative care is the palliative care team's involvement simultaneously or soon after a diagnosis of advance cancer (7).

This study from Pakistan provides valuable insights into the integration of palliative care for patients with gastrointestinal cancer at a tertiary care oncological center. This is the first real-life study from a developing country to evaluate the role of early versus delayed referrals to palliative care services in patients with advanced gastrointestinal cancer and their impact on quality of life.

Materials and Methods

This is a retrospective, observational, cross-sectional study involving all metastatic gastrointestinal cancers, conducted after exemption (EX-03-06-23-01) was granted by the Institutional Review Board of Shaukat Khanum Cancer Hospital and Research Centre. The data were collected from the electronic hospital information system of Shaukat Khanum Memorial Cancer Trust between January 2018 and December 2022.

All consecutive metastatic gastrointestinal (GI) cancers referred to the palliative care team were included in the study. We did not include small bowel cancers, non-GI primary malignancies, non-metastatic cancers, or dual malignancies, as well as primary peritoneal tumors. We also excluded patients for whom the data for the symptom assessment scale were incomplete. These are either rare cancers or the data is incomplete, making it difficult to provide an accurate interpretation. The tumors of the esophagus, stomach, hepatobiliary, peri-ampullary, duodenal, colonic, and rectal were classified as gastrointestinal cancers. We applied the WHO's definition of palliative care, as outlined in 2002. Palliative care is an approach that aims to improve the quality of life for patients and their families affected by a life-threatening disease (8). "Early" palliative care is advised by current palliative care guidelines, albeit the exact timing has not been established in the guidelines. For newly diagnosed patients with advanced cancer, the American Society of Clinical

Oncology (ASCO) expert panel suggests early palliative care involvement within 8 weeks (9).

The definition of early and delayed palliative care requires a diagnosis of advance cancer and then the timing of referral. Advanced cancer can be locally advanced or metastatic cancer. One of the six features of cancer is metastasis, which refers to the process by which cancer cells depart their original place and establish new colonies somewhere else (10). In this study, we defined early palliative care as the initial palliative care encounter received within 90 days of metastatic gastrointestinal cancer diagnosis based on previous literature (11). The initial assessment by the palliative care team within 90 days following the diagnosis of metastases is referred to as the "early group", whereas the evaluation more than 90 days is defined as the "late group".

The Edmonton score (Edmonton Symptom Assessment Scale (ESAS) (Bruera et al., 1991) was used to evaluate palliative illnesses (12). The Edmonton Symptom Assessment Scale (ESAS) is a tool used to assess the severity of symptoms in palliative care. The ESAS was used to evaluate nine core symptoms mainly experienced by cancer patients, including tiredness, shortness of breath, nausea, depression, anxiety, drowsiness, appetite, pain, and feeling of wellbeing. The severity of each symptom at the time of assessment is rated on a scale of 0 to 10, where 0 indicates the symptom is absent and 10 represents the worst possible severity.

The mode of referral to the palliative care team was reviewed, categorizing it as either an elective outpatient consultation or an emergency palliative care consultation without anticipating excessive symptom burden. Additionally, we examined the use of chemotherapy, radiotherapy, and imaging in these patients during their final 30 days of life.

The statistical analysis (descriptive and comparative data analysis) was conducted using SPSS Statistics version 26.0 (IBM, New York, NY, USA). Demographic characteristics are presented as frequencies and percentages for categorical variables. The independent samples Mann-Whitney U test was employed to analyze non-parametric values of ESAS scores. Survival probabilities between the early and delayed groups were compared using Kaplan-Meier survival curves.

Results

A total of 216 consecutive patients with metastatic gastrointestinal cancer who met the inclusion criteria and presented between January 2018 to December 2022 were enrolled in our analysis. There were 123 (57%) patients in the early group and 93 (43%) patients in the delayed group. The average time of referral in the early group was 35 days (0 to 86 days) and 241 days in the delayed group (94-848 days).

The demographic characteristics and the cancer sites included in the analysis are outlined in Table 1. The predominant majority of the patients in both groups were male patients (early group 65 (53%), delayed group 56 (60%)). The mean age was 50.8 years in the early group and 46.9 years in the delayed group. The hepatobiliary patients were higher in the early group, and this was statistically significant (early group 51, delayed group 9, $p=0.00$).

An important parameter was the mode of referral to evaluate the involvement of the palliative care team as an outpatient referral or via an emergency encounter. There were 154 (71%) patients referred electively to the palliative care team and 62 (29%) as an emergency referral due to urgency of the burden of disease. Out of 154 elective referrals, 83 (54%) were in the early group and 71 (46%) in the delayed group. In the emergency referrals, there were 40 (64%) in the early group and 22 (36%) in the late group. The higher number of emergency referrals in the early group suggests that enrollment was more often due

to symptom burden rather than the integration of palliative care. However, this difference was not statistically significant ($p=0.15$) Table 1.

The number of distant metastatic sites was evaluated and showed a higher disease burden in the early group, and this was statistically significant ($p=0.017$). There was a single metastatic site in 78 (63%) vs 46 (27%), two sites 32 (48%) vs 35 (52%) and more than two sites in 13 (52%) vs 12 (48%) patients in early group vs delayed group, respectively. A total of 39 (18%) patients received chemotherapy in the last 30 days of life with 17 (56%) in the early group and 22 (A total of 216 consecutive patients with metastatic gastrointestinal cancer who met the inclusion criteria and presented between January 2018 to December 2022 were enrolled in our analysis. There were 123 (57%) patients in the early group and 93 (43%) patients in the delayed group. The average time to referral in the early group was 35 days (range: 0-86 days), and 241 days in the delayed group (range: 94-848 days).

Table 1. This table compares the demographic and disease characteristics between early group (referred within 90 days) and delayed group (after 90 days) depending on timing of referral to palliative care with metastatic cancer. Hepatobiliary cancer was referred earlier and was statistically significant. Majority of the patients in early group were referred as emergency.

		Total	≤90 days (n=123)	>90 days (n=93)	P-Value
Sex	Male	121	65	56	0.28
	Female	95	58	37	
Type Of cancer	Gastric	51	25	26	0.00
	Hepatobiliary	60	51	9	
	Rectal	37	15	22	
	Esophageal	37	17	20	
	Periampullary	24	14	10	
	Anal Canal	7	1	6	
Mode palliative review	Elective Referral	154	83	71	0.15
	Emergency Referral	62	40	22	
Chemo with in last 30 days of life	No	177	106	71	0.06
	Yes	39	17	22	
Imaging with in last 30 days of life	Yes	109	64	45	0.59
	No	107	59	48	
Use of radiotherapy	No radiotherapy	174	99	75	0.97
	Radiotherapy for symptom control	42	24	18	
Place of death	Outside hospital death	139	74	65	0.14
	Hospital death	76	49	27	
	Alive	1	0	1	
Number of distant metastatic sites	One Site	124	78	46	0.01
	Two Site	67	32	35	
	More than Two Site	25	13	12	

The demographic characteristics and the cancer sites included in the analysis are outlined in Table 1. The majority of patients in both groups were male (early group: 65 (53%), delayed group: 56 (60%)). The mean age was 50.8 years in the early group and 46.9 years in the delayed group. The number of hepatobiliary patients was higher in the early group, and this difference was statistically significant (early group, 51; delayed group, 9; $p = 0.00$).

An important parameter was the mode of referral, used to evaluate the involvement of the palliative care team, whether as an outpatient referral or via an emergency encounter. There were 154 (71%) patients referred electively to the palliative care team and 62 (29%) as emergency referrals due to the urgency of the disease burden. Out of 154 elective referrals, 83 (54%) were in the early group and 71 (46%) in the delayed group. In the emergency referrals, there were 40 (64%) in the early group and 22 (36%) in the late group. The higher number of emergency referrals in the early group suggests that enrollment was more often due to symptom burden rather than the integration of palliative care. However, this difference was not statistically significant ($p = 0.15$), as shown in Table 1.

The number of distant metastatic sites was evaluated and showed a higher disease burden in the early group, which was statistically significant ($p = 0.017$). There was a single metastatic site in 78 (63%) patients versus 46 (27%), two sites in 32 (48%) patients versus 35 (52%), and more than two sites in 13 (52%) patients versus 12 (48%) patients in the early group versus the delayed group, respectively. A total of 39 (18%) patients received chemotherapy in the last 30 days of life, with 17 (56%) in the early group and 22 (44%) in the delayed group. The use of imaging, including Computed tomography (CT) scans and Magnetic resonance imaging (MRI) scans, was performed in 109 (50%) patients, with 64 (59%) in the early group and 45 (41%) in the late group ($p = 0.59$).

The survival evaluation showed one person alive at the time of the study, with 76 (35%) people dying inside the hospital, with 49 (64%) in the early group and 27 (36%) in the late group ($p=0.14$). According to the ESAS parameters, pain, nausea, and wellbeing were better controlled in the early group; however, there was no statistically significant difference, as depicted in Table 2. The Kaplan-Meier survival graphs indicated considerably higher survival in the delayed group. The overall survival was from 0 to 929 days.

Discussion

In our study, most patients were referred within three months (early group, $n = 123$ vs. delayed group, $n = 90$), providing a false sense of reassurance regarding the early integration of palliative care. Further analysis revealed that the palliative care team

Table 2. Is the comparison of symptom scores between patients in early group (<90 Days) and delayed group (>90 Days) after diagnosis. Early group had a better pain control, nausea and wellbeing as compared to delayed group despite. The remaining parameters were equally controlled in both the groups. Although, the results were not statistically significant across as determined by the Mann-Whitney U test.

Variables	<90 days (n=123)	>90 days (n=93)	p-value
Pain	3.00	4.00	0.33
Tiredness	2.00	2.00	0.885
Drowsiness	1.00	1.00	0.717
Nausea	1.00	2.00	0.311
Appetite	3.00	3.00	0.579
*SOB	0.00	0.00	0.574
Depression	2.00	2.00	0.584
Anxiety	2.00	2.00	0.708
Wellbeing	2.00	3.00	0.397
Pain Score last 6 months	1.00	2.00	0.383

*Shortness of breath

saw more patients as emergency referrals (64% vs 36%). This is despite the hospital offering specialized palliative care services. Both the American and European oncological societies have highlighted the importance of early integration of palliative care in advance cancer (13,14). The majority of hospitals in Pakistan do not have a palliative care service available. Literature suggests that early integration of palliative care reduces the likelihood of aggressive treatments at the end of life (15, 16). Furthermore, anticancer treatment in the last month is associated with adverse outcomes (17), and it can increase healthcare costs and consume limited resources without obvious benefit to the patient (18). It has been suggested that less than 10% of patients should receive anticancer treatment during the last 2 weeks of their life (19, 20).

The exceedingly aggressive approach can lead to nearly 10% of patients receiving chemotherapy in the last 14 days of life (19). A national registry-based data from France showed increased use of chemotherapy in the last days of life, if there is no palliative care service available (21). In our study, the overall use of chemotherapy in the last 30 days of life was 18%. However, this was significantly lower in the early group, at 14%, compared to 23% in the delayed group, highlighting the positive impact of palliative care involvement. However, it is still higher than the aspirational level of less than 10% of patients receiving chemotherapy in the last 30 days of life. This may again be due to the involvement of palliative care in emergencies. The study by Bandieri et al. showed that the use of chemotherapy in the last 30 days of life was 3.4% in referrals to palliative care

within 90 days and 9.6% in referrals after the 90-day cutoff (22). The higher use of chemotherapy in Asia has previously been reported in a Korean study (23).

The use of radiotherapy for symptom control was equal in both groups at 19% despite the higher burden of disease in the early group. A population-based study from British Columbia examining the use of Radiotherapy for Bone metastasis found 4% and 10% use in the last 2 weeks and 2-4 weeks, respectively (24). The data from this study also suggested a higher likelihood of receiving Radiotherapy in the last 14 days of life, for gastrointestinal cancers (24).

It is also crucial to ensure an improved quality of life for patients with metastatic cancer, and there is evidence that palliative care interventions can improve these important symptoms over time (22). The analysis of the ESAS score showed better results for pain control, nausea, and wellbeing in the early group; however, there was no statistical difference in these or any of the other ESAS categories. We only examined a single assessment point, and the impact of palliative care intervention cannot be determined.

There is evidence that the preferred place of death is often home for most patients, including cancer patients (25,26). There was a higher number of hospital deaths in the early group in our analysis compared to the delayed group, although this difference was not statistically significant.

Our study highlights significant issues, particularly the late elective referral to palliative care services, even within specialised cancer centres, following the diagnosis of advanced cancer. Integrating palliative care early in the treatment process can significantly enhance patient comfort and provide comprehensive support, addressing physical, emotional, and psychological needs.

The weaknesses of our study include its retrospective nature and the limitation of only a single-point analysis for palliative symptom assessment. The symptoms are assessed using a validated tool (ESAS), ensuring reproducibility.

In conclusion, it is crucial to prioritize enhanced training in palliative care and to educate cancer care providers on the importance of early engagement with palliative services. By involving patients in early decision-making, we can significantly improve their quality of life and overall treatment outcomes. Immediate action in these areas will ensure that patients receive the comprehensive care they deserve from the very beginning of their cancer journey.

Author Contributions: ** add initials of authors across each category **

Conceived and designed the analysis:

Collected the data:

Contributed data or analysis tools:

Performed the analysis:

Wrote the paper:

Acknowledgment

The authors acknowledge the contribution of Amjad Anwar in data collection.

Funding

This research received no specific grant from any funding agency in public, commercial, or not-for-profit sectors.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024 May;74(3):229–63.
2. World Health Organization. Palliative Care: NCC Clin Pract Guidel Oncol [Internet]. Geneva: WHO; 2020 [cited 2025 Oct 31]. Version 1.2020 — February 7, 2020. p. 68–9.
3. Punjwani R, Khatoon A, Dias JM, Kurji ZA, Siddiqui DF, Bana S, Baig-Ansari N. Palliative care in nursing: where are we in Pakistan. *J Palliat Care Med*. 2015;5:002.
4. Wright M, Wood J, Lynch T, Clark D. Mapping levels of palliative care development: a global view. *J Pain Symptom Manage*. 2008 May;35(5):469–85.
5. World Health Organization. Globocan 2020 Pakistan report. *Glob Cancer Obs*. 2021;928:2020–1.
6. Cripe LD, Frankel RM. Dying from cancer: communication, empathy, and the clinical imagination. *J Patient Exp*. 2017 Jun;4(2): 69–73.
7. Engeser P, Glassman J, Leutgeb R, Szecsenyi J, Laux G. Early integration of palliative care for outpatients with advanced cancer in general practice: how is the situation?—a cohort study. *Ann Palliat Med*. 2021 Mar;10(3):2843848–2848.
8. Sepúlveda C, Marlin A, Yoshida T, Ullrich A. Palliative care: the World Health Organization's global perspective. *J Pain Symptom Manage*. 2002 Aug;24(2):91–6.
9. Sanders JJ, Temin S, Ghoshal A, Alesi ER, Ali ZV, Chauhan C, Cleary JF, Epstein AS, Firn JJ, Jones JA, Litzow MR. Palliative care for patients with cancer: ASCO guideline update. *J Clin Oncol*. 2024 May;JCO-24.
10. Hanahan D, Weinberg RA. The hallmarks of cancer. *Cell [Internet]*. 2000 Jan 7 [cited 2023 Nov 18];100(1):57–70. Avail
11. Lammers A, Slatore CG, Fromme EK, Vranas KC, Sullivan DR. Association of early palliative care with chemotherapy intensity in patients with advanced stage lung cancer: a national cohort study. *J Thorac Oncol*. 2019 Feb 1;14(2):176–83.
12. Bruera E, Kuehn N, Miller MJ, Selmser P, Macmillan K. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. *J Palliat Care*. 1991 Jun;7(2):6–9.
13. Ferrell BR, Temel JS, Temin S, Alesi ER, Balboni TA, Basch EM, et al. Integration of palliative care into standard oncology care:

- American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2017;35(1):96–112.
14. Hui D, Bansal S, Strasser F, Morita T, Caraceni A, Davis M, et al. Indicators of integration of oncology and palliative care programs: an international consensus. *Ann Oncol* [Internet]. 2015 Sep 1 [cited 2023 Nov 18];26(9):1953–9.
15. El-Jawahri A, LeBlanc TW, Kavanaugh A, Webb JA, Jackson VA, Campbell TC, et al. Effectiveness of integrated palliative and oncology care for patients with acute myeloid leukemia: a randomized clinical trial. *JAMA Oncol*. 2021 Feb 1;7(2):238–45.
16. El-Jawahri A, Greer JA, Pirl WF, Park ER, Jackson VA, Back AL, et al. Effects of early integrated palliative care on caregivers of patients with lung and gastrointestinal cancer: a randomized clinical trial. *Oncologist*. 2017 Dec 1;22(12):1528–34.
17. Baena-Cañada JM, Campini Bermejo A, Gamez Casado S, Rodríguez Perez L, Quilez Cutillas A, Calvete Cadenas J, et al. Experiences with prescribing large quantities of systemic anticancer therapy near death. *J Palliat Med*. 2019 Dec 1;22(12):1515–21.
18. Bao Y, Maciejewski RC, Garrido MM, Shah MA, Maciejewski PK, Prigerson HG. Chemotherapy use, end-of-life care, and costs of care among patients diagnosed with stage IV pancreatic cancer. *J Pain Symptom Manage*. 2018 Apr 1;55(4):1113–21.
19. Earle CC, Neville BA, Landrum MB, Souza JM, Weeks JC, Block SD, et al. Evaluating claims-based indicators of the intensity of end-of-life cancer care. *Int J Qual Health Care*. 2005 Dec 1;17(6):505–9.
20. Earle CC, Park ER, Lai B, Weeks JC, Ayanian JZ, Block S. Identifying potential indicators of the quality of end-of-life cancer care from administrative data. *J Clin Oncol*. 2003 Mar 15;21(6):1133–8.
21. Rochigneux P, Raoul JL, Beaussant Y, Aubry R, Goldwasser F, Tournigand C, et al. Use of chemotherapy near the end of life: what factors matter? *Ann Oncol* [Internet]. 2017 Apr 1 [cited 2023 Nov 18];28(4):809–17.
22. Bandieri E, Banchelli F, Artioli F, Mucciari C, Razzini G, Cruciani M, et al. Early versus delayed palliative/supportive care in advanced cancer: an observational study. *BMJ Support Palliat Care*. 2020;10(4):e32.
23. Keam B, Kim J, Hong Y, Lee S, Kim D, Im S, et al. Aggressiveness of cancer care near the end of life. *J Clin Oncol* [Internet]. 2006 Jun 20 [cited 2024 Dec 15];24(18_suppl):6103.
24. Kress MAS, Jensen RE, Tsai HT, Lobo T, Satinsky A, Potosky AL. Radiation therapy at the end of life: a population-based study examining palliative treatment intensity. *Radiat Oncol*. 2015;10(1):1–9.
25. Gomes B, Calanzani N, Gysels M, Hall S, Higginson IJ. Heterogeneity and changes in preferences for dying at home: a systematic review. *BMC Palliat Care* [Internet]. 2013 Feb 15 [cited 2023 Nov 19];12(1):1–13.
26. Townsend J, Frank AO, Fermont D, Dyer S, Karran O, Walgrove A, et al. Terminal cancer care and patients' preference for place of death: a prospective study. *BMJ*. 1990;301(6749):415–7.