Nutrition In Palliative Care

NUTRITION AND HYDRATION IN PALLIATIVE CARE

F. Bozzetti (IT)
Nutrition and hydration in palliative care

Federico Bozzetti
NUTRITIONAL INTERVENTION IN THE ONCOLOGIC PRACTICE

CANCER PATIENTS

On oncologic therapy
No more curable
Imminently dying
Disease trajectory of a cancer patient

Life expectancy:

<table>
<thead>
<tr>
<th>YEARS</th>
<th>MONTHS</th>
<th>WEEKS</th>
<th>DAYS</th>
</tr>
</thead>
</table>

Transition of care (place, levels and goals of care)

End of life
Terminally Ill
Terminal care period
Actively dying
Teunissen SC, Wesker W, Kruitwagen C, de Haes HC, Voest EE, de Graeff A.  
**Symptom prevalence in patients with incurable cancer; a systematic review.**  
J Pain Symptom Manage. 2007 Jul;34(1):94-104

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number of Studies</th>
<th>Number of Patients</th>
<th>Pooled Prevalence (%)</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>40</td>
<td>25,074</td>
<td>74</td>
<td>(63; 83)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>17</td>
<td>6,727</td>
<td>74</td>
<td>(63; 83)</td>
</tr>
<tr>
<td>Pain</td>
<td>37</td>
<td>21,917</td>
<td>71</td>
<td>(67; 74)</td>
</tr>
<tr>
<td>Lack of energy</td>
<td>6</td>
<td>1,827</td>
<td>69</td>
<td>(57; 79)</td>
</tr>
<tr>
<td>Weakness</td>
<td>18</td>
<td>14,910</td>
<td>60</td>
<td>(51; 68)</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>37</td>
<td>23,112</td>
<td>53</td>
<td>(48; 59)</td>
</tr>
<tr>
<td>Nervousness</td>
<td>5</td>
<td>727</td>
<td>48</td>
<td>(39; 57)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>17</td>
<td>13,167</td>
<td>46</td>
<td>(34; 59)</td>
</tr>
</tbody>
</table>
SIGNS OF IMPENDING DEATH°

- Profound progressive weakness
- Bed-bound state
- Sleeping much of the time
- Indifference to food and fluid
- Difficulty swallowing
- Disorientation to time
- Low blood pressure (not related to hypovolemia) with rising weak pulse
- Urinary incontinence or retention caused by weakness
- Loss of ability to close eyes
- Oliguria
- Hallucinations of previously deceased important individuals
- References to going home or similar themes
- Changes in respiratory rate and pattern (Cheyne-Stokes breathing, apneas)
- Noisy breathing, airway secretions
- Motting and cooling of the skin due to vasomor instability with venous pooling, particularly tibial
- Mental status changes (delirium, restlessness, agitation, coma)

° Bicanovsky 2008
Bukki et al.
Decision making at the end of life--cancer patients' and their caregivers' views on artificial nutrition and hydration. Support Care Cancer. 2014 Dec;22(12):3287-99

65 non-imminently dying patients

Responses to items PQ 1 (black), RQ 1 (grey), and RQ 2 (white columns). The response option “AN only, no AH” was not chosen by any participant.

\( \chi^2 \)-Test, \( p < 0.05 \) after adjustment for multiple testing (Bonferroni)
LIMITATIONS OF THE STUDY

- 31 patients were randomised out of 116 planned because patients & families were repulsed by the idea of withdrawing/withholding the nutritional support.

- Patients were too ill (ECOG 3-4, massive M+, anemia, lymphopenia, hypoalbuminemia)

- In conclusion: very poor design of the study and gross underestimation of ethical problems
From Lunney et al. JAMA 2003 (data on 897 patients)
## MEAN SURVIVAL OF (HYPO)APHAGIC OBSTRUCTED CANCER PATIENTS WITHOUT NUTRITIONAL SUPPORT

<table>
<thead>
<tr>
<th>TIME</th>
<th>TREATMENT</th>
</tr>
</thead>
</table>

* median 25 d
Modified from Lunney et al. JAMA 2003
The prognosis of incurable cachectic cancer patients on home parenteral nutrition: a multi-centre observational study with prospective follow-up of 414 patients


Multivariate analysis of factors associated with 3- and 6-month survival

- 3 months:
  Glasgow (P=0.00)
  Karnofsky (P<0.00)

- 6 months:
  Glasgow (P=0.00)
  Karnofsky (P<0.01)
  Tumor spread (P=0.01)

Figure 1. Overall survival curve of the entire series.

Median survival: 3 mos
3-mo survival: 50%
6-mo survival: 23%
Development and validation of a nomogram to predict survival in incurable cachectic cancer patients on home parenteral nutrition

F. Bozzetti⁴, P. Cotogni⁵, S. Lo Vullo⁶, L. Pironi⁷, D. Giardiello⁸ & L. Mariani⁹ *

Supplementary Figure S1. Kaplan-Meier overall survival curves for training and testing samples.

Figure 1. Cox modeling based nomogram for predicting 3-, 6-month and median OS. Instructions on how to use the nomogram for building survival estimates are supplied at the bottom of the Results section.
### COMPARISON OF SURVIVAL OF TWO HOMOGENEOUS GROUPS OF PATIENTS RECEIVING OR NOT HPN AFTER BEING ACCEPTED IN THE HPN PROGRAMME

<table>
<thead>
<tr>
<th></th>
<th>HPN+</th>
<th>HPN-</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N patients</td>
<td>89</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Male/female</td>
<td>47/42</td>
<td>21/15</td>
<td>P=0.57</td>
</tr>
<tr>
<td>Age, years, median</td>
<td>68 (62;74)</td>
<td>68 (63;74)</td>
<td>P=0.6</td>
</tr>
<tr>
<td>Stage, No. (%)</td>
<td></td>
<td>P=0.79</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>3 (3%)</td>
<td>1 (3%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>13 (15%)</td>
<td>7 (19%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>73 (82%)</td>
<td>28 (78%)</td>
<td></td>
</tr>
<tr>
<td>Karnofsky PS, median (IQR)</td>
<td>60 (50;70)</td>
<td>60 (50;70)</td>
<td>P=0.57</td>
</tr>
<tr>
<td>ECOG, No. (%)</td>
<td></td>
<td>P=0.49</td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>33 (37%)</td>
<td>11 (31%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>56 (63%)</td>
<td>25 (69%)</td>
<td></td>
</tr>
<tr>
<td>BMI, median (IQR)</td>
<td>21 (19;24)</td>
<td>21 (18;24)</td>
<td>P=0.94</td>
</tr>
<tr>
<td>Weight loss, %</td>
<td>10.9 (7.0;16.7)</td>
<td>11.3 (6.5;16.0)</td>
<td>P=0.99</td>
</tr>
<tr>
<td>C-reactive protein, mg l(^{-1})</td>
<td>17.7 (9.3;47.0)</td>
<td>14.6 (7.2;69.8)</td>
<td>P=0.91</td>
</tr>
<tr>
<td>Albumin, g l(^{-1})</td>
<td>3.4 (3.1;3.6)</td>
<td>3.3 (2.9;3.6)</td>
<td>P=0.53</td>
</tr>
<tr>
<td>mGPS, No. (%)</td>
<td></td>
<td>P=0.73</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>26 (29%)</td>
<td>13 (36%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>21 (24%)</td>
<td>7 (19%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>42 (47%)</td>
<td>16 (44%)</td>
<td></td>
</tr>
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</table>
COMPARISON OF SURVIVAL OF TWO HOMOGENEOUS* GROUPS OF PATIENTS RECEIVING OR NOT HPN AFTER BEING ACCEPTED IN THE HPN PROGRAMME

CRITERIA FOR ENTERING A PROGRAMME OF HPN
(125 patients: 89 finally received HPN and 34 did not)

- failure to meet nutrition requirements by oral or enteral route
- life expectancy > 2 months
- Karnofsky Performance Status ≥ 50
- satisfying control of pain/relevant symptoms
- absence of severe organ dysfunction

REASONS FOR REFUSING HPN AFTER ACCEPTANCE IN THE PROGRAMME (34 patients)

- 8 refused HPN
- 26 admitted to hospice

*No difference in demographic, clinical, oncologic and prognostic variables

Median OS (mos): HPN 4.2 vs noHPN 1.5; p= 0.001
Quality of life and length of survival in advanced cancer patients on home parenteral nutrition

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*Italian Society for Parenteral and Enteral Nutrition, Milan, Italy, and †Unit of Medical Statistics and Biometry, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan (Correspondence to: FB, Istituto Nazionale per lo Studio e la Cura dei Tumori, Via Venezian, 1, 20133 Milano, Italy)

Abstract—Background: The use of home parenteral nutrition (HPN) in patients with advanced cancer is controversial because survival is usually short and there are no data regarding the quality of life (QoL).

Methods: Sixty-nine advanced cancer patients enrolled in a program of HPN in six different Italian centers were prospectively studied as regards nutritional status (body weight, serum albumin, serum transferrin and total lymphocyte count), length of survival and QoL through the Rotterdam Symptom Checklist questionnaire. These variables were collected at the start of HPN and then at monthly intervals. All these patients were severely malnourished, almost aphagic and beyond any possibility of cure.

Results: Nutritional indices maintained stable until death. Median survival was 4 months (range 1–14) and about one-third of patients survived more than 7 months. QoL parameters remained stable till 2–3 months before death.

Conclusions: HPN may benefit a limited percentage of patients who may survive longer than the time allowed by a condition of starvation and depletion. Provided that these patients survive longer than 3 months, there is some evidence that QoL remains stable for some months and acceptable for the patients. © 2002 Elsevier Science Ltd. All rights reserved.
Cancer Medicine

ORIGINAL RESEARCH

Longitudinal study of quality of life in advanced cancer patients on home parenteral nutrition

Paolo Cotogni1,2, Luca De Carli3, Roberto Passera4, Maria Luisa Amerio5, Elena Agnello3, Maurizio Fadda3, Marta Ossola3, Taira Monge3, Antonella De Francesco3 & Federico Bozzetti5

Table 3. Determinants for trend over time for the EORTC QLQ-C30 scales.

<table>
<thead>
<tr>
<th>Determinant</th>
<th>Global QoL</th>
<th>PF</th>
<th>FF</th>
<th>EF</th>
<th>CF</th>
<th>SF</th>
<th>AP</th>
<th>FA</th>
<th>NV</th>
<th>RI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trend over time</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.007</td>
<td>&lt;0.001</td>
<td>0.169</td>
<td>0.202</td>
<td>0.004</td>
<td>0.022</td>
<td>0.266</td>
<td>0.455</td>
</tr>
<tr>
<td>Gender</td>
<td>0.879</td>
<td>0.913</td>
<td>0.993</td>
<td>0.452</td>
<td>0.871</td>
<td>0.617</td>
<td>0.682</td>
<td>0.488</td>
<td>0.066</td>
<td>0.447</td>
</tr>
<tr>
<td>Age</td>
<td>0.479</td>
<td>0.863</td>
<td>0.264</td>
<td>0.931</td>
<td>0.153</td>
<td>0.143</td>
<td>0.202</td>
<td>0.003</td>
<td>0.549</td>
<td>0.002</td>
</tr>
<tr>
<td>Weight loss</td>
<td>0.247</td>
<td>0.106</td>
<td>0.289</td>
<td>0.300</td>
<td>0.968</td>
<td>0.746</td>
<td>0.003</td>
<td>0.936</td>
<td>0.257</td>
<td>0.206</td>
</tr>
<tr>
<td>Karnovsky PS</td>
<td>0.055</td>
<td>0.086</td>
<td>0.120</td>
<td>0.106</td>
<td>0.217</td>
<td>0.677</td>
<td>0.023</td>
<td>0.711</td>
<td>0.712</td>
<td>0.266</td>
</tr>
<tr>
<td>Tumour site</td>
<td>0.419</td>
<td>0.045</td>
<td>0.521</td>
<td>0.298</td>
<td>0.524</td>
<td>0.385</td>
<td>0.161</td>
<td>0.067</td>
<td>0.890</td>
<td>0.113</td>
</tr>
<tr>
<td>Stage</td>
<td>0.712</td>
<td>0.167</td>
<td>0.341</td>
<td>0.648</td>
<td>0.618</td>
<td>0.512</td>
<td>0.877</td>
<td>0.439</td>
<td>0.916</td>
<td>0.520</td>
</tr>
<tr>
<td>Treatment1</td>
<td>0.252</td>
<td>&lt;0.001</td>
<td>0.014</td>
<td>0.040</td>
<td>0.049</td>
<td>0.007</td>
<td>0.162</td>
<td>0.680</td>
<td>0.024</td>
<td>0.284</td>
</tr>
<tr>
<td>Metastasis</td>
<td>0.694</td>
<td>0.985</td>
<td>0.009</td>
<td>0.811</td>
<td>0.264</td>
<td>0.728</td>
<td>0.281</td>
<td>0.098</td>
<td>0.536</td>
<td>0.711</td>
</tr>
<tr>
<td>PG-SGA</td>
<td>0.279</td>
<td>0.739</td>
<td>0.909</td>
<td>0.710</td>
<td>0.367</td>
<td>0.613</td>
<td>0.192</td>
<td>0.009</td>
<td>0.228</td>
<td>0.363</td>
</tr>
</tbody>
</table>

PF: physical functioning, RF: role functioning, AP: appetite loss
...about water restriction in the imminently dying...

**Pros**
- Has analgesic effect
- ↓ accumulation of secretions
- ↓ pulmonary congestion

**Cons**
- ↑ mental confusion
- ↑ renal failure
- ↑ opioid toxicity
- ↑ hypercalcemia
Clin Nutr. 2016 Dec;35(6):.

Bozzetti F

**Fig 2.** Overall survival by hydration status. The median survival was 21 days (range, 13 to 29 days) for the hydration group (gold) and 15 days (range, 12 to 18 days) for the placebo group (blue), with a \( P \) value of .83 (log-rank test).
**PURPOSE:**

The vast majority of patients with cancer at the end of life receive parenteral hydration in hospitals and no hydration in hospice, with limited evidence supporting either practice. In this randomized controlled trial, we determined the effect of hydration on symptoms associated with dehydration, quality of life, and survival in patients with advanced cancer.

**PATIENTS AND METHODS:**

We randomly assigned 129 patients with cancer from six hospices to receive parenteral hydration (normal saline 1 L per day) or placebo (normal saline 100 mL per day) daily over 4 hours. The primary outcome was change in the sum of four dehydration symptoms (fatigue, myoclonus, sedation and hallucinations, 0 = best and 40 = worst possible) between day 4 and baseline. Secondary outcomes included Edmonton Symptom Assessment Scale (ESAS), Memorial Delirium Assessment Scale (MDAS), Nursing Delirium Screening Scale (NuDESC), Unified Myoclonus Rating Scale (UMRS), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Dehydration Assessment Scale, creatinine, urea, and overall survival. Intention-to-treat analysis was conducted to examine the change by day 4 ± 2 and day 7 ± 2 between groups.

**RESULTS:**

The hydration (n = 63) and placebo (n = 66) groups had similar baseline characteristics. We found no significant differences between the two groups for change in the sum of four dehydration symptoms (-3.3 v -2.8, P = .77), ESAS (all nonsignificant), MDAS (1 v 3.5, P = .084), NuDESC (0 v 0, P = .13), and UMRS (0 v 0, P = .54) by day 4. Results for day 7, including FACIT-F, were similar. Overall survival did not differ between the two groups (median, 21 v 15 days, P = .83).

**CONCLUSION:**

Hydration at 1 L per day did not improve symptoms, quality of life, or survival compared with placebo.
Some limitations of Bruera study

• Fluid administration (1L) not tailored to BW (which is not reported in the paper): for instance, 1L saline may be insufficient for a ≥ 70 kg patient (14 ml/kg/d)

• Na/Cl ratio 1 to 1 of normal saline is not physiologic (risk of hyperchloremic acidosis)
  (Hartmann or Ringer solution likely preferable)

• NICE GL suggest 25-50 g glucose
CONCLUSION on PALLIATIVE NUTRITION and HYDRATION

• In (hypo)aphagic patients with a life-expectancy longer than 2 months, HPN is a reasonable proposal if QoL is acceptable

• In the imminently dying patient, there is no demonstration of either benefit or harm with hydration

• Anyway, mode of hydration should be more «physiologic»:
  - water: 20-25 mL/Kg, give more Na than Cl or K, add 50 g glucose

• In doubtful cases (imminently-dying yes or no), a trial-and-error attempt with PN should be considered
...knowledge is the enemy of disease...

Federico Bozzetti gave independent lectures at scientific and educational events also sponsored by nutritional industries. There is no conflict of interest.