Opportunities to improve palliative care: towards a more patient-centred and proactive approach

Verhoef, M.J.

CHAPTER 4

End-of-Life Trajectories of Patients with Haematological Malignancies and Patients with Advanced Solid Tumours visiting the Emergency Department: the Need for a Proactive Integrated Care Approach

Verhoef M, de Nijs EJM, Ootjers CS, Fiocco M, Fogteloo AJ, Heringhaus C, Marijnen CAM, Horeweg N, van der Linden YM.

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ABSTRACT

Purpose

Patients with haematological malignancies (HM) have more unpredictable disease trajectories compared to patients with advanced solid tumours (ST) and miss opportunities for a palliative care approach. They often undergo intensive disease-directed treatments until the end of life with frequent emergency department (ED)-visits and in-hospital deaths. Insight into end-of-life trajectories and quality of end-of-life care can support arranging appropriate care according to patients' wishes.

Methods

Mortality follow-back study to compare of end-of-life trajectories of HM- and ST-patients who died <3 months after their ED-visit. Five indicators based on Earle et al. for quality of end-of-life care were assessed: intensive anti-cancer treatment <3 months; ED-visits <6 months; in-hospital death; death in the ICU; in-hospice death.

Results

We included 78 HM-patients and 420 ST-patients, median age 63 years, 35% had ECOG performance status 3-4. At the ED, common symptoms were dyspnoea (22%), pain (18%) and fever (11%). After ED-visit, 91% of HM-patients versus 76% of ST-patients were hospitalized (p=0.001). Median survival was 17 days (95%CI 15-19); 15 days in HM-patients (95%CI 10-20) versus 18 days in ST-patients (95%CI 15-21), p=0.028. Compared to ST-patients, HM-patients more often died in-hospital (68% vs 30%, p<0.0001) and in the ICU or ED (30% vs 3%, p<0.0001).

Conclusion

Because end-of-life care is more aggressive in HM-patients compared to ST-patients, a proactive integrated care approach with early start of palliative care alongside curative care is warranted. Timely discussions with patients and family about advance care planning and end-of-life choices can avoid inappropriate care at the end of life.

INTRODUCTION

The disease trajectories of patients with a haematological malignancy (HM) are diverse; from diseases with an acute manifestation and poor survival, to those with a chronic nature. Treatments for HMs, even in patients with a poor clinical condition, are often intensive and are associated with a high risk of severe toxicity (such as graft versus host disease), infection and even death.[1] Because disease trajectories of HM-patients are unpredictable and life-threatening, recognition of those who could benefit from a palliative care approach is complicated.[2-6] As a consequence, HM-patients are seldom referred to palliative care consultation teams (PCCTs) or hospices; and if they are referred, they often die within days or weeks.[2,7,8] It is known that palliative care needs of HM-patients are often unmet.[9] According to the definition of the World Health Organization, the aim of a palliative care approach is to improve quality of life of both patients and family; in addition, it can concur with curative systemic treatment along the disease trajectory.[10] This approach includes conversations about the end of life, supportive care, symptom management and psychosocial support.[9] Insight into the end-of-life trajectory of HM-patients may help identifying cues for initiation of a palliative care approach.

With the occurrence of disease progression or metastases, the palliative phase in patients with a solid tumour (ST) is easier to identify.[6,7,11] According to Murray, their physical decline is stable and predictable until a steep and short period of decline before death. During the stable phase health care providers can proactively assess and support palliative care needs and the end of life.[12] A palliative care approach has been shown effective in a various populations of ST-patients in improving quality of life, symptom burden and even survival.[13-15] In HM-patients, palliative care can improve the quality of life after hematopoietic stem cell transplantation already after two weeks, as a randomized controlled study by El-Jawahri et al. showed.[16] However, literature indicates that HM-patients need a different proactive approach for early palliative care than the disease trajectory of advanced ST-patients. Conceptual models of integrated palliative care for HM-patients depict palliative care as concurrent with curative care to aim for both cure and care.[17-19] So-called trigger-events can help identifying HM-patients with palliative care needs to arrange appropriate care.[20] An ED-visit is shown to be a potential trigger.[21]

Many HM-patients are urged to visit the emergency department (ED) with uncontrollable symptoms or a high symptom burden at home. Consecutively, they are often admitted to the hospital or even to an intensive care unit (ICU), where many of them die.[2,22,23] These situations can diminish the quality of the end of life of HM-patients and their families.[24] To measure the quality of end-of-life care provided to patients with incurable diseases, Earle et al. constructed the following indicators: receiving chemotherapy in the last 14 days

of life; starting a new chemotherapy in the last 30 days of life; >1 emergency room visit in the last month of life; >1 hospitalization in the last month of life; ICU-admission in the last month of life; death in an acute care hospital; lack of hospice-admission; admission to hospice <3 days before death.[24,25]

The primary objective of this study was to provide insight into the end-of-life trajectory of HM-patients visiting the ED during the last three months of life and to compare with ST-patients. Secondary objective was to compare the quality of end-of-life care in HM- and ST-patients.

PATIENTS AND METHODS

Setting

This mortality follow-back study was conducted at Leiden University Medical Center (LUMC) in Leiden, the Netherlands. LUMC's ED is open 24 hours a day, 7 days a week. On average, 80 patients visit the ED every day and about 30.000 patients are evaluated every year. Since 2011, LUMC has a palliative care consultation team (PCCT), which is available to all departments of our centre for consultation after patients are referred by their health care professional. This study was part of a larger study on end-of-life trajectories of all patients visiting the ED between 2011 and 2013, approved by LUMC's Committee of Medical Ethics on May 27, 2013. Written consent was not required according to Dutch Law (WGBO, article 458) and European Law (General Data Protection Regulation).

Patients

All adult HM-patients who died within three months after their last ED-visit were included. They were compared to ST-patients with advanced cancer, which was defined as not having any curative options or receiving anti-cancer treatment not aimed at curation. Detailed analysis of ST-patients is published elsewhere.[26] The period of three months was chosen because in the Netherlands, an estimated life-expectancy of <3 months justifies referral to intensive palliative care at home, in nursing homes and in hospices. Data-collection occurred from May 2011 - January 2013.

Data collection

For transparent and solid data collection, a code book was designed by two members of our PCCT which contained inclusion and exclusion criteria and description and coding of all variables.[27] Characteristics of disease, referral, ED-visit, and follow-up from ED-arrival until death were extracted from electronic patient records (EPRs) of eligible patients by four trained research assistants. One expert of the PCCT checked

for interrater agreement. EPRs were searched for any correspondence with general practitioners (GPs) or PCCT-consultations during the three months before the ED-visit and proactive symptom-management plans in files or letters up to six weeks before the ED-visit. Limitations on life-sustaining treatments (LSTs) were orders on no resuscitation; no ventilation; and no admission to the intensive care unit (ICU). LST-discussions did not occur routinely and notes about LSTs were collected by the research assistants. Arrival at the hospital within office hours was defined as from Monday to Friday between 8 am and 6 pm. Performance status was scored using the Eastern Cooperative Oncology Group (ECOG)-scale.[28] The main symptom was defined as the referring symptom reported by the attending physician and is part of the structure of reporting in the EPR. This symptom was considered 'new' if it was not mentioned in the EPR three months before the ED-visit; it was considered 'acute' if the onset of the symptom was <24h. The clinical diagnosis was defined as the conclusion reported by the attending physician in the EPR. Date and place of death were obtained from EPRs. Cause of death in HM-patients was discussed between one expert of the PCCT (EN) and a haematologist (CO) until agreement was reached. Cues for proactive care were communication about the patient's condition between a health care professional or PCCT of the hospital and the patient's general practitioner (GP) via a letter, telephone, or transfer; proactive care plans (care plan for anticipation of symptoms; care plans informing the general practitioner, care plans written by the PCCT; PCCT-referrals); and limitations on LSTs before the current ED-visit. Quality of end-of-life care was assessed using indicators for proactive end-of-life care and indicators of Earle et al.: intensive anti-cancer treatment in the previous 3 months before the ED-visit (intensive anti-cancer treatments include chemotherapy, targeted therapy, stem cell transplantation and surgery); the number of ED-visits in the 6 months before the current ED-visit; in-hospital death; death in an acute hospital department (the ED or the ICU); death in a hospice (as a positive measure).[24]

Statistics

Characteristics of patients, referrals, ED-visits, and follow-up were analysed using descriptive statistics. To test differences between HM- and ST-patients, we performed Chi-square tests for nominal variables; Mann-Whitney U tests for not-normally distributed continuous or ordinal variables; and Fisher-Freeman-Halton tests for variables with three or more categories. Kaplan-Meier's methodology was used to estimate survival from the ED-visit and survival between HM-patients and ST-patients was tested using a log-rank test. Complete case analyses were performed, using SPSS 23.0 software and a two-sided p-value <0.05 was considered statistically significant.

RESULTS

Patient and disease characteristics

Seventy-eight HM-patients and 420 ST-patients died within three months after their ED-visit (Table 1); more men were in the HM-group (68% versus 55% of ST-patients, p=0.026), median age was 63 years (range: 22-94 years). ECOG-performance score did not differ between HM- and ST-patients. Acute myeloid leukaemia and multiple myeloma were the most common HM-types (26% and 17%, respectively); most solid tumours were located in the digestive tract (27.6%) and in the lung (16.0%; Appendix 1). Before the ED-visit, limitations on life-sustaining treatments (LSTs) were discussed with 171 patients (34.3%): with 13 (16.7%) HM-patients and 158 (37.6%) ST-patients (p<0.0001). Four (5.1%) HM-patients and 142 ST-patients (33.8%) had documented limitations; 'no limitations' were documented in 9 (11.5%) HM-patients and 16 (3.8%) ST-patients (p<0.0001). Up to three months before the ED-visit, the PCCT was consulted in 27 patients (1 HM-patient and 26 ST-patients, p=0.10). Communication via letters, telephone and transfers between medical specialists and the patient's GP had occurred in 67 (85.9%) HM-patients and 332 (79.0%) ST-patients (p=0.15). Proactive care plans were documented for 13 (16.7%) HM-patients and 66 (15.7%) ST-patients (p=0.83).

Table 1. Characteristics of 78 patients with a haematological malignancy and 420 patients with a solid tumour visiting the emergency department.

	Total n=498		**HM-patients n=78**		**ST-patients n=420**		
Characteristics	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**P-value**
Male	282	(56.6)	53	(67.9)	229	(54.5)	0.026
Age in years, median (range)	63	(22-94)	61	(27-94)	61	(22-92)	0.147
Disease-modifying treatment in the past 3 months[a]							
Chemotherapy	202	(40.6)	34	(43.4)	168	(40.0)	0.554
Radiotherapy	118	(23.7)	14	(17.9)	104	(24.8)	0.182
Targeted therapy/immunotherapy	96	(19.3)	21	(26.9)	75	(17.9)	0.065
Stem-cell transplantation	10	(2.0)	9	(11.5)	1	(0.2)	<0.0001
None	125	(25.1)	14	(17.9)	111	(26.4)	0.102
Limitations on LSTs[b]							<0.0001
Discussed, no documented limitations	25	(5.0)	9	(11.5)	16	(3.8)	
Discussed, documented limitations	146	(29.3)	4	(5.1)	142	(33.8)	
Not discussed	327	(65.7)	65	(83.3)	262	(62.4)	

Table 1. Characteristics of 78 patients with a haematological malignancy and 420 patients with a solid tumour visiting the emergency department. (continued)

	Total n=498		HM-patients n=78		ST-patients n=420		
Characteristics	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**P-value**
PCCT consulted during last 3 months	27	(5.4)	1	(1.3)	26	(6.2)	0.100
Proactive symptom-management plan in the prior 6 weeks	62	(12.4)	11	(14.1)	51	(12.1)	0.612
Number of ED-visits during the last 6 months, median (range)	1	(0-9)	1	(0-9)	1	(0-7)	0.147
Patient had a family caregiver							0.608
Yes	433	(86.9)	67	(85.9)	366	(87.1)	
No	31	(6.2)	6	(7.7)	25	(6.0)	
Unknown	34	(6.8)	5	(6.4)	29	(6.9)	
Patient had homecare before the ED visit							0.462
Yes	110	(22.1)	19	(24.4)	91	(21.7)	
No	280	(56.2)	44	(56.4)	236	(56.2)	
Unknown	108	(21.7)	15	(19.2)	93	(22.1)	
Living situation							0.120
Alone	90	(18.1)	10	(12.8)	80	(19.0)	
With someone	369	(74.1)	65	(83.3)	304	(72.4)	
Unknown	39	(7.8)	3	(3.8)	36	(8.6)	
Housing							0.075
Home	447	(89.8)	66	(84.6)	381	(90.7)	
Residential home	9	(1.8)	2	(2.6)	7	(1.7)	
Nursing home	18	(3.6)	6	(7.7)	12	(2.9)	
Hospice	6	(1.2)	1	(1.3)	5	(1.2)	
Other	5	(1.0)	2	(2.6)	3	(0.7)	
Unknown	13	(2.6)	1	(1.2)	12	(2.9)	
ECOG-performance score							0.078
0-2	90	(18.1)	17	(21.8)	73	(17.4)	
3-4	173	(34.7)	50	(64.1)	123	(29.3)	
Unknown	235	(47.2)	11	(14.1)	224	(53.3)	

List of abbreviations: ED: emergency department; HM: haematological malignancy; ST: solid tumour; IQ-range: interquartile range; LSTs: life-sustaining treatments; PCCT: palliative care consultation team; ECOG: Eastern Cooperative Oncology Group.

[a] Numbers may exceed 100% because patients may have received multiple disease-modifying therapies in the past.

[b] Limitations on LSTs were defined as orders on: no resuscitation; no ventilation; and no admission to the intensive care unit.

Referral characteristics

Patients or their family initiated the ED-visit in 37.3% (Table 2). Two hundred-and-fifty-eight (51.8%) came outside office hours. Most common main symptoms were dyspnoea (22.1%), pain (17.5%) and fever (11.2%). HM-patients more often presented with fever (23.1% versus 9.0% of the ST-patients, p=0.001); ST-patients more often with nausea or vomiting (9.3% versus 2.6% of the HM-patients). Patients had a median of 2 symptoms.

Table 2. Emergency department-referral characteristics of 78 patients with a haematological malignancy and 420 patients with a solid tumour.

	Total n=498		**HM-patients n=78**		**ST-patients n=420**		
ED-referral	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**P-value**
Referrer							0.420
GP or elderly care physician	189	(38.0)	25	(32.1)	164	(39.0)	
Medical specialist	123	(24.7)	23	(29.5)	100	(23.8)	
Patient or informal caregiver	186	(37.3)	30	(38.5)	156	(37.1)	
Referral outside office hours	258	(51.8)	40	(51.3)	218	(51.9)	0.919
Main symptom							
Dyspnoea	110	(22.1)	22	(28.2)	88	(21.0)	0.166
Pain	87	(17.5)	9	(11.5)	78	(18.6)	0.117
Fever	56	(11.2)	18	(23.1)	38	(9.0)	0.001
Neurologic deterioration[a]	41	(8.4)	8	(10.3)	33	(7.9)	0.491
Nausea or vomiting	41	(8.2)	2	(2.6)	39	(9.3)	0.025
Weakness or loss of strength	25	(5.0)	6	(7.7)	19	(4.5)	0.256
Bleeding	23	(4.6)	3	(3.8)	20	(4.8)	>0.999
Obstipation or diarrhoea	17	(3.4)	1	(1.3)	16	(3.8)	0.493
Fatigue	12	(2.4)	4	(5.1)	8	(1.9)	0.102
Difficulty swallowing or passage problems	9	(1.8)	0	(0.0)	9	(2.1)	0.367
Seizure	9	(1.8)	1	(1.3)	8	(1.9)	>0.999
Oedema	8	(1.6)	0	(0.0)	8	(1.9)	0.617
Ascites	7	(1.4)	0	(0.0)	7	(1.7)	0.603
Other	53	(10.6)	4	(5.1)	49	(11.7)	0.062
Admission for							
New problem[b]	254	(51.0)	35	(44.9)	219	(52.1)	0.238
Acute problem[c]	179	(35.9)	24	(30.8)	155	(36.9)	0.295
Number of symptoms, median (range)	2	(0-8)	2	(0-8)	2	(0-7)	0.055

List of abbreviations: HM: haematological malignancy; ST: solid tumour; ED: emergency department; GP: general practitioner.
[a] Confusion, drowsiness, reduced consciousness.
[b] Not reported in the patient records in the last three months.
[c] Onset within the last 24 hours.

Visit and follow-up characteristics

Patients underwent diagnostic imaging in 64.1% and laboratory tests in 84.1% (Table 3). Most patients were diagnosed with infection or fever (24.5%), bronchopulmonary insufficiency (14.3%) or renal insufficiency (11.8%). In HM-patients, treatment for their main symptoms was initiated at the ED more often than in ST-patients (69.2% versus 54.8%, p=0.010). After their ED-visit, more HM-patients were hospitalized than in ST-patients (91.0% versus 76.0%, p=0.001). The ED-visit triggered discussions about LSTs in both HM-patients and ST-patients. After the ED-visit, LSTs were documented for 41 (52.6%) HM-patients and 307 (73.1%) ST-patients (p<0.0001). Among these patients, 39 (95.1%) HM-patients and 297 (96.7%) ST-patients had limitations on LSTs (p=0.64). Median survival from the ED-visit was 17 days (95% CI 15-19) and was significantly shorter in HM-patients (15 days versus 18 days, p=0.028). In-hospital death occurred in 67.9% of the HM-patients versus 29.5% of the ST-patients; HM-patients died at home in 15.4% versus 38.3% of the ST-patients (p<0.0001). In HM-patients, causes of death were disease progression (46.2%), treatment toxicity (39.7%), or both (9.0%).

Quality of end-of-life care

Quality of end-of-life care in HM- and ST-patients is shown in Table 4. Intensive anti-cancer treatment was administered to 375 (72.4%) of all patients up to 6 months before the ED-visit; to 75.6% of the HM-patients versus 71.8% of the ST-patients, p=0.48. HM-patients died more often in-hospital compared to ST-patients (67.9% versus 29.5%, p<0.0001), in an acute hospital setting (29.5% versus 2.7%, p<0.0001) and less often in a hospice (2.6% versus 10.5%, p=0.011).

Table 3. Emergency department-visit and follow-up characteristics of 78 patients with a haematological malignancy and 420 patients with a solid tumour.

	Total n=498		**HM-patients n=78**		**ST-patients n=420**		
ED-visit	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**P-value**
Diagnostic imaging	319	(64.1)	53	(67.9)	266	(63.3)	0.326
Laboratory tests	419	(84.1)	69	(88.5)	350	(83.3)	0.204
Clinical diagnosis							
Infection or fever	122	(24.5)	36	(46.2)	86	(20.5)	<0.0001
Bronchopulmonary insufficiency	71	(14.3)	17	(21.8)	54	(12.9)	0.051
Renal insufficiency or hydronephrosis	59	(11.8)	12	(15.4)	47	(11.2)	0.308
Cachexia	44	(8.8)	4	(5.1)	40	(9.5)	0.177
Pleural effusion	36	(7.2)	5	(6.4)	31	(7.4)	0.750
Ascites	35	(7.0)	1	(1.3)	34	(8.1)	0.010
Bleeding	33	(6.6)	3	(3.8)	30	(7.1)	0.250
Jaundice	24	(4.8)	1	(1.3)	23	(5.5)	0.151
Neuropathy or plexopathy	20	(4.0)	3	(3.8)	17	(4.0)	>0.999
Ileus or passage disturbances	18	(3.6)	0	(0.0)	18	(4.3)	0.091
Urine retention	14	(2.8)	1	(1.3)	13	(3.1)	0.707
Seizure	14	(2.8)	1	(1.3)	13	(3.1)	0.707
Fracture	10	(2.0)	0	(0.0)	10	(2.4)	0.375
Deep venous thrombosis	8	(1.6)	1	(1.3)	7	(1.7)	>0.999
Coma	8	(1.6)	0	(0.0)	8	(1.9)	0.617
Delirium	8	(1.6)	2	(2.6)	6	(1.4)	0.365
Pulmonary embolism	8	(1.6)	1	(1.3)	8	(1.9)	0.617
Spinal cord compression	5	(1.0)	0	(0.0)	5	(1.2)	>0.999
Treatment for main symptom initiated at ED	284	(57.0)	54	(69.2)	230	(54.8)	0.010
Time spent at ED in hours:minutes, median (range)	3:32	(0:12-18:01)	3:37	(0:42-12:12)	3:39	(0:12-18:01)	0.708
Follow-up							
ED-visit followed by hospital admission	390	(78.3)	71	(91.0)	319	(76.0)	0.001
Observed survival in days, median (95% C.I.)	17	(15-19)	15	(10-20)	18	(15-21)	0.028
Place of death							<0.0001
Clinical ward	143	(28.7)	30	(38.5)	113	(26.9)	
ICU or ED	34	(6.8)	23	(29.5)	11	(2.6)	
Home	173	(34.7)	12	(15.4)	161	(38.3)	
Nursing or residential home	12	(2.4)	3	(3.8)	9	(2.1)	
Hospice	47	(9.4)	2	(2.6)	45	(10.7)	
Unknown	89	(17.9)	8	(10.3)	81	(19.3)	

List of abbreviations: ED: emergency department; HM: haematological malignancy; ST: solid tumour; ICU: intensive care unit.

Table 4. Comparison of indicators of quality of end-of-life care between 78 patients with a haematological malignancy and 420 patients with a solid tumour.

Indicators of quality of end-of-life care	Total n=498		HM-patients n=78		ST-patients n=420		
	n	(%)	n	(%)	n	(%)	P-value
Intensive anti-cancer treatment[a]	375	(72.4)	59	(75.6)	316	(71.8)	0.48
Number of ED-visits[b], median (range)	1.00	(0-9)	1.00	(0-9)	1.00	(0-7)	0.12
In-hospital death	183	(35.3)	53	(67.9)	130	(29.5)	<0.0001
Death in an acute hospital setting[c]	35	(6.8)	23	(29.5)	12	(2.7)	<0.0001
Death in hospice	48	(9.2)	2	(2.6)	46	(10.5)	0.011

List of abbreviations: HM: haematological malignancy; ST: solid tumour; ED: emergency department; ICU: intensive care unit

[a] Number of intensive anti-cancer treatments received in the 3 months before ED-visit. Intensive anti-cancer treatments included: chemotherapy, targeted therapy, stem cell transplantation, surgery, radiotherapy, hormonal therapy, nuclear therapy.

[b] Number of ED-visits in 6 months before current ED-visit.

[c] Acute hospital settings included the ED and the ICU.

DISCUSSION

This study gives insight into the disease trajectory of haematological malignancy (HM)-patients and in the differences compared to the disease trajectory of patients with a solid tumour (ST) visiting the ED in the last three months of their lives. Limitations on life-sustaining treatments (LST) were often not discussed in HM-patients before their ED-visit; and if these were discussed, patients often had no limitations on LSTs. End-of-life care was considerably more aggressive in HM-patients compared to ST-patients. HM-patients had a worse survival than ST patients, and more often died in-hospital and in the ICU and seldom in a hospice.

Our results show that end-of-life care implicates aggressive in HM-patients: they scored poorly on five of the indicators of quality of end-of-life care by Earle.[24] Our findings are in accordance with international literature reporting that HM-patients receive intensive treatments until death. In a study by Hui et al., HM-patients received significantly more chemotherapy (21%) and targeted therapy (17%) than ST-patients (6% and 5%, respectively).[2] Other studies report that HM-patients often received G-CSF, blood transfusions and antibiotics and underwent diagnostic imaging, blood sampling, endoscopy and bone marrow examination in the last seven days of life.[23,29] A French study in patients who died from metastatic lung cancer showed that end-of-life care was less aggressive the earlier palliative care needs were reported in their EPRs: patients sooner stopped anticancer treatment and they underwent less often invasive ventilation.[30] In patients with pancreatic cancer in the last thirty days of life who were referred to a

palliative care service, those with an early referral to a palliative care team visited the ED less often and were less often hospitalized.[31] It thus seems that when palliative care is integrated into oncology care, ST-patients are at a lower risk of aggressive end-of-life care. In our study, limitations on LSTs were seldom discussed with HM-patients and remarkably, if it was discussed, it was often explicitly stated in their electronic patient dossiers that there were no limitations on LSTs. A recent integrative systematic review provided more insight into the aspects of this 'curative mindset': haematologists feel uncomfortable with hospice-referrals and discussing approaching death with patients and family; disease-progression is considered as personal failure; and they are concerned that mentioning palliative care early in the disease trajectory might scare patients and their relatives.[6] A qualitative study by Prod'homme et al. showed that end-of-life discussions are avoided by haematologists as long as cure is possible; these discussions are perceived to damage the doctor-patient relationship, especially when the patient's prognosis is uncertain.[32] In addition, haematologists interpret palliative care more often as end-of-life care than medical oncologists do and are less used to involve a palliative care specialist than medical oncologists.[33] It is known that if HM-patients are referred to palliative care, it generally occurs very late in their disease trajectory.[3,7,11] Although a curative care approach towards HM-patients could be appropriate, the way it is currently practiced discourages timely initiation of a palliative care approach and conversations about the end of life. El-Jawahri et al. reported that 27% of the hospital-admissions in AML-patients could have been avoided.[34] Reasons were: being discharged too soon after the previous admission, visits for problems that would have been manageable at home and the lack of timely out-patient follow-up appointments. These reasons are starting points for initiating a palliative care approach to avoid possible aggressive and harmful treatments in vulnerable patients.

Our study suggests that in many patients the ED-visit marked deterioration and a transition in disease trajectory and often even the start of the dying phase. After the ED-visit or following hospital-admission, limitations on LSTs were discussed and documented in 73% of the ST-patients and 53% of the HM-patients. Although efforts were made to discuss these LSTs, still 36% of the HM-patients were subsequently transferred to the ICU. This is in line with literature demonstrating that HM-patients are frequently and more often admitted to ICUs than ST-patients (39% and 8%, respectively).[2] Failure to recognize patients in the end-of-life phase makes them at risk of receiving aggressive treatments in the hospital and may even result in death: in our study, 33% of the HM-patients died in the ICU, compared to 4% of the ST-patients ($p<0.0001$).[2] Sixty-nine percent of our HM-patients died in the hospital and 40% died as a result of treatment toxicity. Howell et al. showed that, compared to ST-patients, HM-patients had a twice higher risk to die in the hospital.[22] Our findings confirm that HM-patients have unpredictable disease trajectories that can

suddenly change from curative to dying: most of our patients died shortly after the ED-visit with a median survival of only 15 days. Reasons for difficulties to predict survival and to recognize the transition to the end-of-life trajectory are: possibly reversible conditions such as infections, increasing availability of systemic therapies that stimulate continuance of active treatment and increase the risk of lethal complications.[1,35] Long-lasting physician-patient relationships are also known to hamper accurate recognition of deterioration.[6] The combination of these factors makes it difficult for physicians to recognize approaching death in HM-patients and to timely prepare them for their approaching death.

A proactive integrated care approach

We advocate, as Zimmermann, Bruera, LeBlanc, El-Jawahri, Chung and Button do, the use of an integrated care approach with two concurrent tracks: a curative approach and palliative care approach (Figure 1).[16-19,36,37] Integrated care should be initiated early in the disease trajectory if the disease is potentially life-threatening (which can be at diagnosis). The first track consists of conventional disease treatment aimed at cure. The second track consists of supportive care following the four-dimensional principles of palliative care: physical, psychological, social, and spiritual. Importantly, the second track also includes discussions about future problems, treatment choices, hospital-admissions, LSTs and place of death. The palliative care approach has shown to benefit symptom-control[37] and quality of life,[38] to decrease ED-visits, hospital- and ICU-admissions and in-hospital deaths[39,40] and might even prolong survival.[41] In the integrated care approach, multidisciplinary discussions and communication across specializations within and outside the medical field are crucial to satisfy care needs. The randomized clinical trial by El-Jawahri et al. demonstrated that in-patient palliative care improved the quality of life of HM-patients already within two weeks after hematopoietic stem cell transplantation had taken place.[16]

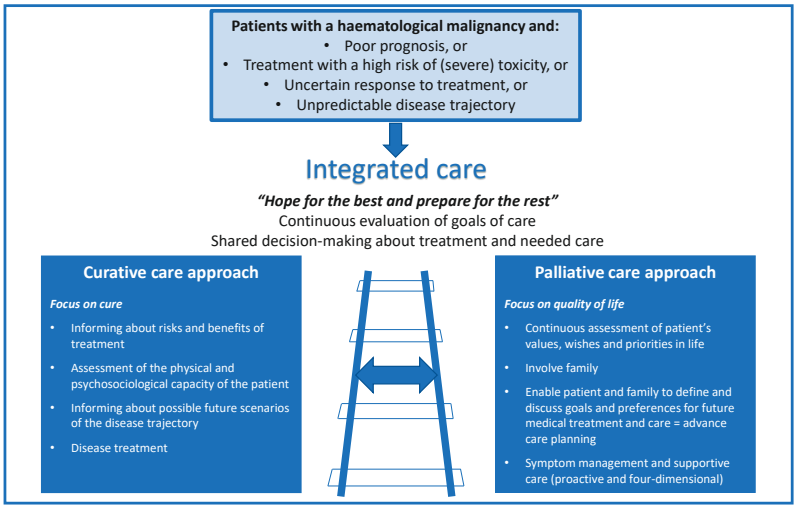

Figure 1. A proactive integrated care approach for patients with a haematological malignancy: a curative and a supportive track.

Our pragmatic study provides insight into the care for HM-patients visiting the ED in their end-of-life trajectory and compared is with the disease trajectory of ST-patients. The inclusion of only those patients who died within 3 months after the ED-visit is inherent to the mortality-follow-back design of this study, but it has introduced selection bias. Although data were collected from 2011-2013, they are still relevant since new life-prolonging systemic treatments only further emphasize the need for an integrated care approach. Further research should be directed to identifying the specific palliative care needs of HM-patients and their families and developing interventions to address to those.

CONCLUSION

HM-patients who visited the ED in the last 3 months of life are more often hospitalized and die in-hospital compared to ST-patients. To improve care during the end-of-life trajectory, especially for HM-patients, palliative care should be timely integrated in standard oncological care.

Authors' Note

As approved by the Medical Ethics Committee of the LUMC and according to Dutch and European law, informed consent from patients was not necessary because of the retrospective design of this study.

Declaration of Conflicting Interests

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