### **Original** Article

# Parenteral Hydration in Dying Patients With Cancer: A National Registry Study

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### Abstract

**Context.** Clinically assisted hydration during end-of-life care among patients with cancer is controversial; practice varies between clinical settings and countries, and there is a lack of evidence.

**Objectives.** To examine whether breathlessness, respiratory secretion, or confusion correlates with receiving parenteral hydration during end of life, adjusted for sex, age, and place of death.

**Methods.** The Swedish Register of Palliative Care database was used to collect data about the usage of parenteral hydration during the last day of life, and the occurrence of three symptoms during the last week. Adults dying from cancer during 2011 –2021 in hospitals, in residential care homes, and within specialized palliative care were included. Correlation between parenteral hydration and symptoms was examined using  $\chi^2$ -test and logistic regression.

**Results.** A total of 147,488 patients were included in the study. Parenteral hydration was more often prescribed to younger persons, to men, and in acute hospitals (compared to other settings), p < 0.001 in all three comparisons. Patients with hematological malignancies (20%) and ovarian cancer (16%) were most likely to receive parenteral hydration, while those with brain tumors (6%) were least likely. The presence of all three analyzed symptoms during the last week (breathlessness, respiratory secretion, and confusion) were significantly correlated with having received parenteral hydration during the last day of life (p < 0.001). In the final logistic regression model adjusted for age, sex, and place of death, the only symptom with remaining correlation to parenteral hydration was breathlessness (OR 1.56, 95% CI 1.50–1.6).

**Conclusion.** There is an association between parenteral hydration and increased breathlessness in patients with cancer. Provision of parenteral hydration is more prevalent in men, younger patients, and those with hematological malignancies or ovarian cancer, and most widespread in acute hospital settings. J Pain Symptom Manage 2024;000:1–9. © 2024 The Authors. Published by Elsevier Inc. on behalf of American Academy of Hospice and Palliative Medicine. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

### Key Words

Palliative care, end-of-life care, parenteral hydration, symptoms

### Key Message

This article describes a retrospective cohort study that describes the correlation between parenteral hydration and three symptoms during the last week of life for patients with cancer. A correlation between

© 2024 The Authors. Published by Elsevier Inc. on behalf of American Academy of Hospice and Palliative Medicine. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/) parenteral hydration and increased breathlessness was found. These data may be used as a basis for future advance care planning, as well for dialogues with relatives, who often request hydration to their immediately dying family member.

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List of abbreviations: aOR, adjusted odds ratio; CI, confidence interval; SRPC, Swedish Register of Palliative Care Address correspondence to: Lisa Martinsson, MD, PhD, Department of Radiation Sciences, Umea University, SE-90187 Umea, Sweden. E-mail: lisa.martinsson@umu.se

### Introduction

Most patients at the end of life have a reduction or cessation of oral intake. The administration of clinically assisted hydration (CAH), defined as fluids given parenterally either intravenously or subcutaneously, or enterally via a tube into the stomach or small bowel, in these patients is controversial; practice varies between clinical settings and countries, and there is a lack of evidence.<sup>1,2</sup> Different opinions regarding CAH during end-of-life care have been found among patients, caregivers, and health care professionals. In general, patients and their caregivers are positive about CAH and negative about withholding CAH, while the view of health care professionals varies considerably, with a range of 22% - 100%preferring to give CAH.<sup>3</sup> There is a broad variation (10%-88%) among patients with cancer receiving CAH at the end of life.<sup>4</sup> One important aspect is that CAH might increase the proportion of patients dying in care settings, especially hospitals, as CAH cannot always be provided in the home setting, unless the home care service is designed for such health care interventions, which is the case in Sweden.<sup>5</sup> Also, the practice of enteral tube feeding during end of life varies - it is controversial and is very uncommon in Sweden.<sup>6</sup>

A Cochrane review<sup>1</sup> found that there is a lack of good-quality studies on CAH for palliative care patients on which to base definite recommendations, and it is unclear whether CAH impacts symptoms, quality of life, and survival in end of life. In a review from Kingdon et al.,<sup>7</sup> CAH was not associated with severity of respiratory secretions in the majority of studies<sup>8-13</sup> although one paper showed increased secretions in those receiving CAH<sup>12</sup>. In addition, delirium might be delayed, but no decrease in incidence was shown.<sup>9</sup> No association between terminal restlessness and CAH has been shown, although increased restlessness was shown in those with higher fluid intake in the final hours.<sup>8</sup> Regarding breathlessness, no impact on severity of symptoms was seen in patients receiving CAH in end of life.<sup>9,10,14</sup> However, one retrospective observational study based on data from medical records found increased breathlessness in those receiving higher volumes close to end of life.<sup>10</sup>

The evidence regarding parenteral hydration in end-of-life care in patients with cancer is still controversial, and general clinical guidelines do not give clear guidance. Further, there is no information on how parenteral hydration is related to symptoms in different cancer diagnoses, and there is a lack of studies including patients in the last days of life.

### Aim

To examine whether breathlessness, respiratory secretions, or confusion (delirium) correlated with administration of parenteral hydration during end of life in patients with cancer, adjusted for sex, age, and place of death. A secondary aim was to examine whether the usage of parenteral hydration during end of life had changed during an 11-year period and whether there were differences in the usage between different cancer diagnoses.

### Methods

All adults reported to the Swedish Register of Palliative Care (SRPC) between 2011 and 2021 who had died from cancer in one of the three most common places of deaths (hospitals wards, specialized palliative care, and residential care homes including short-term stays) were identified. Cause of death data are collected by the SRPC from the Cause of Death registry at the National Board of Health and Welfare and were merged into SRPC data before data collection for this study. Of all cancer deaths in Sweden during 2011-2021 about 80% are registered in the SRPC. Further information about the development of the SPCR and validity for the questionnaire used for data collection has been previously described.<sup>15</sup> The following cancer diagnoses according to the International Classification of Diseases 10 (ICD-10) were included: gastrointestinal C15-C26, lung C34, breast C50, gynecological C51 -C58, prostate C61, urinary tract and kidney C64 -C68, central nervous system C69-C72, and lymphoma and hematological malignancies C81-C96.

Data about parenteral hydration and occurrence of symptoms (breathlessness, respiratory secretions, and confusion) during the last week in life were collected from the SRPC. In the SRPC symptoms of pain, nausea and anxiety are also reported but these were excluded from the study as they are not expected to be directly correlated to parenteral infusion. The question about parenteral hydration used to collect data in the SRPC database was "Did the person receive parenteral hydration/nutrition or enteral-tube feeding during the last 24 hours of life?" with Yes / No / Don't know, as alternatives. Parenteral hydration does not include small infusions for drug administration or subcutaneous infusions. During 2011 to 2014, the question used to collect symptom data was "Did the person display any of the following symptoms at any time during the last week of life?" From 2015, the symptom question was formulated as "Did the person display breakthrough of any of the following symptoms at any time during the last week of life?" These questions had Yes / No / Don't know, as alternatives. Symptoms were assessed by health care professionals according to local routines and data were entered in the SRPC by health care professionals after the patients' death.

Whether the occurrence of three symptoms (breathlessness, respiratory secretions, and confusion) was dependent on parenteral hydration was examined using  $\chi^2$ -test. Correlations between parenteral hydration, and sex, age categories, and place of death were analyzed using  $\chi^2$ -test. The usage of parenteral hydration between 2011 and 2021 was described for the different places of death. Further analyses of the correlations with adjustment for sex, age, and place of death were performed using logistic regression. Those reported as unexpected deaths were excluded, due to lack of data on the usage of parenteral hydration and occurrence of symptoms.

Analyses were performed using IBM SPSS Statistics version 28.0.1.1.<sup>18</sup>

### Results

A total of 153,250 adult persons who died from cancer during 2011 to 2021 within either specialized palliative care, hospitals, or residential care homes were identified in the database. Of these, 4741 were reported as unexpected deaths and therefore excluded, together with 1061 persons who had "Don't know" reported as answer to the question about parenteral hydration. In all, 147,448 persons remained in the study.

#### Demographics and the Use of Parenteral Hydration

A total of 72 255 women (49.0%) and 75 193 men (51.0%) were included. Mean age was 74.7 years (median 76.0), ranging from 18 to 109. Young age was associated with a higher probability of receiving parenteral hydration. Parenteral hydration was more commonly given to men (14.0%) compared to women (12.0%) (Table 1). The usage of parenteral hydration during the last day in life was most common in hospital wards (34.7%) and least common in residential care homes (2.4%). In specialized palliative patient care, 7.1% received parenteral hydration (Table 1).

The usage of parenteral hydration was least common for central nervous system malignancies (6.4%)

and most common for lymphoma and hematological malignancies (20.3%) (Table 2). The usage of parenteral hydration for the ovarian cancer group (ICD-10 C56 including subgroups) was 15.6% (679/4344). The usage of parenteral hydration for the colon cancer group (ICD-10 C18 including subgroups) was 12.0% (1668/13884).

During the study period, the usage of parenteral hydration overall declined from 14.0% during 2011 to 9.7% during 2021. In specialized palliative care it declined from 8.2% to 5.2%, and in hospitals from 36.6% to 32.6%, while usage in residential care homes went from 2.5% to 2.1% during the same time period (Table 3).

### *Symptoms*

The presence of all three analyzed symptoms during the last week (breathlessness, respiratory secretion, and confusion) was significantly correlated with parenteral hydration during the last day of life (p < 0.001) (Table 4).

All three symptoms were more common for younger patients compared to older (Table 5), and for men compared to women (Table 6).

In the first logistic regression model, adjustment was done for age and sex. In that model, the correlation between all three symptoms and the usage of parenteral hydration remained (data not shown). In the final model, also adjusted for place of death, the only symptom with remaining correlation to parenteral hydration was breathlessness (aOR 1.56, 95% CI 1.50-1.6) (Table 7).

### Discussion

Our extensive data on over 147,000 deceased persons with cancer in palliative care settings, nursing homes, and acute care hospitals shows that on average

The correlation between parenteral hydration and age categories, sex, and place of death, respectively				
	Parenteral hydration	No parenteral hydration	Total	p value
Age (years)				
18-64	4360 (17.0%)	21 291 (83.0%)	25651	<.001
65-74	6297 (15.2%)	35 255 (84.8%)	41552	
75-84	5861 (12.1%)	42 720 (87.9%)	48581	
85 and older	2669 (8.4%)	28 996 (91.6%)	1644	
Total	19 187 (13.0%)	128 261 (87.0%)	$147\ 448$	
Sex				
Women	8675 (12.0%)	63 580 (88.0%)	72255	<.001
Men	10 512 (14.0%)	64 681 (86.0%)	75193	
Total	19 187 (13.0%)	128 261 (87.0%)	$147\ 448$	
Place of death				
Specialized palliative care	5348 (7.1%)	70 322 (92.9%)	$75\ 670$	<.001
Residential care homes (long-term and short-term stays)	833 (2.4%)	33 416 (97.6%)	34249	
Hospitals	13 006 (34.7%)	24 523 (65.3%)	37529	
Total	19 187 (13.0%)	128 261 (87.0%)	$147\ 448$	

Table 1

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The usage of parenteral hydration for the different cancer diagnosis groups				
Cancer type	Parenteral hydration	No parenteral hydration	Total	
Gastrointestinal C15–C26	7218 (13.2%)	47 375 (86.8%)	54 593	
Lung C34	3629 (13.3%)	23 626 (86.7%)	$27\ 255$	
Breast C50	1209 (11.0%)	9794 (89.0%)	11 003	
Gynecological C51–C58	1322 (13.6%)	8423 (86.4%)	9745	
Prostate C61	1668 (10.0%)	15 029 (90.0%)	16~697	
Urinary tract and kidney C64-C68	1071 (10.8%)	8855 (89.2%)	9926	
Central nervous system C69–C72	291 (6.4%)	4255 (93.6%)	4546	
Lymphoma and hematological malignancies C81–C96	2779 (20.3%)	10 904 (79.7%)	13 683	
Total	19 187 (13.0%)	128 261 (87.0%)	147 448	

 Table 2 

 The usage of parenteral hydration for the different cancer diagnosis groups

during the last week of life, parenteral hydration was prescribed in 13% of the cases but significantly more often in hospitals (35%). The provision of parenteral hydration to a dying person was also associated with being male, being younger, or having ovarian cancer or a hematological diagnosis, with a somewhat reduced used from the years 2011 to 2021. In a logistic regression model adjusted for age, sex, and place of death, the receipt of parenteral hydration was significantly associated with breathlessness (aOR = 1.56), but not with respiratory secretion or confusion/delirium.

The use of parenteral hydration in the acutely dying remains a controversial issue.<sup>1,2</sup> A palliative intervention such as provision of parenteral hydration is intended to produce a palliative effect in the form of symptom control and improved quality of life, with limited adverse effects. For this reason, randomized controlled trials (RCTs) have been conducted to study possible benefits, as well as adverse effects.<sup>16–18</sup> As reported in a Cochrane report from 2015,<sup>1</sup> there might be some improvement in certain symptoms such as myoclonus or sedation in selected patients but the overall conclusion made by Cochrane is that the studies do not show a clinically relevant benefit, and there are insufficient studies of good quality for definite recommendations.

Still, clinically assisted hydration (CAH) is widely used, but not in a uniform way. In the last week of life, different cancer studies report CAH in 12%-88%, according to a systematic review by Raijmakers et al.<sup>4</sup> Palliative care experts have raised concerns about providing hydration to immediately dying persons, as some studies indicate that in this phase of general organ failure and impaired heart function, hydration might result in higher degrees of pleural effusions, ascites and / or peripheral edema, as shown in a prospective, observational study by Morita et al.<sup>11</sup> and reproduced by Nakajima et al.<sup>12</sup>

Despite concerns, studies have only occasionally shown associations between hydration and respiratory secretion and only in smaller studies,<sup>12</sup> whereas other studies have failed to show clear-cut associations,<sup>8–10</sup> well in line with our own data, when adjusted for age, sex, and place of death. These conflicting data might be related to the occurrence of two types of secretion. Type 1 secretion is explained as "real death rattle," which is related to secretion and exudation in the upper airways. Type 2 secretion is described as "pseudo death rattle," which sounds similar but is typically produced in the lungs, for example, as a consequence of debris from necrotic tumors or widespread pneumonias,<sup>19</sup> and thus, is secretion with a less obvious association with hydration.

Based on the limited data on associations between hydration and pleural effusions and / or peripheral edema,<sup>11,12</sup> an association with breathlessness would be more expected. Such an association was found in a study by Fritzon et al.,<sup>10</sup> who also showed that there was a correlation between the proportion of patients with dyspnea and the administered volume. This is of interest, as, for example, in two of the methodologically well performed studies, where Bruera et al. used 1000 mL normal saline in their intervention groups (compared with 100 ml in the control groups),  $^{16,17}$  which restricts generalizability of the data to situations when low or moderate volumes are administered. However, a few studies have found no correlation<sup>9,14</sup> but most of the performed studies have been limited in size. In contrast, we found a significant association, based on a very large number of registrations (over 147,000 deceased patients), even after controlling for age, sex, and place of death.

The proportion of patients receiving parenteral hydration varied a lot between places of death, from only 2.4% in residential care homes, to 7.1% in specialized palliative care and 34.7% in acute hospitals. Such large differences are not likely to reflect merely differences in medical needs, but also in psychological needs. A person in residential care or in palliative care is expected to die within a limited period of time, and it is more likely that advance care directives are in place. Moreover, in residential

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Place of death	Year of death	Parenteral hydration	No parenteral hydration	Total
Specialized palliative care	2011	490 (8.2%)	5457 (91.8%)	5947
	2012	533 (8.5%)	5765 (91.5%)	6298
	2013	529 (8.1%)	6024 (91.9%)	6553
	2014	523 (7.8%)	6201 (92.2%)	6724
	2015	500 (7.3%)	6388 (92.7%)	6888
	2016	492 (6.9%)	6635 (93.1%)	7127
	2017	499 (6.8%)	6792 (93.2%)	7291
	2018	522 (7.3%)	6617 (92.7%)	7139
	2019	472 (6.6%)	6662(93.4%)	7134
	2020	411 (5.6%)	6961 (94.4%)	7372
	2021	377(5.2%)	6820(94.8%)	7197
	Total	5348(7.1%)	70322(92.9%)	75 670
Residential care home (long-term and short-term stays)	2011	75 (2.5%)	2870 (97.5%)	2945
residential care nome (rong term and short term stays)	2012	82 (2.5%)	3149(97.5%)	3231
	2013	102(30%)	3346 (97.0%)	3448
	2013	78(24%)	3232 (97.6%)	3310
	2011	103(31%)	3168 (96.9%)	3971
	2015	70(2.2%)	3046 (97.8%)	3116
	2010	70(2.270) 71(9.9%)	3150 (97.8%)	3991
	2017	69(9.9%)	3038 (97.8%)	3107
	2010	61(2.270)	9075 (08.0%)	3036
	2019	62(9.9%)	2575(56.070) 9740(07.872)	9803
	2020	50(2.270)	2740(97.876) 9709(07.076)	2003
	2021 Tatal	39(2.170)	2702(97.970) 99.416(07.67)	2701
Hamital	10121	633(2.4%)	33410(97.0%)	34 249
Hospital	2011	1111(30.0%) 1490(97.9%)	1920(03.4%)	2027
	2012	1409(37.3%) 1500(27.6%)	2500(62.7%)	3909
	2015	1590(37.0%)	2040 (02.4%)	4230
	2014	1505 (35.9%)	2785(64.1%)	4348
	2015	1349 (35.8%)	2417(64.2%)	3700
	2016	1242 (32.9%)	2529 (67.1%)	3771
	2017	1189 (33.3%)	2380 (66.7%)	3569
	2018	996 (33.2%)	2001 (66.8%)	2997
	2019	908 (30.9%)	2035 (69.1%)	2943
	2020	817 (31.8%)	1752 (68.2%)	2569
	2021	752 (32.6%)	1558 (67.4%)	2310
	Total	13 006 (34.7%)	24 523 (65.3%)	37 529
All places of death	2011	1676 (14.0%)	10 253 (86.0%)	11 929
	2012	2104 (15.6%)	11 414 (84.4%)	13 518
	2013	2221 (15.6%)	12 010 (84.4%)	14 231
	2014	2164 (15.0%)	12 218 (85.0%)	$14\ 382$
	2015	1952 (14.0%)	11973~(86.0%)	13925
	2016	1804 (12.9%)	12 210 (87.1%)	14014
	2017	1759 (12.5%)	12 322 (87.5%)	$14\ 081$
	2018	1587 (12.0%)	11 656 (88.0%)	13243
	2019	1441 (11.0%)	11 672 (89.0%)	13 113
	2020	1291 (10.1%)	11 453 (89.9%)	$12\ 744$
	2021	1188 (9.7%)	11 080 (90.3%)	12 268
	Total	19 187 (13.0%)	128 261 (87.0%)	147 448

Table 3

care nurses are not available 24/7, making parenteral hydration more difficult due to practical reasons. Persons who are acutely admitted to a hospital are probably less prepared on a psychological level, and in a review of attitudes towards CAH, Gent et al. conclude that the symbolic value of CAH, including for the family, is a commonly expressed motive.<sup>20</sup> In the same literature review, beliefs and misconceptions about CAH as a means to alleviate thirst in the acutely dying were also discussed as a motive, as were cultural, ethical, and legal aspects.<sup>20</sup> In our data, younger patients were more likely to receive CAH, for unexplored reasons, but a possibility is that the mentioned symbolic value of "not giving up"<sup>20</sup> is more likely to be present in the care of younger patients.

In line with several other studies,<sup>11,12,17,18</sup> we found no association between hydration and delirium. However, as a secondary finding in a multiple logistic regression model, we found an association between acute care hospitals as place of death and confusion / delirium, with an aOR of 1.22 compared with palliative care settings. Considering our retrospective design, we cannot conclude whether this difference is a real difference, for example, due to a higher degree of delirium in dying patients who are acutely admitted to hospitals,

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Correlation between parenteral hydration and breathlessness, respiratory secretions, and confusion				
	Breathlessness	No breathlessness	Total	p value
Parenteral hydration	7246 (40.9%)	10 492 (59.1%)	17 738	< 0.001
No parenteral hydration	29 156 (23.5%)	95 105 (76.5%)	124 261	
Total	36 402 (25.6%)	105 597 (74.4%)	141 999	
	Respiratory secretions	No respiratory secretions	Total	p value
Parenteral hydration	9821 (53.0%)	8702 (47.0%)	18523	< 0.001
No parenteral hydration	63 822 (50.4%)	62 884 (49.6%)	126 706	
Total	73 643 (50.7%)	71 586 (49.3%)	145 229	
	Confusion	No confusion	Total	p value
Parenteral hydration	5114 (31.0%)	11 366 (69.0%)	16 480	< 0.001
No parenteral hydration	33 993 (28.6%)	84 958 (71.4%)	118 951	
Total	39 107 (28.9%)	96 324 (71.1%)	135 431	

Table 4

Table 5

# Correlation between three symptoms (breathlessness, respiratory secretions, and confusion) and age, divided into four categories

Age (years)	Breathlessness	No breathlessness	Total	p value
18-64	7381 (29.7%)	17 432 (70.3%)	24 813	<.001
65 - 74	11 282 (28.2%)	28 738 (71.8%)	40 020	
75-84	11 622 (24.9%)	35 144 (75.1%)	46 766	
85 and older	6117 (20.1%)	24 283 (79.9%)	30 400	
Total	36 402 (25.6%)	10 5597 (74.4%)	141 999	
	Respiratory secretions	No respiratory secretions	Total	p value
18-64	12 965 (51.3%)	12314(48.7%)	25 279	<.001
65 - 74	21 590 (52.7%)	19 350 (47.3%)	40 940	
75-84	24 311 (50.8%)	23 553 (49.2%)	47864	
85 and older	14777 (47.4%)	16 369 (52.6%)	31 146	
Total	73 643 (50.7%)	71 586 (49.3%)	145 229	
	Confusion	No confusion	Total	p value
18-64	7096 (29.7%)	16 768 (70.3%)	23 864	<.001
65 - 74	11 193 (29.2%)	27 116 (70.8%)	38 309	
75-84	12 971 (29.1%)	31 569 (70.9%)	44540	
85 and older	7847 (27.3%)	20 871 (72.7%)	28 718	
Total	39 107 (28.9%)	96 324 (71.1%)	135 431	

or whether this is due to a higher awareness among the hospital staff who register the symptom.

When comparing different diagnoses, persons with hematological malignancies were by far most likely to receive parenteral hydration during their last week of life. In hematology, hydration is widely used, for example, to counteract tumor lysis syndrome,<sup>21</sup> a feared

complication of hematological malignancies. In addition, these patients receive more aggressive care at end of life compared to patients with solid tumors,<sup>22</sup> probably affecting the use of parenteral hydration. The high frequency of 20% of patients receiving parenteral hydration in this data set could thus partly be explained by more aggressive care, although only patients where

Table 6	
Correlation between three symptoms (breathlessness, respiratory secretions, and confusion) ar	nd sex

Sex	Breathlessness	No breathlessness	Total	p value
Women	17 649 (25.3%)	52 171 (74.7%)	69 820	.002
Men	18 753 (26.0%)	53 426 (74.0%)	72 179	
Total	36 402 (25.6%)	105 597 (74.4%)	141 999	
	Respiratory secretions	No respiratory secretions	Total	p value
Women	34 424 (48.3%)	36 826 (51.7%)	$71\ 250$	<.001
Men	39 219 (53.0%)	34 760 (47.0%)	73 979	
Total	73 643 (50.7%)	71 586 (49.3%)	145 229	
	Confusion	No confusion	Total	p value
Women	17 562 (26.3%	49 089 (73.7%)	66 651	<.001
Men	21 545 (31.3%)	47 235 (68.7%)	68 780	
Total	39 107 (28.9%)	96 324 (71.1%)	135 431	

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aOR Lower 95% CI Upper 95% CI Breathlessness Parenteral hydration Yes 1.56 1.50 1.61	p value <.001 .41 <.001
Breathlessness Parenteral hydration Yes 1.56 1.50 1.61	<.001 .41 <.001
Parenteral hydration Yes 1.56 1.50 1.61	<.001 .41 <.001
	.41 <.001
No Ref.	.41 <.001
Sex Men 1.01 .99 1.04	<.001
Women Ref.	<.001
Age categories (years) 18–64 1.38 1.32 1.44	
65-74 1.31 1.26 1.36	<.001
75-84 1.17 1.13 1.22	<.001
85 and older Ref.	
Place of death Residential care homes 0.69 0.66 0.71	<.001
Hospitals 1.79 1.74 1.85	<.001
Specialized palliative care Ref.	
Respiratory secretions	
Parenteral hydration Yes 0.98 0.95 1.02	.28
No Ref.	
Sex Men 1.20 1.18 1.22	<.001
Women Ref.	
Age categories (years) 18–64 1.19 1.15 1.23	<.001
65-74 1.24 1.20 1.28	<.001
75-84 1.14 1.11 1.18	<.001
85 and older Ref.	
Place of death Residential care homes 1.06 1.03 1.09	<.001
Hospitals 1.26 1.23 1.30	<.001
Specialized palliative care Ref.	
Confusion	
Parenteral hydration Yes 1.00 .96 1.04	.94
No Ref.	
Sex Men 1.27 1.24 1.30	<.001
Women Ref.	
Age categories (years) 18-64 1.11 1.07 1.15	<.001
65-74 1.07 1.03 1.11	<.001
75-84 107 103 110	< .001
85 and older Ref.	
Place of death Residential care homes 0.97 0.94 100	.06
Hospitals 1.22 1.19 1.259	<.001
Specialized palliative care Ref.	

Table 7

Logistic regression model examining whether the presence of three symptoms (breathlessness, respiratory secretions, and confusion) was dependent on parenteral hydration, adjusted for sex, age, and place of death

death was expected were included. The second highest proportion was seen in ovarian cancer, with 16%, which is reasonable, considering the high risk of terminal bowel obstruction in this group of patients, implying that they cannot consume oral food or fluids. The lowest proportion by far (6%) was seen in persons with brain tumors. We do not know the rationale behind this low figure, but a possible reason is that patients with brain tumors at the end of life are known to be at risk of cerebral edema, which may result in a restrictive policy as regards artificial hydration. The low percentage in this study also differs from a previous study with 87% of patients with brain tumors receiving hydration in end of life,<sup>23</sup> possibly related to different treatment traditions.

The proportion of patients who received parenteral hydration decreased by about 30% from 2011 to 2021, which was seen in all three settings. We do not know the exact reason, but this change is seen in parallel with an increased awareness of palliative care on different levels. In 2013 the National Board of Health and

Welfare published national guidelines for palliative care,<sup>24</sup> in 2015 palliative medicine became a subspecialty in Sweden, and, in parallel, it was decided that all young physicians, regardless of their future specialty, need to have an obligatory course in palliative medicine for their specialist degree, and this has probably influenced their clinical decision-making. Moreover, there is a national care program in place, with detailed advice for daily clinical work.<sup>25</sup>

### Strengths and Limitations

The results of this study are based on a questionnaire with the same questions, regardless of place of care. Therefore, it is possible to compare different settings. As the data are relatively complete for persons who died of cancer, with approximately 80% coverage, data can be generalized to a high degree.

A drawback is that the central question about parenteral hydration is formulated in the following way: "Did the person receive parenteral fluids/nutrition or enteral-

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tube feeding during the last 24 hours of life?" That is, enteral-tube feeding was included in the question. However, based on a previous study, it is known that the usage of enteral-tube feeding in Sweden is very low. Orrevall et al. studied 1083 Swedish patients with cancer cared for within specialized palliative care and found only four receiving enteral-tube feeding, out of whom three had head-and-neck cancers.<sup>6</sup> Symptoms during the dying phase could be affected by different diseases or medications, such as dyspnea by lung cancer and delirium by brain metastasis or different medications. As data in the SPCR does not include all this information, adjustments for these factors were not possible.

Symptoms were assessed by health care professionals according to local routines and data were entered in the SRPC by health care professionals after the patients' death. This implies that there may be variability in the evaluation of symptom severity among evaluators. As only symptoms during the last week of life are included in the SRPC, most symptoms are at rest, i.e. patients are bedridden. It cannot be excluded that some symptoms are assessed during physical activity, but there is no information about this in the SRPC. It would be interesting to examine the correlation between parenteral hydration and fatigue or peripheral edema, but these symptoms are not registered in the SRPC.

### Conclusions

There is an association between parenteral hydration and increased breathlessness in patients with cancer. Provision of parenteral hydration to dying persons is more likely in men, in younger patients, and to persons with hematological malignancies or ovarian cancer, and it is by far most prevalent in acute care hospital settings. These data may be used as a basis for future advance care planning, as well for dialogue with relatives, who often request hydration to their immediately dying family member.

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Ethics approval: The working procedure and study design were examined by the Regional Ethical Review Board in Region Stockholm, EPN 2017/1141-31/4, who had no ethical objections to the study. The official national ethical review board gave permission to use the information about the deceased and health care, and required no informed consent from next of kin, in accordance with Swedish law.

### **Consent for Publication**

Not applicable.

### Availability of Data and Materials

The data set contains personally identifying information, such as personal identity numbers, and potentially identifying information, such as date of death, and therefore is subject to ethical and legal restrictions on public sharing. We cannot share the data set, which is on individual level, because it is not permitted according to the laws that apply in Sweden.

### Authors' Contributions

All authors together planned the study. LM performed the statistical analysis, and all authors together interpreted the results. CH, LM, and PS wrote the first manuscript draft, and SL made critical revisions. All authors approved the final version. All authors meet criteria for authorship.

### References

1. 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:Cd006273.

**2.** 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;6:365–370.

**3.** Raijmakers NJ, Fradsham S, van Zuylen L, et al. Variation in attitudes towards artificial hydration at the end of life: a systematic literature review. Curr Opin Support Palliat Care 2011;5:265–272.

**4.** Raijmakers NJH, van Zuylen L, Costantini M, et al. Artificial nutrition and hydration in the last week of life in cancer patients. A systematic literature review of practices and effects. Ann Oncol 2011;22:1478–1486.

**5.** Nordström M, Strang P. High Degree of Satisfaction With the Support Given by Multidisciplinary Palliative Home Care Teams in the County of Stockholm. J Palliat Care 2018;33:109–114.

**6.** Orrevall Y, Tishelman C, Permert J, Lundström S. A national observational study of the prevalence and use of enteral tube feeding, parenteral nutrition and intravenous glucose in cancer patients enrolled in specialized palliative care. Nutrients 2013;5:267–282.

**7.** Kingdon A, Spathis A, Brodrick R, et al. What is the impact of clinically assisted hydration in the last days of life? A systematic literature review and narrative synthesis. BMJ Support Palliat Care 2021;11:68–74.

**8.** Lokker ME, van der Heide A, Oldenmenger WH, van der Rijt CCD, van Zuylen L. Hydration and symptoms in the last days of life. BMJ Support Palliat Care 2021;11:335–343.

**9.** Davies AN, Waghorn M, Webber K, et al. A cluster randomised feasibility trial of clinically assisted hydration

in cancer patients in the last days of life. Palliat Med 2018;32:733-743.

**10.** Fritzson A, Tavelin B, Axelsson B. Association between parenteral fluids and symptoms in hospital end-of-life care: an observational study of 280 patients. BMJ Support Palliat Care 2015;5:160–168.

**11.** Morita T, Hyodo I, Yoshimi T, et al. Association between hydration volume and symptoms in terminally ill cancer patients with abdominal malignancies. Ann Oncol 2005;16:640–647.

**12.** Nakajima N, Hata Y, Kusumuto K. A clinical study on the influence of hydration volume on the signs of terminally ill cancer patients with abdominal malignancies. J Palliat Med 2013;16:185–189.

**13.** Krishna LK, Poulose JV, Goh C. Artificial Hydration at the end of Life in an Oncology Ward in Singapore. Indian J Palliat Care 2010;16:168–173.

14. Otani S, Yoshimoto M, Tokuyasu N, et al. PP088-MON THE ASSOCIATION BETWEEN ARTIFICIAL HYDRATION AND SYMPTOMS IN TERMINALLY ILL CANCER PATIENTS. Clinical Nutrition 2013;32:S155.

**15.** Martinsson L, Heedman PA, Lundström S, Axelsson B. Improved data validity in the Swedish Register of Palliative Care. PLoS One 2017;12:e0186804.

**16.** Bruera E, Sala R, Rico MA, et al. Effects of parenteral hydration in terminally ill cancer patients: a preliminary study. J Clin Oncol 2005;23:2366–2371.

**17.** Bruera E, Hui D, Dalal S, et al. Parenteral hydration in patients with advanced cancer: a multicenter, double-blind, placebo-controlled randomized trial. J Clin Oncol 2013;31:111–118.

**18.** Cerchietti L, Navigante A, Sauri A, Palazzo F. Hypodermoclysis for control of dehydration in terminal-stage cancer. Int J Palliat Nurs 2000;6:370–374.

**19.** Wildiers H, Menten J. Death rattle: prevalence, prevention and treatment. J Pain Symptom Manage 2002;23:310–317.

**20.** Gent MJ, Fradsham S, Whyte GM, Mayland CR. What influences attitudes towards clinically assisted hydration in the care of dying patients? A review of the literature. BMJ Support Palliat Care 2015;5:223–231.

**21.** Durani U, Hogan WJ. Emergencies in haematology: tumour lysis syndrome. Br J Haematol 2020;188:494–500.

**22.** Hui D, Didwaniya N, Vidal M, et al. Quality of end-of-life care in patients with hematologic malignancies: a retrospective cohort study. Cancer 2014;120:1572–1578.

**23.** Pompili A, Telera S, Villani V, Pace A. Home palliative care and end of life issues in glioblastoma multiforme: results and comments from a homogeneous cohort of patients. Neurosurg Focus 2014;37:E5.

24. The National Board of Helath and welfare (Socialstyrelsen). National knowledge support for good palliative care at the end of life; guidance, recommendations and indicators (Nationellt kunskapsstöd för god palliativ vård i livets slutskede; vägledning, rekommendationer och indikatorer). 2013. Available from: https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/kunskapsstod/ 2013-6-4.pdf. Accessed November 06, 2023.

25. Regionala cancercentrum i samverkan. The Swedish National Palliative Care Guidelines (Nationellt vårdprogram Palliativ vård). 2023. Available from: https://kunskaps-banken.cancercentrum.se/diagnoser/palliativ-vard/vardprogram/. Accessed November 06, 2023.