BMC Palliative Care

RESEARCH Open Access

Fluid therapy is associated with lower care quality and higher symptom burden during last days of life of patients with cancer – a population-based register study

Magnus Lindskog[1,2,3*], Hanna Mogensen[3,4], Björn Tavelin[5], Johanna Eknert[6], Sta□an Lundström[7] and Peter Strang[7]

Abstract

Background Parenteral □uid (PF) therapy of patients in end-of-life (EOL) is controversial. The purpose of this study was to assess associations between PF, quality of the EOL care process and symptom burden in dying cancer patients, using a population-based approach.

Methods This was a nationwide retrospective register study of all adult cancer deaths with documented information on PF in the last 24 h of life as reported to the Swedish Register of Palliative Care during a three-year period ($n = 41,709$). Prevalence and relief of symptoms during the last week of life as well as EOL care process quality indicators were assessed in relation to PF in those patients who had a documented decision to focus on EOL care (immediately dying, $n = 23,112$). Odds ratios were calculated, adjusting for place of death (hospital vs. non-hospital).

Results PF was administered to 30.9% of immediately dying patients in hospitals compared to 6.5% outside of hospitals. PF was associated with a higher likelihood for breathlessness and nausea. In patients screened for EOL symptoms with a validated instrument, PF was inversely associated with the likelihood of complete relief of breathlessness, respiratory secretions, anxiety, nausea and pain. Several palliative care quality indicators were inversely associated with PF, including EOL conversations and prescriptions of injectable drugs as needed. These associations were more pronounced in hospitals.

Conclusions Parenteral □uid therapy in the last 24 h of life was associated with inferior quality of the EOL care process and with increased symptom burden in imminently dying cancer patients.

Keywords Fluid therapy, Palliative care, End-of-life, Cancer, Quality, Symptoms

*Correspondence:
Magnus Lindskog
magnus.lindskog@igp.uu.se
[1]Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden
[2]Department of Pelvic Cancer, Genitourinary Oncology Unit, Karolinska University Hospital, Eugeniavägen 3, Solna 171 76, Stockholm, Sweden
[3]Department of Immunology, Genetics and Pathology, Cancer Precision Medicine, Uppsala University, Uppsala, Sweden
[4]Unit of Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
[5]Department of Radiation Sciences, Umeå University, Umeå, Sweden
[6]Upper GI Unit, Theme Cancer, Karolinska University Hospital, Stockholm, Sweden
[7]Stockholms Sjukhem Foundation and Department of Oncology-Pathology, Stockholm, Sweden

Background

Methods

Population

Variables

Statistical methods

Results

Study population

Associations between PF and quality of the EOL care process

Table 1 Study base

Category	ALL	PF	non-PF
Number of patients, n (%)	41,709	5,781 (13.9)	35,928 (86.1)
Age in years, median (range)	74 (18–105)	70 (18–102)	74 (18–105)
Place of death			
Hospital, n (%)	10,357	3,627 (35.0)	6,730 (65.0)
Spec PC in-patient unit, n (%)	13,136	1,256 (9.6)	11,880 (90.4)
Spec PC home care, n (%)	7,402	502 (6.8)	6,900 (93.2)
Gen PC home care, n (%)	2,813	135 (4.8)	2,678 (95.2)
Nursing home short term stay, n (%)	4,635	167 (3.6)	4,468 (96.4)
Nursing home permanent stay, n (%)	3,189	74 (2.3)	3,115 (97.7)
Other, n (%)	177	20 (11.3)	157 (88.7)
Cancer diagnoses (ICD-10) with PF use > median			
Head and neck cancer[1], n (%)	474 (100)	146 (30.8)	328 (69.2)
Esophageal cancer[2], n (%)	786 (100)	218 (27.7)	568 (72.3)
Ovarian cancer[3], n (%)	1,203 (100)	251 (20.1)	952 (79.1)
Hematological cancer[4], n (%)	2,633 (100)	517 (19.6)	2,116 (80.4)
Gastric cancer[5], n (%)	1,488 (100)	283 (19.0)	1,205 (81.0)

PF = Parenteral fluid therapy in the last 24 h of life. [1]C0-C14, C32-C33; [2]C15; [3]C56.9; [4]C81-C88, C90-C96; [5]C16

Table 2 Characteristics of adult cancer patients dying in hospital versus dying outside hospital as reported to the SRPC in 2011–2013

	Hospital deaths PF	Hospital deaths Non-PF	OR	95% CI	*P*	Non-Hospital deaths PF	Non-Hospital deaths Non-PF	OR	95% CI	*P*
N* (%)	1687 (30.9)	3772 (69.1)	NA	NA	NA	1148 (6.5)	16,505 (93.5)	NA	NA	NA
Age (SD)	70.5 (12.17)	72.2 (11.99)	NA	NA	< 0.0001	68.7 (12.63)	73.9 (12.18)	NA	NA	< 0.0001
Sex, % female	48.9	49.5	0.98	0.87–1.10	0.69	51.4	49.5	1.08	0.96–1.22	0.21
Received specialised palliative care (%)	NA	NA	NA	NA	NA	955 (83.2)	10,985 (66.6)	NA	NA	< 0.0001
Pain[#] Yes/No (% yes)	1279/327 (75.8)	3052/640 (80.9)	0.82	0.71–0.95	0.009	955/181 (83.2)	13,655/2744 (82.7)	1.06	0.90–1.25	0.48
Anxiety[#] Yes/No (% yes)	787/593 (46.7)	1974/1328 (52.3)	0.89	0.79–1.01	0.081	613/445 (53.4)	8565/7108 (51.9)	1.14	1.01–1.30	0.037
Nausea[#] Yes/No (% yes)	420/991 (24.9)	685/2618 (18.2)	1.62	1.41–1.87	< 0.0001	429/675 (37.4)	3633/12,279 (22.0)	2.15	1.89–2.44	< 0.0001
Breathlessness[#] Yes/No (% yes)	604/952 (35.8)	1065/2485 (28.2)	1.48	1.31–1.68	< 0.0001	329/785 (28.7)	3273/12,927 (19.8)	1.66	1.45–1.89	< 0.0001
Respiratory secretions[#] Yes/No (% yes)	920/714 (54.5)	2029/1674 (53.8)	1.02	0.95–1.20	0.31	623/517 (54.3)	8331/8039 (50.5)	1.16	1.03–1.31	0.014

PF = parenteral fluid therapy during the last 24 h of life. *Only patients with a documented decision to focus on end-of-life care and with documented PF status (yes or no) were included (*N* = 23,112). [#]For each specific symptom, only patients for which a documented presence or absence (yes or no) of that symptom were included in the analysis

Discussion

Table 3 Quality indicators of the care process in patients with or without parenteral fluid therapy*, stratified by place of death

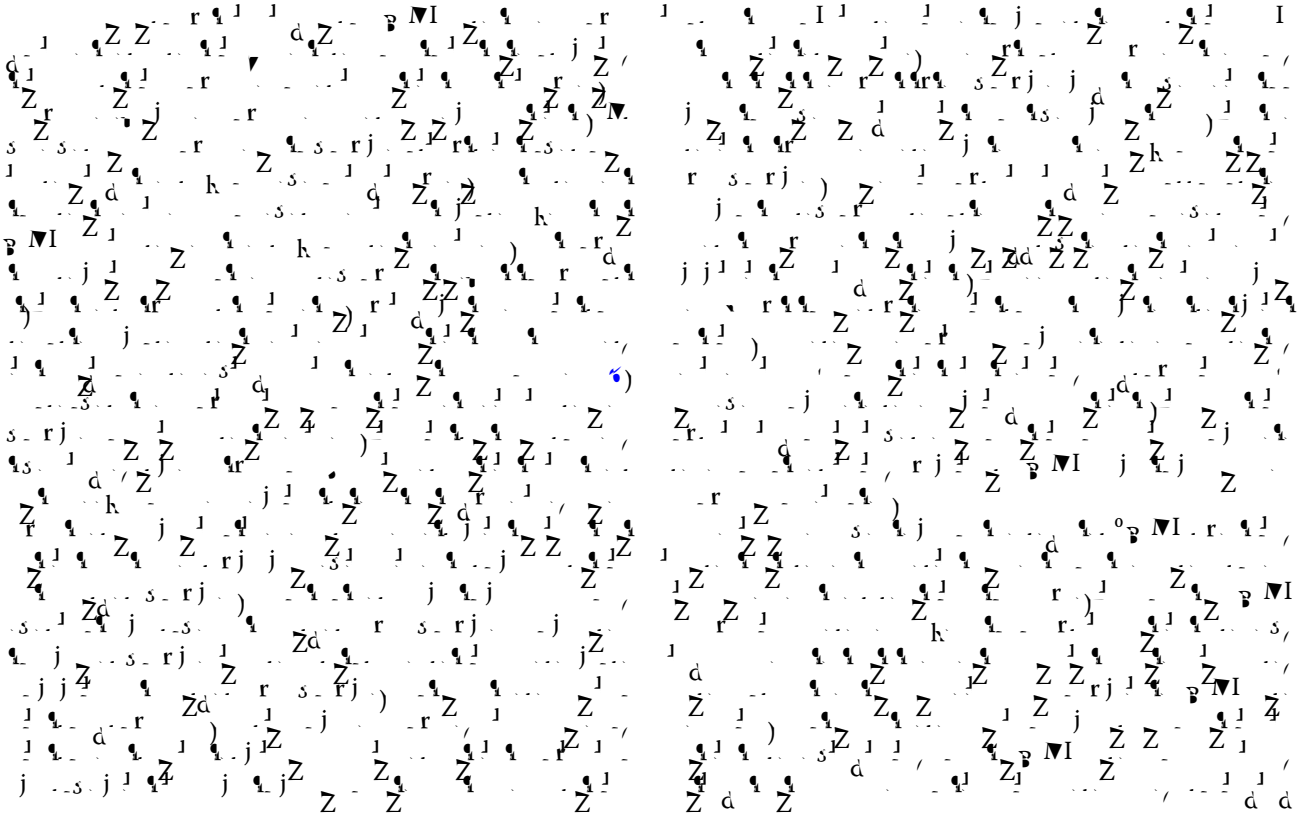
	Hospital deaths					Non-hospital deaths				
	PF	Non-PF	OR	95% CI	p	PF	Non-PF	OR	95% CI	p
EOL conversation, patients, yes/no (%[¤])	886/420 (68)	2464/641 (79)	0.55	0.47–0.63	< 0.001	948/119 (89)	13655/1604 (89)	0.94	0.77–1.14	0.51
EOL conversation, family, yes/no (%[¤])	1351/148 (90)	3232/232 (93)	0.66	0.53–0.81	< 0.001	1020/66 (94)	15638/845 (95)	0.89	0.69–1.15	0.39
Symptom screening										
Pain, yes/no (%[¤])	359/1073 (25)	878/2499 (26)	0.95	0.93–1.10	0.50	486/601 (45)	7084/8790 (45)	0.99	0.88–1.13	1.00
Other symptoms, yes/no (%[¤])	136/1171 (10)	3662792 (12)	0.89	0.72–1.09	0.25	260/789 (25)	3824/11787 (25)	1.02	0.88–1.17	0.83
Analgesic[#], yes/no (%[¤])	1585/95 (94)	3644/121 (97)	0.55	0.42–0.73	< 0.001	1122/25 (98)	16258/233 (99)	0.64	0.42–0.98	0.04
Sedative[#], yes/no (%[¤])	1351/308 (81)	3368/369 (90)	0.48	0.41–0.57	< 0.001	1088/59 (95)	15902/503 (97)	0.68	0.51–0.89	0.01
Antiemetic[#], yes/no (%[¤])	1042/599 (63)	2565/1123 (70)	0.76	0.67–0.86	< 0.001	1053/92 (92)	14997/1464 (91)	1.10	0.90–1.39	0.32
Antimuscarinic[#], yes/no (%[¤])	1215/439 (73)	3223/512 (86)	0.44	0.38–0.51	< 0.001	1047/98 (91)	15750/734 (96)	0.50	0.40–0.62	< 0.001
Oral health assessed, yes/no (%[¤])	931/388 (71)	2493/700 (78)	0.67	0.58–0.78	< 0.001	831/226 (79)	12468/2892 (81)	0.85	0.73–0.99	0.04
Died alone, yes/no (%[¤])	239/1437 (14)	563/3150 (15)	0.94	0.80–1.10	0.44	129/1015 (11)	1801/14641 (11)	1.03	0.85–1.25	0.74

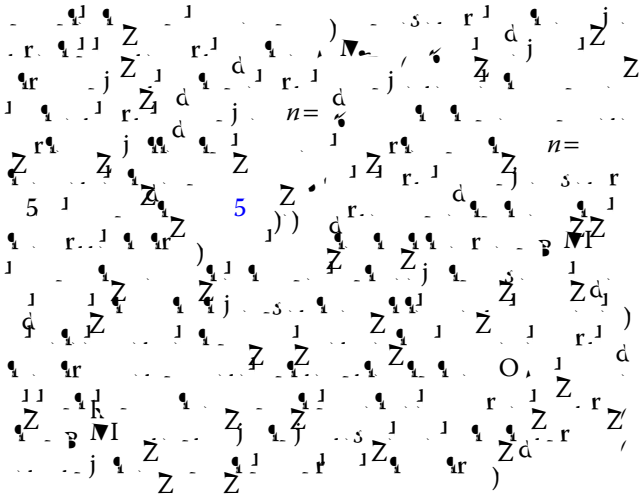
PF = parenteral fluid therapy in the last 24 hours of life. OR = odds ratio with 'non-PF' as reference. CI = confidence intervals *Only patients with a documented decision to focus on end-of-life care included (*N* = 23,112); [¤]% refers to the proportion of "yes", for each comparison. [#]Prescription in medical chart of injectable drug to be used as needed. Patients for whom data was missing about the respective care quality indicator were excluded from that specific analysis. The proportion of missing data per care quality indicator were 10% (information to patients), 2.5% (information to families), 6% (screening for pain), 9% (screening for symptoms other than pain), 0% (analgesic), 1% (sedative), 1% (antiemetic), 0% (antimuscarinic), 9.5% (oral health assessment) and 0.5% (died alone)

Table 4 Likelihood of complete symptom relief[#] in relation to parenteral fluid therapy in the last 24 h of life

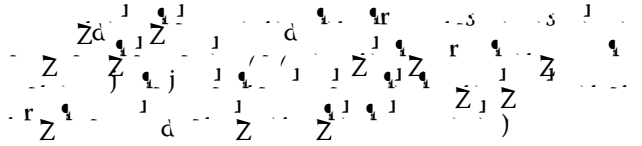
Symptom completely relived	PF	non-PF	OR*	95% CI	*p*
Pain [#], yes / no (%[¤])	2,792 / 1,621 (63)	21,606 / 7,440 (74)	0.70	0.66–0.76	<0.001
Anxiety [#], yes / no (%[¤])	1,443 / 1,327 (52)	11,517 / 6,421 (64)	0.73	0.67–0.80	<0.001
Nausea [#], yes / no (%[¤])	649 / 954 (41)	4,216 / 3,348 (56)	0.58	0.51–0.65	<0.001
Breathlessness [#], yes / no (%[¤])	558 / 1,332 (30)	3,167 / 4,454 (42)	0.73	0.65–0.82	<0.001
Respiratory secretions [#], yes / no (%[¤])	960 / 2,045 (32)	8,412 / 9,565 (47)	0.66	0.61–0.72	<0.001

[#]Only patients with a documented symptom screen detecting the specific symptom are included. PF = parenteral fluid therapy; [¤]% refers to the proportion of "yes", for each comparison; *OR = odds ratio with 'no PF' as reference, adjusted for place of death. CI = confidence interval





Conclusions



Abbreviations

PF	Parenteral □uid therapy
EOL	End-of-life
SRPC	The Swedish Registry of Palliative Care

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12904-024-01504-5.

Supplementary Material 1

Acknowledgements
Not applicable.

Author contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by M.L., B.T. and S.L. The □rst draft of the manuscript was written by M.L. and P.S. H.M. provided epidemiological expertise and took active part in the writing of the manuscript. J.E. contributed with signi□cant input on data interpretation. All authors commented on previous versions of the manuscript. All authors read and approved the □nal manuscript.

Funding
Open access funding provided by Karolinska Institute. Dr. Strang received grants from The Cancer Research Funds of Radiumhemmet (no. 201241), Region Stockholm (ALF project 20200472), and Stockholm's Sjukhem Foundation´s Jubilee Fund during the conduct of the study. Dr Lindskog received grants from Region Uppsala (ALF-941921) and the research foundation Stiftelsen Onkologiska Klinikens i Uppsala Forskningsfond.

Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Human ethics and consent to participate
The study was approved by the Ethics Committee of University of Linköping, Dnr 2013/289 – 31 which in their written decision con□rmed that informed consent was not required since this observational study was entirely based on anonymised data in a national quality register and since all the procedures registered were part of the routine care. The study was conducted in compliance with Good Clinical Practices protocol and also in compliance with the Declaration of Helsinki principles, when applicable (deceased persons with encrypted id-numbers).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 20 September 2023 / Accepted: 8 July 2024
Published online: 18 July 2024

References

1. Kehl KA, Kowalkowski JA. A systematic review of the prevalence of signs of impending death and symptoms in the last 2 weeks of life. Am J Hosp Palliat Care. 2013;30(6):601–16.
2. Hiratsuka Y, Suh SY, Won SH, Kim SH, Yoon SJ, Koh SJ, Kwon JH, Park J, Ahn HY, Cheng SY, et al. Prevalence and severity of symptoms and signs in patients with advanced cancer in the last days of life: the east Asian collaborative cross-cultural study to elucidate the dying process (EASED). Support Care Cancer. 2022;30(6):5499–508.
3. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. J Pain Symptom Manage. 2006;31(1):58–69.
4. Morita T, Shima Y, Adachi I, Japan Palliative Oncology Study G. Attitudes of Japanese physicians toward terminal dehydration: a nationwide survey. J Clin Oncol. 2002;20(24):4699–704.
5. Raijmakers NJH, van Zuylen L, Costantini M, Caraceni A, Clark J, Lundquist G, Voltz R, Ellershaw JE, van der Heide A. Opcare: Arti□cial nutrition and hydration in the last week of life in cancer patients. A systematic literature review of practices and e□ects. Ann Oncol. 2011;22(7):1478–86.
6. Hui D, Dev R, Bruera E. The last days of life: symptom burden and impact on nutrition and hydration in cancer patients. Curr Opin Support Palliat Care. 2015;9(4):346–54.
7. Buchan EJ, Haywood A, Syrmis W, Good P. Medically assisted hydration for adults receiving palliative care. Cochrane Database Syst Rev. 2023;12(12):Cd006273.
8. Dev R, Dalal S, Bruera E. Is there a role for parenteral nutrition or hydration at the end of life? Curr Opin Support Palliat Care. 2012;6(3):365–70.
9. Druml C, Ballmer PE, Druml W, Oehmichen F, Shenkin A, Singer P, Soeters P, Weimann A, Bischo□ SC. ESPEN guideline on ethical aspects of arti□cial nutrition and hydration. Clin Nutr. 2016;35(3):545–56.
10. Good P, Richard R, Syrmis W, Jenkins-Marsh S, Stephens J. Medically assisted hydration for adult palliative care patients. Cochrane Database Syst Rev. 2014;2014(4):CD006273.
11. Morita T, Hyodo I, Yoshimi T, Ikenaga M, Tamura Y, Yoshizawa A, Shimada A, Akechi T, Miyashita M, Adachi I, et al. Association between hydration volume and symptoms in terminally ill cancer patients with abdominal malignancies. Ann Oncol. 2005;16(4):640–7.
12. Bozzetti F, Arends J, Lundholm K, Micklewright A, Zurcher G, Muscaritoli M. Espen: ESPEN guidelines on Parenteral Nutrition: non-surgical oncology. Clin Nutr. 2009;28(4):445–54.
13. Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, Fearon K, Hutterer E, Isenring E, Kaasa S, et al. ESPEN guidelines on nutrition in cancer patients. Clin Nutr. 2017;36(1):11–48.
14. McCann RM, Hall WJ, Groth-Juncker A. Comfort care for terminally ill patients. The appropriate use of nutrition and hydration. JAMA. 1994;272(16):1263–6.
15. Lundstrom S, Axelsson B, Heedman PA, Fransson G, Furst CJ. Developing a national quality register in end-of-life care: the Swedish experience. Palliat Med. 2012;26(4):313–21.
16. Brooke HL, Talback M, Hornblad J, Johansson LA, Ludvigsson JF, Druid H, Feychting M, Ljung R. The Swedish cause of death register. Eur J Epidemiol. 2017;32(9):765–73.
17. Elmstedt S, Mogensen H, Hallmans DE, Tavelin B, Lundstrom S, Lindskog M. Cancer patients hospitalised in the last week of life risk insu□cient care

quality - a population-based study from the Swedish Register of Palliative Care. Acta Oncol. 2019;58(4):432–8.
18. Bruera E, Franco JJ, Maltoni M, Watanabe S, Suarez-Almazor M. Changing pattern of agitated impaired mental status in patients with advanced cancer: association with cognitive monitoring, hydration, and opioid rotation. J Pain Symptom Manage. 1995;10(4):287–91.
19. Fritzson A, Tavelin B, Axelsson B. Association between parenteral uids and symptoms in hospital end-of-life care: an observational study of 280 patients. BMJ Support Palliat Care. 2015;5(2):160–8.
20. Yamaguchi T, Morita T, Shinjo T, Inoue S, Takigawa C, Aruga E, Tani K, Hara T, Tamura Y, Suga A, et al. E ect of parenteral hydration therapy based on the Japanese national clinical guideline on quality of life, discomfort, and symptom intensity in patients with advanced cancer. J Pain Symptom Manage. 2012;43(6):1001–12.
21. Bruera E, Hui D, Dalal S, Torres-Vigil I, Trumble J, Roosth J, Krauter S, Strickland C, Unger K, Palmer JL, et al. Parenteral hydration in patients with advanced cancer: a multicenter, double-blind, placebo-controlled randomized trial. J Clin Oncol. 2013;31(1):111–8.
22. Piili RP, Lehto JT, Luukkaala T, Hinkka H, Kellokumpu-Lehtinen PI. Does special education in palliative medicine make a di erence in end-of-life decision-making? BMC Palliat Care. 2018;17(1):94.
23. Broad JB, Gott M, Kim H, Boyd M, Chen H, Connolly MJ. Where do people die? An international comparison of the percentage of deaths occurring in hospital and residential aged care settings in 45 populations, using published and available statistics. Int J Public Health. 2013;58(2):257–67.
24. Jordhoy MS, Fayers P, Loge JH, Ahlner-Elmqvist M, Kaasa S. Quality of life in palliative cancer care: results from a cluster randomized trial. J Clin Oncol. 2001;19(18):3884–94.
25. de la Cruz M, Noguera A, San Miguel-Arregui MT, Williams J, Chisholm G, Bruera E. Delirium, agitation, and symptom distress within the nal seven days of life among cancer patients receiving hospice care. Palliat Support Care. 2015;13(2):211–6.
26. Bruera E, Sala R, Rico MA, Moyano J, Centeno C, Willey J, Palmer JL. E ects of parenteral hydration in terminally ill cancer patients: a preliminary study. J Clin Oncol. 2005;23(10):2366–71.
27. Lawlor PG, Gagnon B, Mancini IL, Pereira JL, Hanson J, Suarez-Almazor ME, Bruera ED. Occurrence, causes, and outcome of delirium in patients with advanced cancer: a prospective study. Arch Intern Med. 2000;160(6):786–94.
28. Strang P, Martinsson L, Bergstrom J, Lundstrom S. COVID-19: symptoms in dying residents of nursing homes and in those admitted to hospitals. J Palliat Med. 2021;24(7):1067–71.

Publisher's Note