# Non-nutritional calories:

## Are they relevant in the critically ill?

**Arthur R.H. van Zanten, MD PhD**
**Internist-intensivist**
**Gelderse Vallei Hospital**
**Ede, The Netherlands**
**E-mail: zantena@zgv.nl**
**www.criticalcarenutrition.nl**

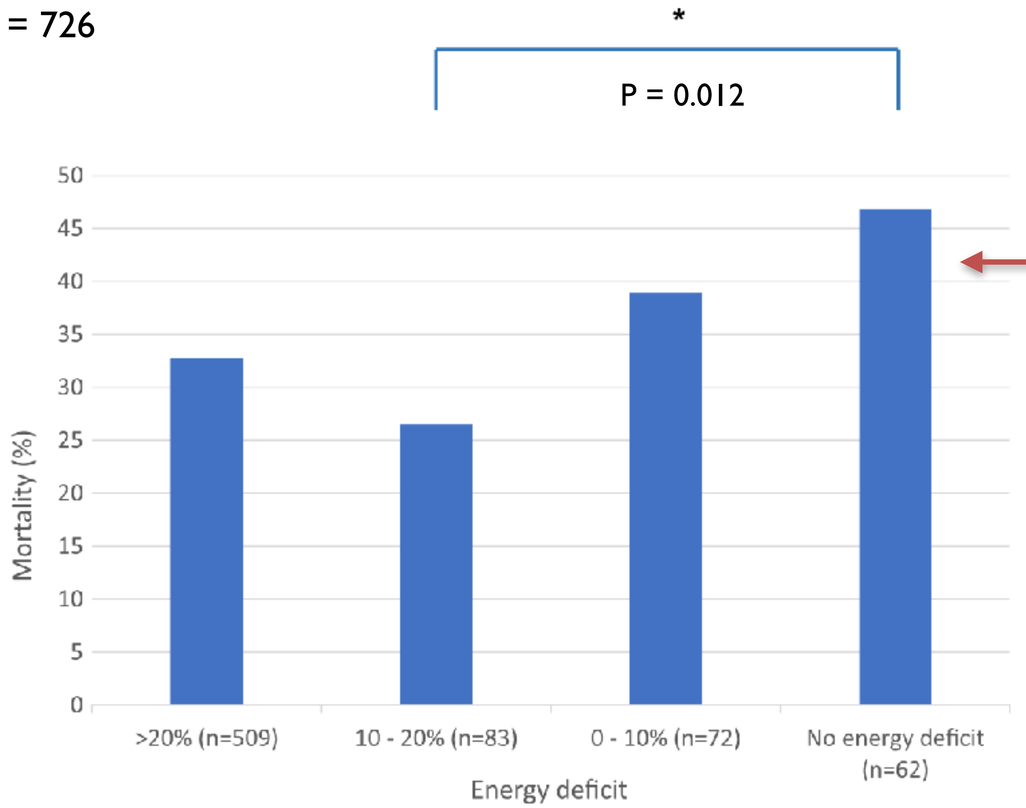
# Consequences of overfeeding

- Azotemia
- Fat-overload syndrome
- Hepatic steatosis
- Hypercapnia
- Hyperglycemia
- Hypertonic dehydration
- Hypertriglyceridemia
- Metabolic acidosis
- Refeeding syndrome

# Hospital mortality and cumulative energy deficit

n = 726

during first 4 days of ICU stay for non-septic patients




Increased mortality due to overfeeding

Reference is the measured resting energy expenditure of the patient.

Weijs P. Crit Care 2014; 18:201

# Energy overfeeding is harmful

| N=843 | OR | 95% CI | P-value |
|---|---|---|---|
| Daily protein intake groups [a] | 0.85 | 0.73-0.99 | 0.047 |
| Energy overfeeding (y/n) [b] | 1.62 | 1.07-2.44 | 0.022 |
| Sepsis (y/n) | 1.77 | 1.18-2.65 | 0.005 |
| APACHE-II score | 1.04 | 1.02-1.05 | <0.001 |

[a] Protein intake groups were <0.8, 0.8 - <1.0, 1.0 - <1.2, and ≥1.2 g/kg.
[b] day 4 energy overfeeding was defined as an energy intake of more than 110% of measured energy expenditure

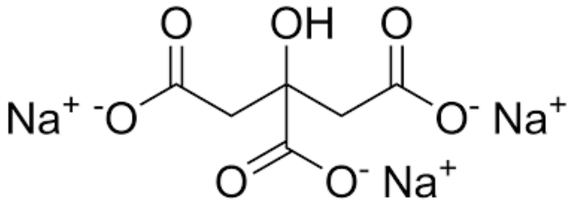
Weijs P. Crit Care 2014; 18:201

# Non-nutritional Calories

- Glucose


- Propofol


- Trisodium Citrate




Bousie E, Van Zanten AR. Eur J Clin Nutr. 2016;70(12):1443-50

# Glucose 5%

- 5% glucose solution means the solution contains 5g/100ml of solution
- Glucose provides energy: 4 kcal/gram,
- So, a 5% glucose solution of 1 liter of glucose 5% provides 200 kcal.

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# propofol

- The currently available preparation is 1-2% propofol, 10% soybean oil, and 1.2% purified egg phosholipid as an emulsifier, with 2.25% glycerol as a tonocity-adjusting agent, and sodium hydroxide to adjust the pH.

- 1.1 kcal /mL.

- Example: 15 ml/hour over 24 hours = 15*1.1*24 = 396 kcal


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# Citrate energy provision during CVVH

- Depends on concentration
- Depends on blood flow/infusion rate
- Depends of filtration fraction into the ultrafiltrate over time
- Depends on filter

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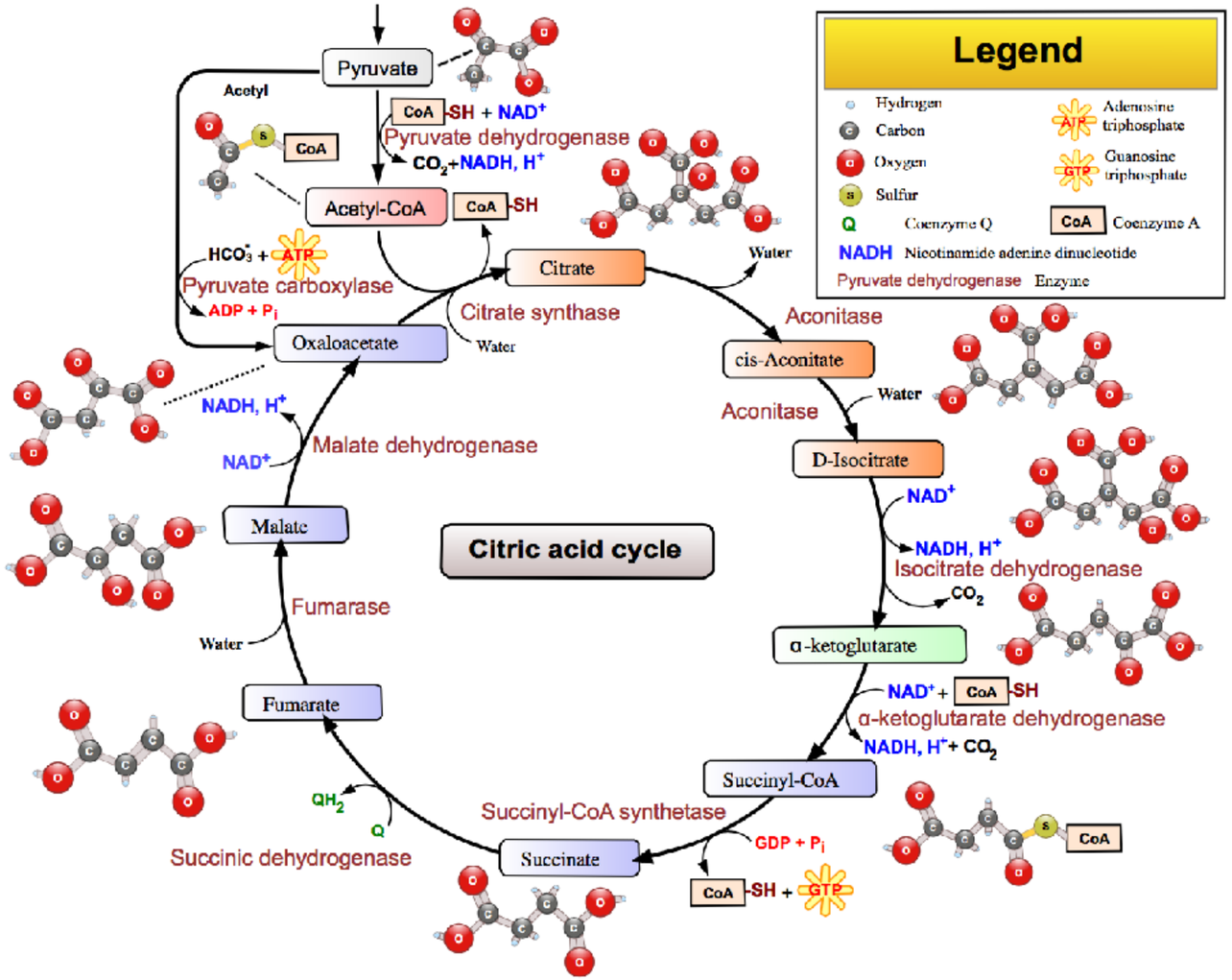
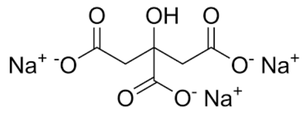
# Citrate energy provision in the Citric Acid Cycle




**Citrate ($C_6H_5O_7$) is a source of energy, conferring 3 kcal/g (0.59 kcal/mmol) is rapidly metabolized in the citric acid (Krebs) cycle - especially in the liver, muscle and renal cortex**

Food energy - methods of analysis and conversion factors. FAO Food and Nutrition Paper 77 [ftp://ftp.fao.org/docrep/fao/006/y5022e/y5022e00.pdf
Citric acid [http://www.ecama.org/level_2/SDS/1CAM22April1998.doc]

# Non-nutritional Calories

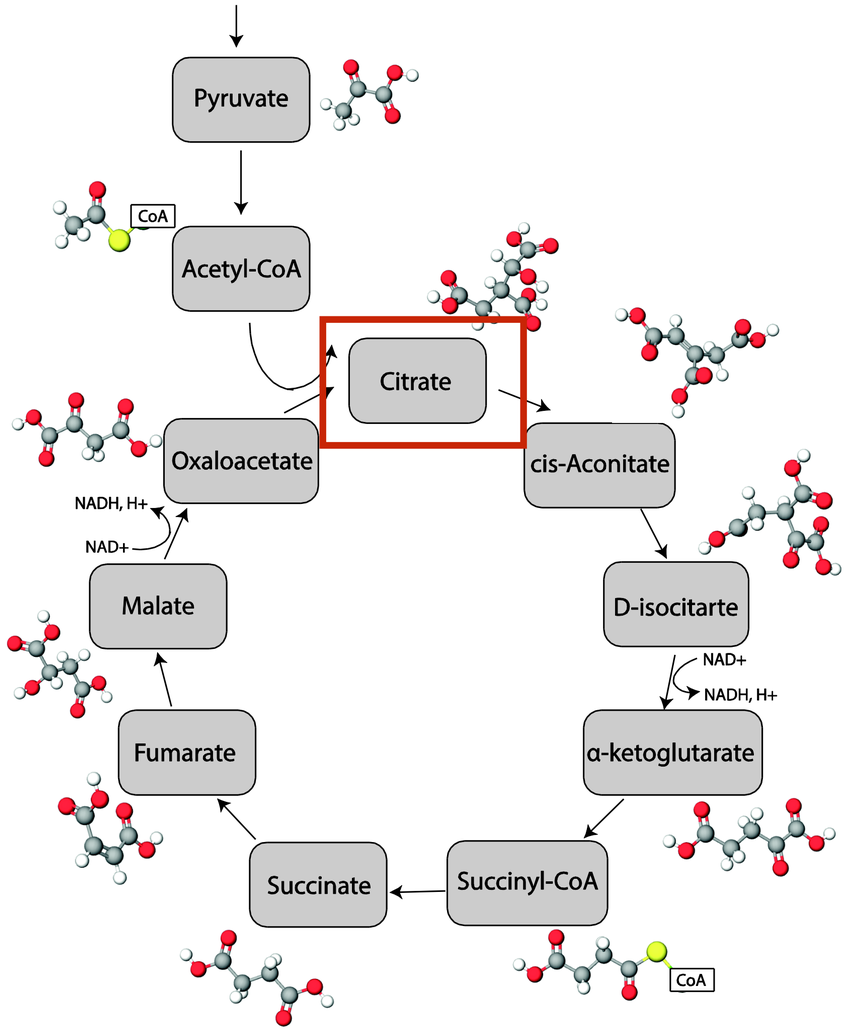



**Trisodium citrate ($Na_3C_6H_5O_7$), contains 0.59 kcal/mmol (= 3 kcal/g).**

**Actual caloric load due to citrate dialysis depends on a number of factors such as:**

Trisodium Citrate

- **concentration of trisodium citrate used,**
- **the infusion rate,**
- **the blood flow in the filter,**
- **the filtration fraction into the ultrafiltrate over time (Sieving coefficient) and the**
- **filter characteristics.**

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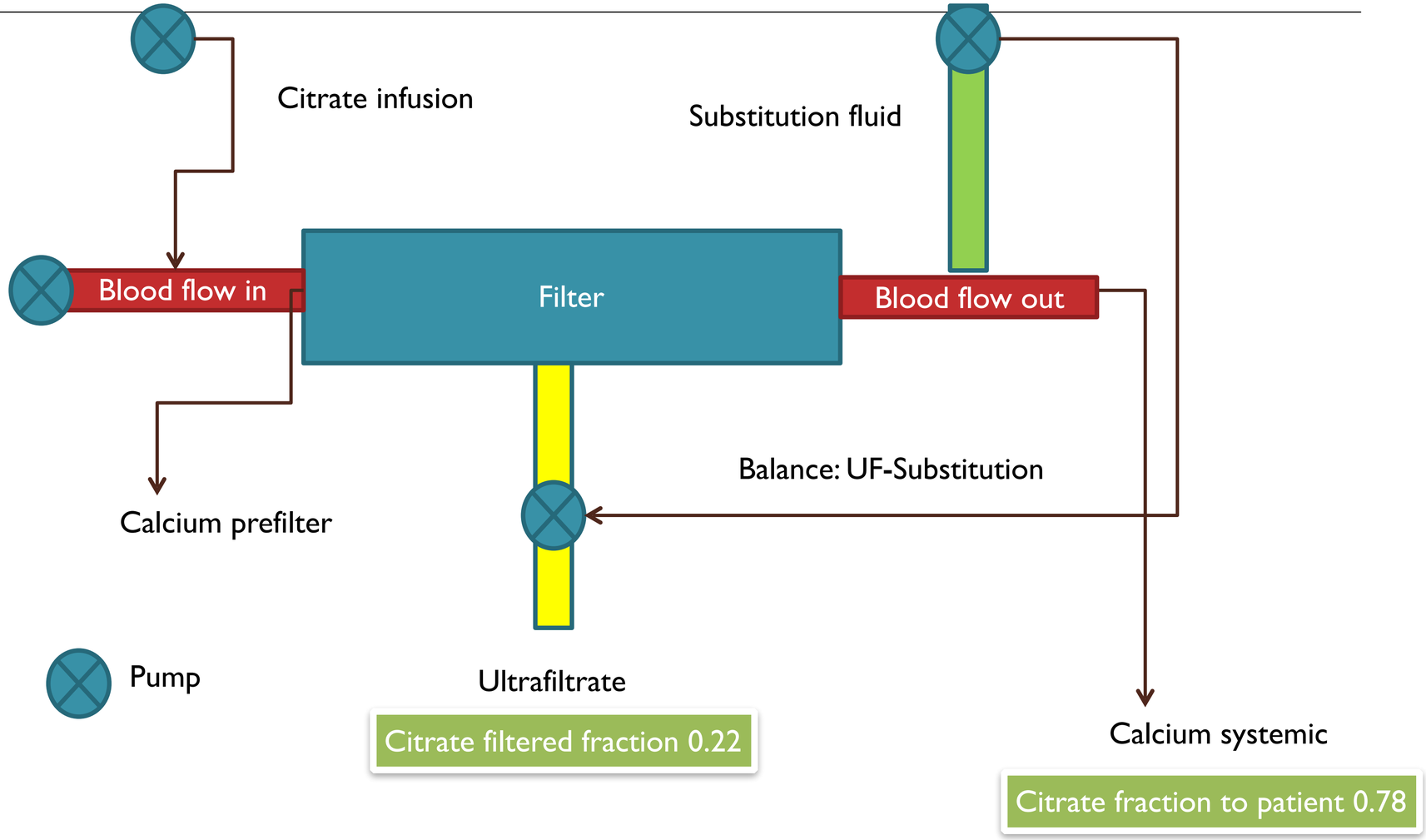
# Citrate during CVVH

| | |
|---|---|
| Citrate concentration TCA (mmol/L) | 500 |
| Caloric value citrate (kJ/mmol) | 2.48 |
| Caloric value citrate (kcal/mmol) | 0.59 |

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# Citrate Energy infusion calculations

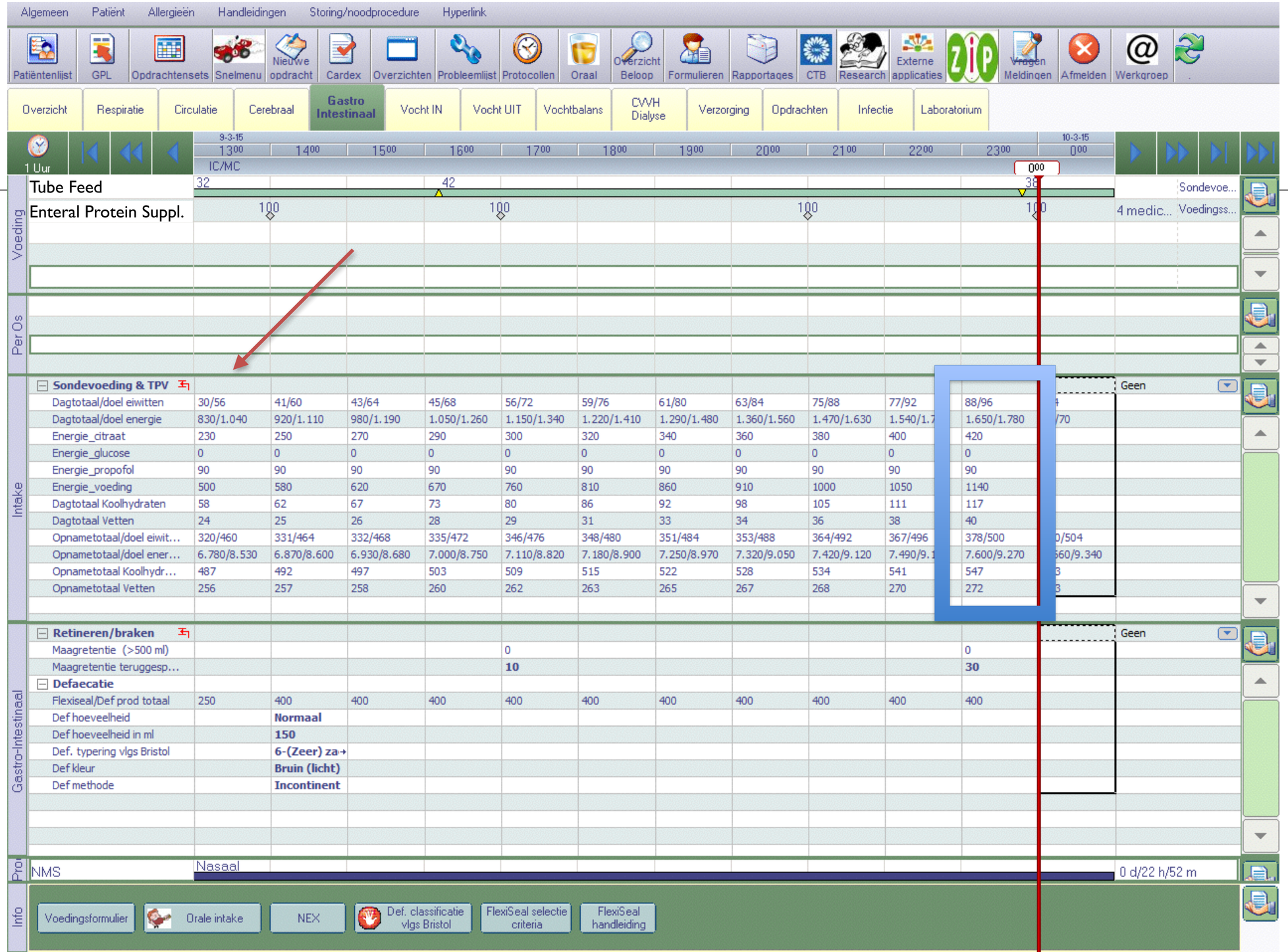
- $E_c = f_c * Q_c * 7{,}080$
- $E_c$: Energy from citrate per 24 hours (kcal)
- $f_c$: fraction of citrate not filtered (normally 0.78)
- $Q_c$: citrate infusion rate (ml/hour)
- $f_c$ is : $1-(Q_u/(Q_b*60))$.
- $Q_s$: Ultrafiltrate rate (ml/hour)
- $Q_b$: Blood flow (ml/min)
- $E_c$ in kJ per 24 hours : $E_c = f_c * Q_c * 29{,}76$

Bousie E, Van Zanten AR. Eur J Clin Nutr. 2016;70(12):1443-50

# Non-nutritional calories

- Overall (n = 843) mean energy intake at day 4 was 1710 ± 699 kcal corresponding to 95% of measured EE.
- Energy from sources other than nutrition (glucose and propofol) comprised **median 132 kcal/day**
- 7.9% of the total energy intake; 10.1% in the non-overfed vs. 6.4% in the overfed cohort ($p < 0.001$).

Weijs P. Crit Care 2014; 18:201




| Sondevoeding & TPV | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dagtotaal/doel eiwitten | 30/56 | 41/60 | 43/64 | 45/68 | 56/72 | 59/76 | 61/80 | 63/84 | 75/88 | 77/92 | 88/96 | |
| Dagtotaal/doel energie | 830/1.040 | 920/1.110 | 980/1.190 | 1.050/1.260 | 1.150/1.340 | 1.220/1.410 | 1.290/1.480 | 1.360/1.560 | 1.470/1.630 | 1.540/1.7 | 1.650/1.780 | /70 |
| Energie_citraat | 230 | 250 | 270 | 290 | 300 | 320 | 340 | 360 | 380 | 400 | 420 | |
| Energie_glucose | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Energie_propofol | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 | |
| Energie_voeding | 500 | 580 | 620 | 670 | 760 | 810 | 860 | 910 | 1000 | 1050 | 1140 | |
| Dagtotaal Koolhydraten | 58 | 62 | 67 | 73 | 80 | 86 | 92 | 98 | 105 | 111 | 117 | |
| Dagtotaal Vetten | 24 | 25 | 26 | 28 | 29 | 31 | 33 | 34 | 36 | 38 | 40 | |
| Opnametotaal/doel eiwit... | 320/460 | 331/464 | 332/468 | 335/472 | 346/476 | 348/480 | 351/484 | 353/488 | 364/492 | 367/496 | 378/500 | 0/504 |
| Opnametotaal/doel ener... | 6.780/8.530 | 6.870/8.600 | 6.930/8.680 | 7.000/8.750 | 7.110/8.820 | 7.180/8.900 | 7.250/8.970 | 7.320/9.050 | 7.420/9.120 | 7.490/9.1 | 7.600/9.270 | 660/9.340 |
| Opnametotaal Koolhydr... | 487 | 492 | 497 | 503 | 509 | 515 | 522 | 528 | 534 | 541 | 547 | 3 |
| Opnametotaal Vetten | 256 | 257 | 258 | 260 | 262 | 263 | 265 | 267 | 268 | 270 | 272 | 3 |

| Retineren/braken | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Maagretentie (>500 ml) | | | | | 0 | | | | | | 0 | |
| Maagretentie teruggesp... | | | | | **10** | | | | | | **30** | |
| **Defaecatie** | | | | | | | | | | | | |
| Flexiseal/Def prod totaal | 250 | 400 | 400 | 400 | 400 | 400 | 400 | 400 | 400 | 400 | 400 | |
| Def hoeveelheid | | **Normaal** | | | | | | | | | | |
| Def hoeveelheid in ml | | **150** | | | | | | | | | | |
| Def. typering vlgs Bristol | | **6-(Zeer) za→** | | | | | | | | | | |
| Def kleur | | **Bruin (licht)** | | | | | | | | | | |
| Def methode | | **Incontinent** | | | | | | | | | | |

# Snapshot ICU PDMS Gelderse Vallei Hospital Ede The Netherlands

Actual intake

Cumulative target

Intake

| Sondevoeding & TPV | 13:00 h |
|---|---|
| Dagtotaal/doel eiwitten | 30/56 |
| Dagtotaal/doel energie | 830/1.040 |
| Energie_citraat | 230 |
| Energie_glucose | 0 |
| Energie_propofol | 90 |
| Energie_voeding | 500 |
| Dagtotaal Koolhydraten | 58 |
| Dagtotaal Vetten | 24 |
| Opnametotaal/doel eiwit… | 320/460 |
| Opnametotaal/doel ener… | 6.780/8.530 |
| Opnametotaal Koolhydr… | 487 |
| Opnametotaal Vetten | 256 |

Daily parameters

Cumulative ICU stay

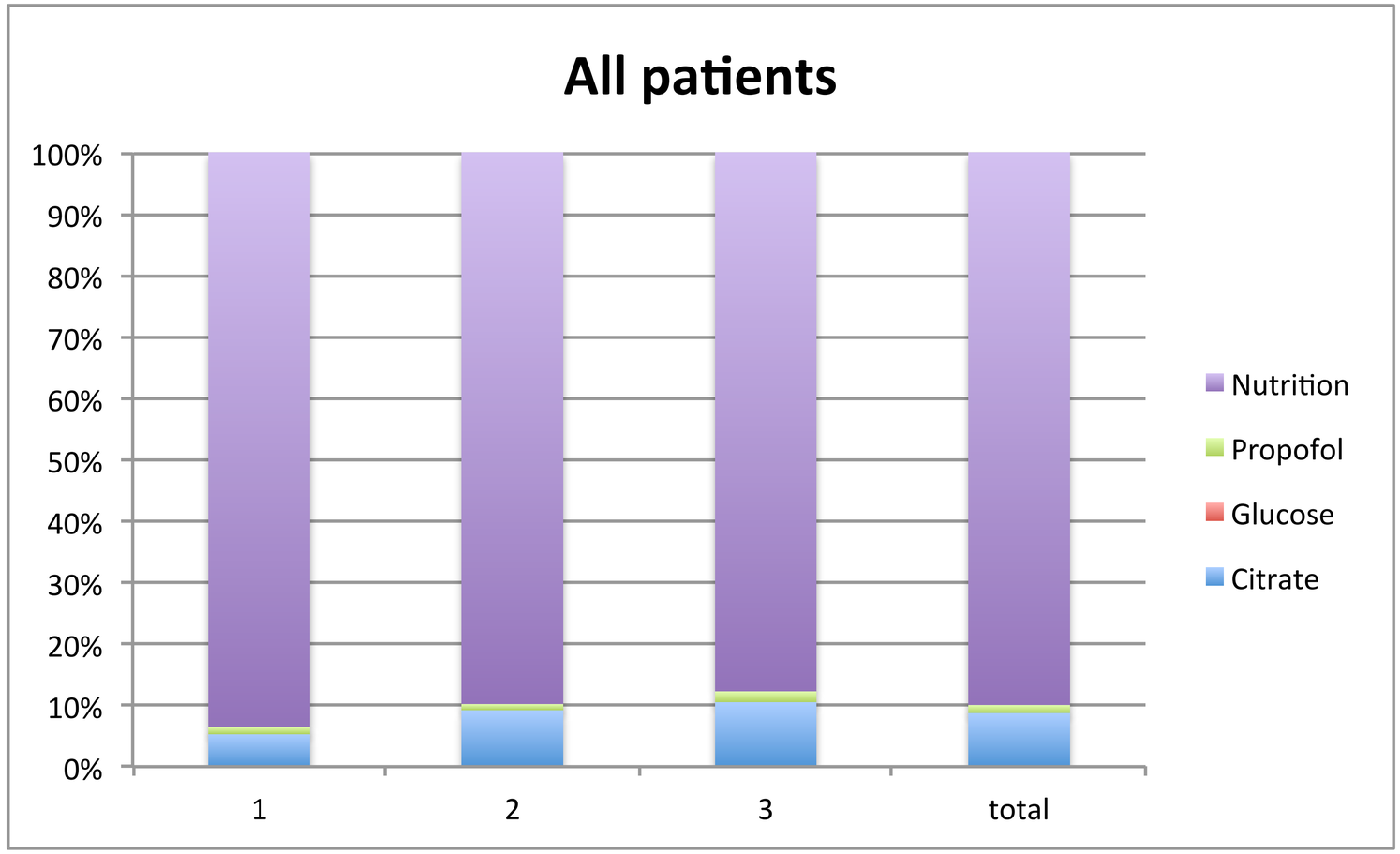
# Patient characteristics

| | All patients | | Citrate | | Propofol | | Non-nutrional | |
|---|---|---|---|---|---|---|---|---|
| | N=26 | | N=9 | | N=5 | | N=13 | |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| Gender male, % | 58% | | 78% | | 60% | | 46% | |
| Age, y | 66,4 | 13,7 | 66,9 | 12,1 | 56,4 | 18,3 | 69,3 | 11,6 |
| Body mass index, kg/m$^2$ | 27,0 | 6,7 | 28,4 | 7,5 | 27,2 | 7,0 | 26,5 | 6,5 |
| Admission type medical, % | 73% | | 67% | | 80% | | 77% | |
| Sepsis yes, % | 58% | | 56% | | 60% | | 62% | |
| APACHE II score | 25,3 | 7,4 | 27,4 | 9,6 | 22,4 | 6,8 | 25,3 | 5,6 |
| SOFA score | 7,7 | 3,1 | 9,3 | 2,8 | 6,4 | 4,9 | 7,4 | 2,3 |
| Hospital mortality % | 35% | | 33% | | 20% | | 38% | |

Bousie E, Van Zanten AR. Eur J Clin Nutr. 2016;70(12):1443-50

# Caloric intake all patients

## 10% total non-nutritional calories intake

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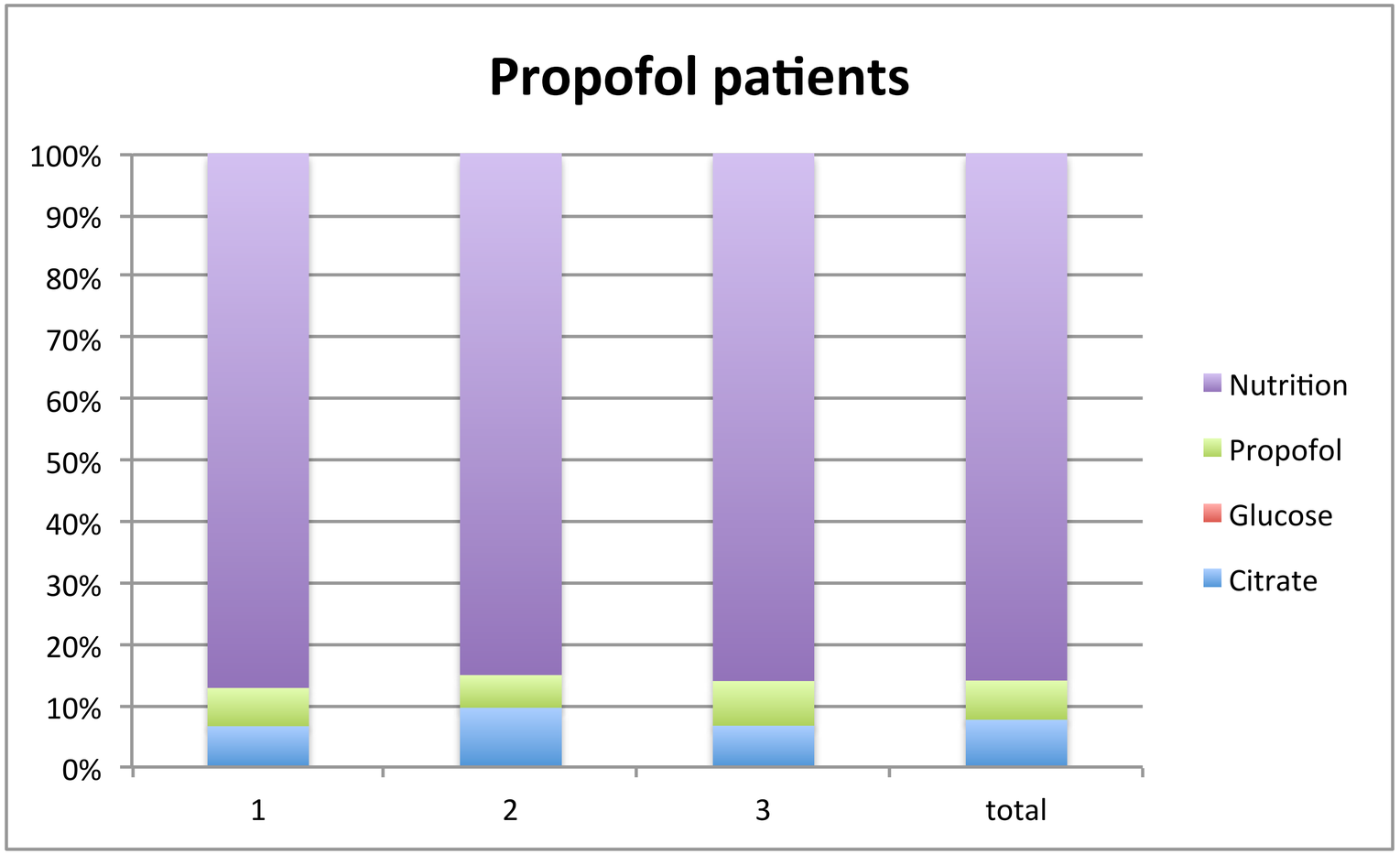
# Caloric intake propofol patients

## 14% total non-nutritional calories intake

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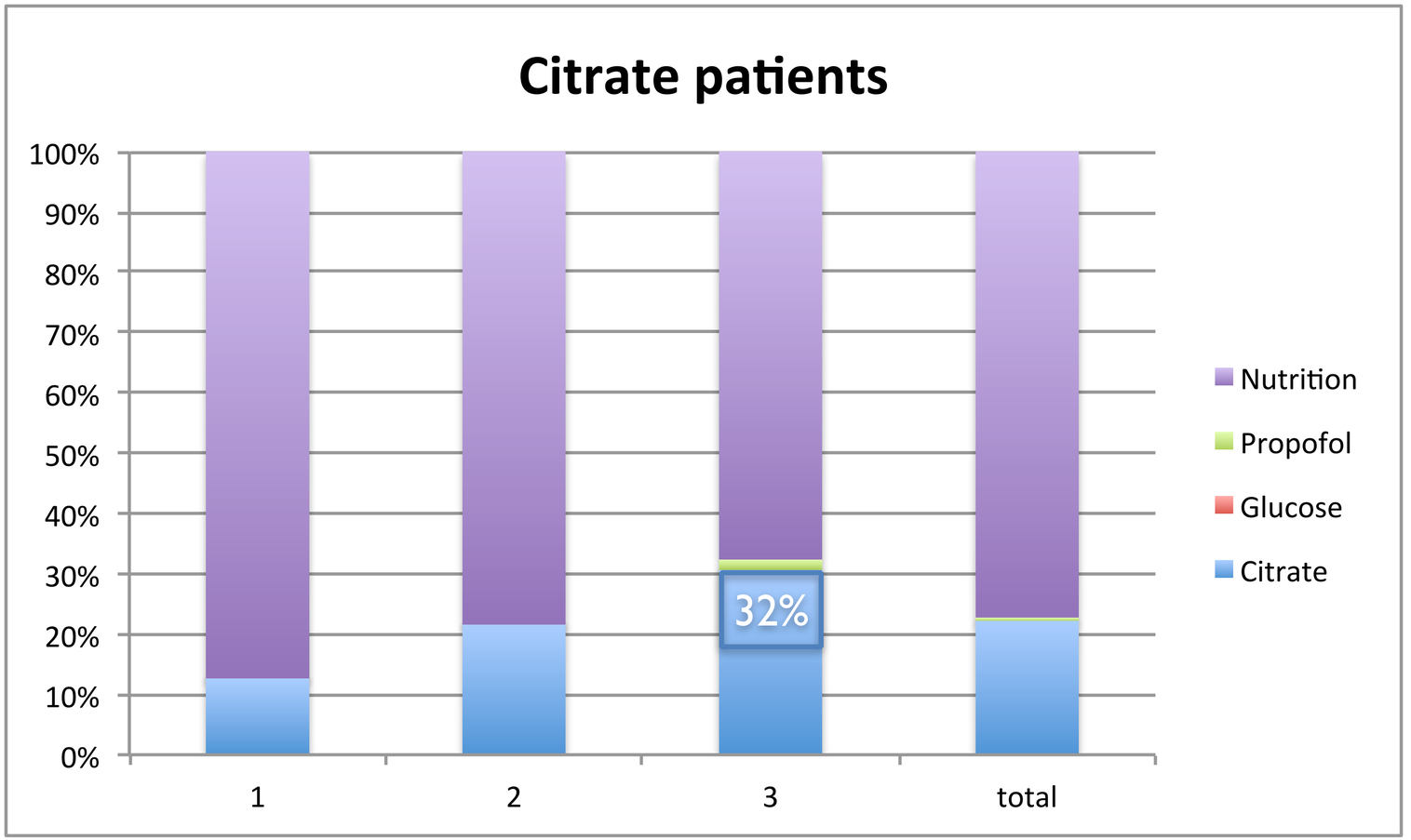
# Caloric intake

## 23% total non-nutritional calories intake

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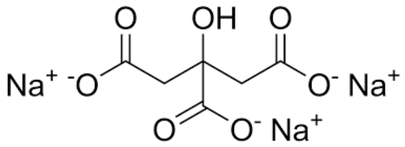
# Relevance of non-nutritional calories in mechanically ventilated patients

- **Glucose**


- **Propofol**


- **Trisodium Citrate**





In some patients 30% of daily intake: risk of overfeeding

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# Nonnutritional Caloric intake

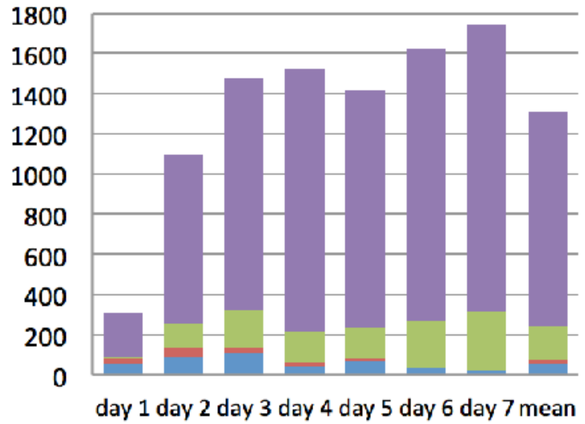
## subgroup analysis (% kcal of total intake)


n=142

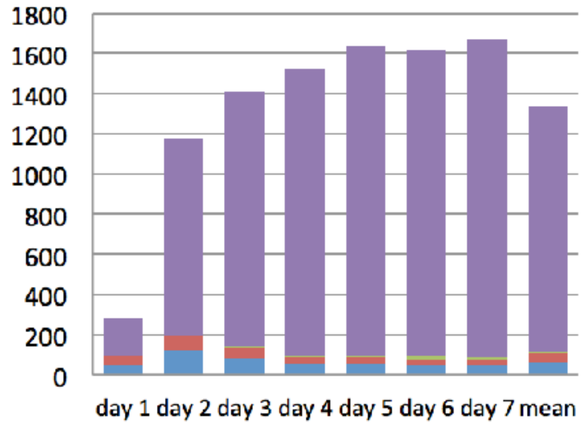
Preliminary results Bousie E, Van Zanten AR, unpublished

# Subgroup analyses absolute total daily kcal intake

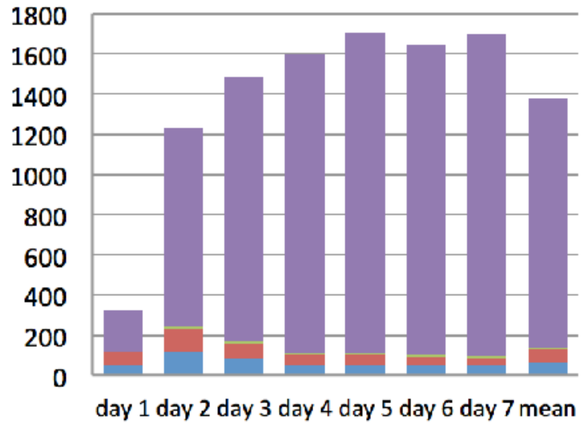
Patients with citrate renal replacement therapy (N=11)



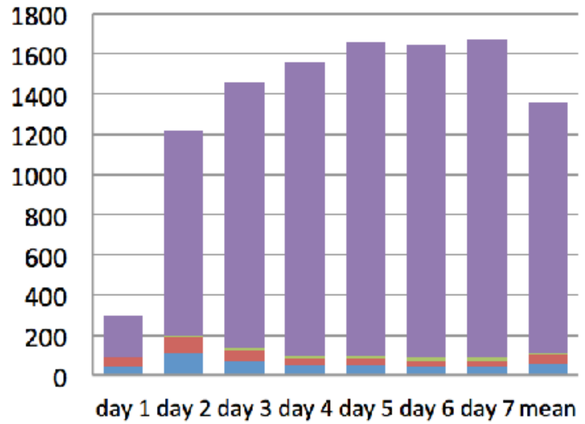

Patients with dextrose infusion (N=131)




Patients with propofol (N=100)




All patients (N=146)

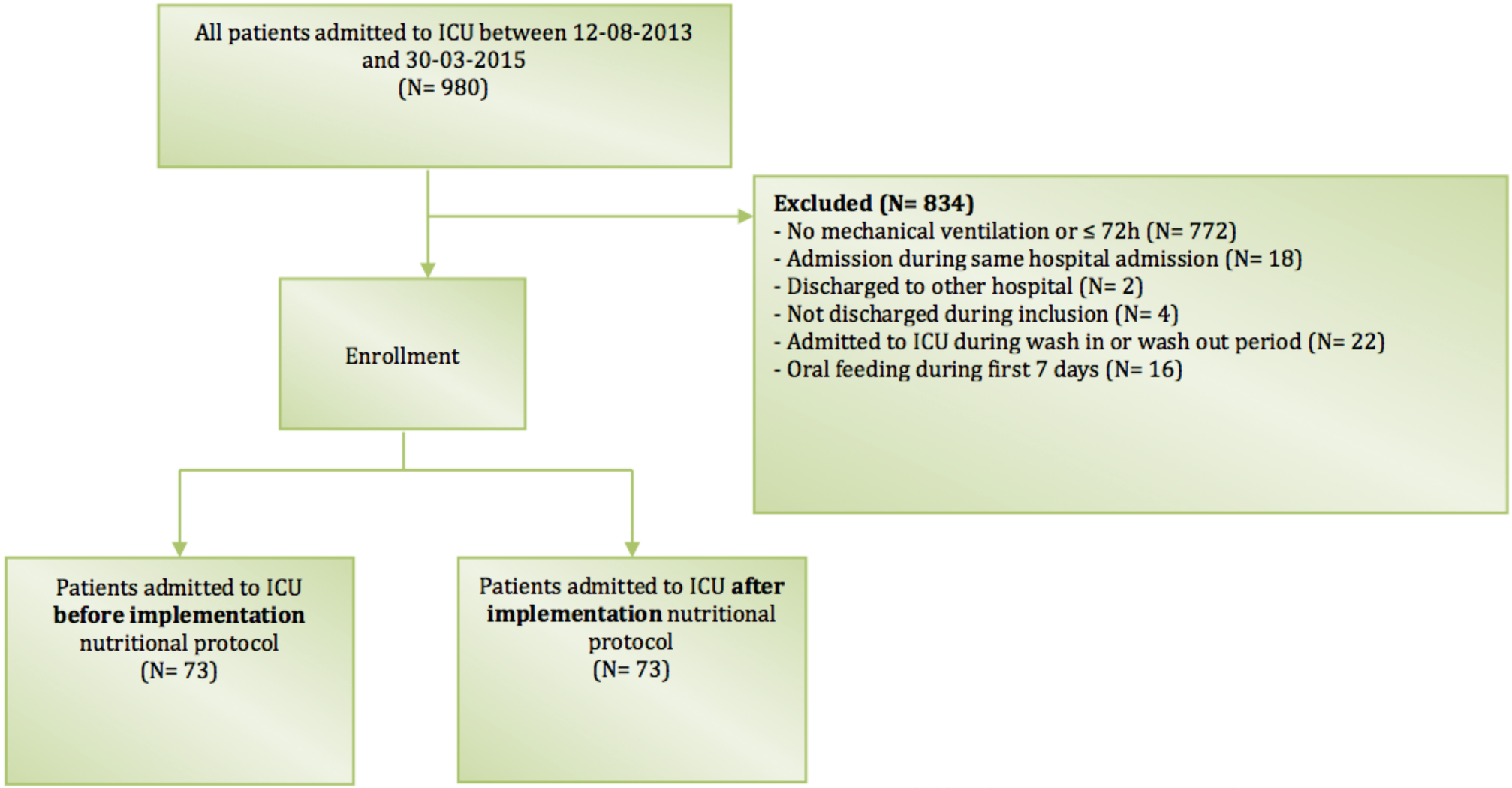



nutrition citrate propofol dextrose

**In individual patients 30% of daily intake**

Bousie E, Van Zanten AR. Eur J Clin Nutr. 2016;70(12):1443-50

# Effects of implementation of a computerized nutritional protocol in mechanically ventilated critically ill patients: A Single-Centre Before and After Study




Bousie E, van Blokland D, van Zanten AR. Clin Nutr. 2016;11:e47-e54.

# Computerized nutritional protocol in MV ICU patients: Before and After Study

**TABLE 1. Patient characteristics**

| | Before implementation N= 73 | | After implementation N= 73 | | P-value |
|---|---|---|---|---|---|
| | Mean (SD) | N (%) | Mean (SD) | N (%) | |
| Age (years) | 66.1 (13.3) | | 65.7 (15.3) | | 0.88 |
| Gender, male | | 43 (58.9%) | | 47 (64.6%) | 0.50 |
| BMI[1] (kg/m$^2$) | 27.1 (6.1) | | 26.8 (5.8) | | 0.78 |
| Primary admission diagnosis | | | | | |
| *Cardiovascular* | | 31 (42.5%) | | 26 (35.6%) | 0.40 |
| *Gastro-intestinal* | | 11 (15.1%) | | 21 (28.8%) | 0.046* |
| *Metabolic* | | 1 (1.4%) | | 0 (0%) | 0.32 |
| *Neurological* | | 5 (6.9%) | | 7 (9.6%) | 0.55 |
| *Renal* | | 0 (0%) | | 1 (1.4%) | 0.32 |
| *Respiratory* | | 25 (34.2%) | | 18 (24.7%) | 0.60 |
| Baseline APACHE II-score[2] | 22.5 (7.6) | | 20.6 (7.2) | | 0.13 |
| Baseline SOFA-score[3] | 3.8 (2.6) | | 4.1 (2.7) | | 0.42 |
| Baseline blood tests[6] | | | | | |
| *Haemoglobin (mmol/L)* | 7.7 (1.4) | | 7.4 (1.3) | | 0.27 |
| *Leukocytes (x10$^9$/L)* | 14.3 (9.0) | | 13.2 (8.0) | | 0.45 |
| *Platelets (x10$^9$/L)* | 249 (141) | | 268(174) | | 0.45 |
| *Creatinine (µmol/L)* | 110 (104) | | 104 (72) | | 0.68 |
| *Sodium (mmol/L)* | 139 (5.1) | | 138 (4.8) | | 0.14 |
| *Potassium (mmol/L)* | 4.0 (0.7) | | 3.9 (0.7) | | 0.50 |
| *Phosphate (mmol/L)* | 1.32 (0.55) | | 1.31 (0.63) | | 0.92 |
| *Albumin (g/L)* | 30 (7.8) | | 26 (7.2) | | 0.010* |
| *Magnesium (mmol/L)* | 0.86 (0.90) | | 0.70 (0.17) | | 0.13 |
| *Bilirubin (µmol/L)* | 9.8 (7.1) | | 12.2 (7.9) | | 0.053 |
| *Glucose (mmol/L)* | 9.6 (3.9) | | 8.6 (3.1) | | 0.12 |
| Sepsis, yes | | 34 (46.6%) | | 28 (38.4%) | 0.32 |
| Admission type | | | | | |
| *Medical* | | 45 (61.6%) | | 46 (63.0%) | 0.87 |
| *Elective surgery* | | 12 (16.4%) | | 11 (15.1%) | 0.82 |
| *Non-elective surgery* | | 16 (21.9%) | | 16 (21.9%) | 1.00 |
| Number of co-morbid conditions | 1.7 (0.9) | | 2.0 (1.1) | | 0.23 |
| *Diabetes mellitus* | | 18 (24.7%) | | 7 (9.6%) | 0.016* |
| *Hepatic* | | 1 (1.4%) | | 9 (12.3%) | 0.009* |
| *Gastro-intestinal* | | 13 (17.8%) | | 21 (28.8%) | 0.12 |
| *Renal* | | 6 (8.2%) | | 8 (11.0%) | 0.58 |
| *Respiratory* | | 32 (43.8%) | | 38 (52.1%) | 0.40 |
| *Cardiovascular* | | 36 (49.3%) | | 38 (52.1%) | 0.74 |
| *Neurological* | | 18 (24.7%) | | 21 (28.8%) | 0.58 |
| Nutritional risk score | | | | | |
| *MUST-score ≥ 2*[4] | | 24 (33.3%) | | 24 (32.9%) | 0.95 |
| *NUTRIC-score*[5] | 4.3 (1.5) | | 4.0 (1.8) | | 0.28 |
| Patients with non-nutritional calories | | | | | |
| *Glucose infusion*[7] | | 66 (90.4%) | | 65 (89.0%) | 0.79 |
| *Propofol*[7] | | 51 (69.9%) | | 49 (67.1%) | 0.72 |
| *Trisodium citrate*[7] | | 5 (6.8%) | | 6 (8.2%) | 0.76 |

[1]BMI, body mass index; [2]APACHE II, Acute Physiology and Chronic Health Evaluation; [3]SOFA, Sequential Organ Failure Assessment, [4]MUST, Malnutrition Universal Screening Tool; [5]NUTRIC, Nutrition Risk in Critically ill. [6]To convert to conventional units in mg/dL (g/dL for haemoglobin), divide by 0.6206 for haemoglobin, 8.4 for creatinine, 0.323 for phosphate, 0.411 for magnesium, 17.1 for bilirubin and 0.0555 for glucose; [7] patients who received non-nutritional calories during the first 7 days of ICU admission.

* = significantly different.

Bousie E, van Blokland D, van Zanten AR. Clin Nutr. 2016;11:e47-e54.

# Effect of Computerized nutritional protocol

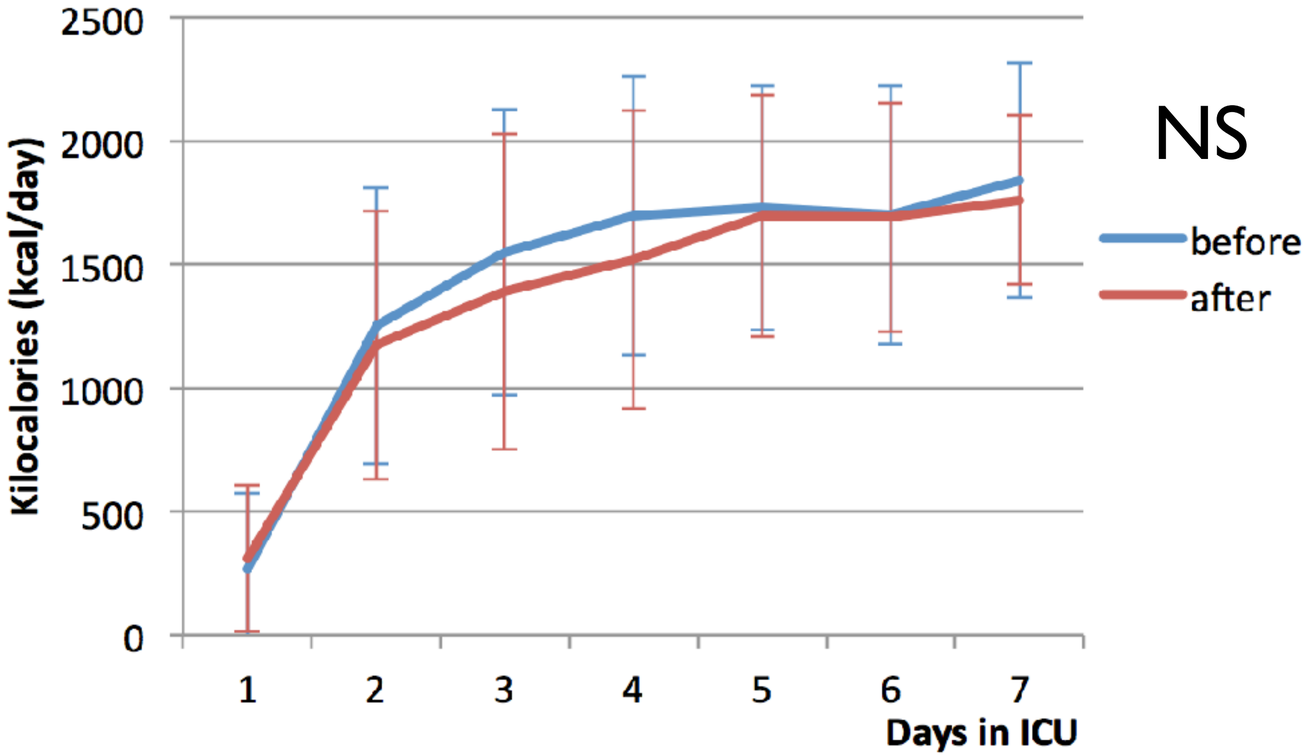



**FIGURE 2. Mean Total caloric Intake per day (kcal/day) before and after protocol implementation**

Mean caloric intake with standard deviations on day 1-7 before (blue line) and after implementation (red line) of the computerized nutritional protocol with hourly feedback of feeding and non-nutritional calories intake.

Bousie E, van Blokland D, van Zanten AR. Clin Nutr. 2016;11:e47-e54.

# Effect of Computerized nutritional protocol

**TABLE 6. Mean proteins per day**

| | Before implementation | After implementation | |
|---|---|---|---|
| | Proteins (g/kg/day) | Proteins (g/kg/day) | **P-value** |
| Day 1 | 0.15 (0.22) | 0.17 (0.21) | 0.47 |
| Day 2 | 0.89 (0.45) | 0.90 (0.52) | 0.89 |
| Day 3 | 1.19 (0.50) | 1.07 (0.58) | 0.19 |
| Day 4 | 1.33 (0.42) | 1.27 (0.51) | 0.47 |
| Day 5 | 1.38 (0.37) | 1.40 (0.37) | 0.80 |
| Day 6 | 1.35 (0.46) | 1.39 (0.36) | 0.63 |
| Day 7 | 1.45 (0.35) | 1.40 (0.36) | 0.52 |
| Total | 1.18 (0.32) | 1.08 (0.37) | 0.092 |

Values are mean (SD); proteins in g/kg/day; weight is corrected for BMI > 27 for the weight for BMI = 27; in the total the admission day and the day of discharge were excluded. * = significantly different.

Bousie E, van Blokland D, van Zanten AR. Clin Nutr. 2016;11:e47-e54.

# Effect of Computerized nutritional protocol

**TABLE 7. Secondary outcomes**

| | Before implementation N= 73 | | After implementation N= 73 | | P-value |
|---|---|---|---|---|---|
| | Mean (SD) | N (%) | Mean (SD) | N (%) | |
| LOS ICU [1,2] | 15.4 (12.4) | | 15.1 (19.1) | | 0.89 |
| Hospital LOS [1,2] | 31.2 (29.1) | | 28.0 (24.5) | | 0.47 |
| Duration of TF[2,3] | 13.3 (10.3) | | 14.1 (18.3) | | 0.77 |
| Duration of MV[2,4] | 9.5 (6.7) | | 10.4 (8.6) | | 0.56 |
| Patients with PN[5] | | 6 (8.2%) | | 7 (9.6%) | 0.77 |
| ICU mortality | | 10 (13.7%) | | 6 (8.2%) | 0.29 |
| Hospital mortality | | 13 (17.8%) | | 8 (11.0%) | 0.24 |

[1]LOS, length of stay; [2]LOS ICU, LOS hospital, duration of tube feeding and duration of mechanical ventilation are in days; [3]TF, tube feeding; [4]MV, mechanical ventilation; [5]PN, parenteral nutrition. * = significantly different.

Bousie E, van Blokland D, van Zanten AR. Clin Nutr. 2016;11:e47-e54.

# Effect of Computerized nutritional protocol

**TABLE 8. Electrolyte and glucose abnormalities[1]**

| | Before implementation N= 73 | After implementation N= 73 | P-value |
|---|---|---|---|
| Hypernatraemia | 41 (56.2%) | 30 (41.9%) | 0.068 |
| Hyponatraemia | 10 (13.7%) | 14 (19.2%) | 0.37 |
| Hyperkalaemia | 20 (27.4%) | 13 (17.8%) | 0.16 |
| Hypokalaemia | 43 (58.9%) | 28 (38.4%) | 0.013* |
| Hyperphosphaetemia | 23 (32.4%) | 22 (31.4%) | 0.86 |
| Hypophosphataemia | 53 (74.6%) | 46 (65.7%) | 0.21 |
| Hypermagnesaemia | 13 (18.3%) | 7 (10%) | 0.15 |
| Hypomagnesaemia | 22 (31%) | 30 (42.9%) | 0.17 |
| Hyperglycaemia | 28 (38.4%) | 18 (25.4%) | 0.075 |
| Hypoglycaemia | 9 (12.3%) | 5 (7%) | 0.26 |

Values are in N (%); [1]the frequencies and percentages of the electrolyte abnormalities are the number of patients with ≥ 1 time during the first 7 days of ICU admission (except from the admission day). * = significantly different.

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# Effect of Computerized nutritional protocol

**TABLE 9. Electrolyte and glucose abnormalities as separate variables**

| | Before | After | P-value |
|---|---|---|---|
| Hypernatraemia | 118/404 (29.2%) | 71/374 (19.0%) | <0.001* |
| Hyponatraemia | 30/404 (7.4%) | 11/374 (2.9%) | 0.005* |
| Hyperkalaemia | 24/404 (5.9%) | 18/375 (4.8%) | 0.48 |
| Hypokalaemia | 58/404 (14.4%) | 34/375 (9.1%) | 0.022* |
| Hyperphosphataemia | 33/296 (11.1%) | 34/267 (12.7%) | 0.56 |
| Hypophosphataemia | 87/296 (29.4%) | 70/267 (26.2%) | 0.40 |
| Hypermagnesaemia | 21/260 (8.1%) | 12/254 (4.7%) | 0.12 |
| Hypomagnesaemia | 29/260 (11.2%) | 48/254 (18.9%) | 0.014* |
| Hyperglycaemia | 39/402 (9.7%) | 28/368 (7.6%) | 0.30 |
| Hypoglycaemia | 10/402 (2.5%) | 5/368 (1.4%) | 0.26 |

Values are in n/total (%) [1]the frequencies and percentages of the abnormalities are the number of abnormalities during the first 7 days of ICU admission (except from admission day) divided by the total determined values. * = significantly different.

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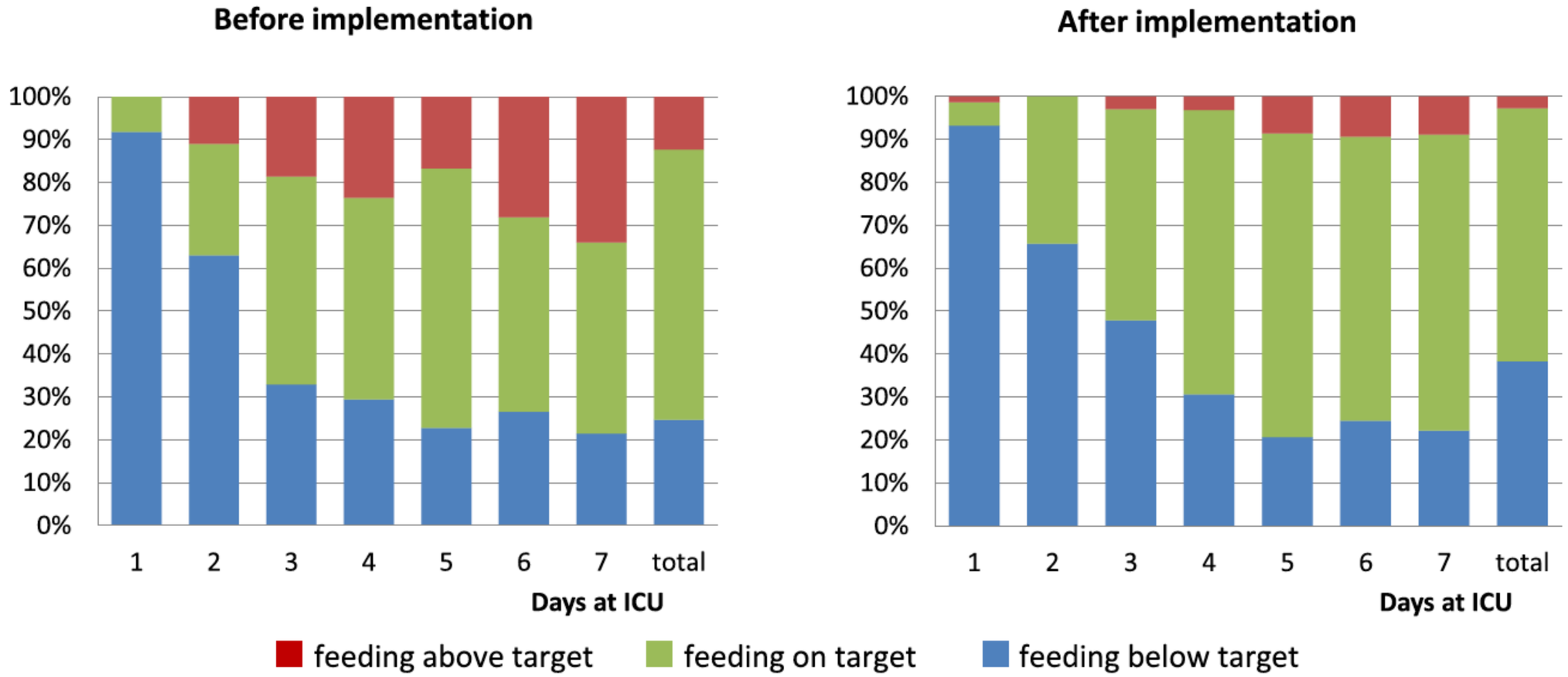
# ICU protocol and feedback promotes optimal nutrition




**Percentage of patients with feeding below target (blue; <80% of calculated target), feeding on target (green; 80-110% of calculated target) and feeding above target (red; >110% of calculated target)**

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# Conclusions

- Hypercaloric feeding should be avoided in critically ill
- Glucose, propofol and citrate provide non-nutritional calories
- Non-nutrional calories may be non-relevant in some patients, but in patients treated with both propofol and citrate they may account for 1/3 of total energy intake
- Feeding intake should be corrected in response to prevent overfeeding
- When feeding intake is reduced protein intake is compromised
- Protein & micronutrients targets then can only be achieved by adding protein & micronutrient supplements