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# Nutrición Hospitalaria

Trabajo Original

Paciente crítico

# Nitrogenous content in parenteral nutrition: a four-year experience in a general hospital. Critically-ill patient specificity

## *Contenido nitrogenado de la nutrición parenteral: un estudio de cuatro años en un hospital general. Especificidad en paciente crítico*

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## Abstract

**Introduction:** There have been several studies focusing on caloric intake during the last years, while protein content relevance has been underestimated. Some recent evidence has shown that protein deficiency has also an impact on patient outcomes. We have studied the nitrogen (N) content in parenteral nutrition (PN) bags administered to adult patients in a Spanish tertiary level hospital for four years.

**Material and methods:** Patients who received parenteral nutrition in the general ward and Intensive Care Unit (ICU) were recorded. Caloric and protein content were registered and adjusted to weight and length of stay. Data were compared among three group of patients: those in the general ward, those in the ICU and those requiring renal replacement therapy (RRT). The one-factor analysis of variance (ANOVA) test was used after checking data normality and homoscedasticity

**Results:** There was an increase in the mean g N/stay year after year ($p < 0.01$) from 14 to 15.5 g, with a decrease in non-protein caloric content ($p < 0.001$) from 111.6 to 101.8 kcal/g N. The range was established from 4.1 to 32.6 g. PN diets with ≥ 18 g N% ranged from 12.8% (2010) to 19.6% (2013). There were significant differences among the groups when comparing the variable g N/stay ($p < 0.0001$): 13.5 general ward *vs* 15.9 ICU patients *vs* 17.6 ICU with RRT, also when referring to adjusted weight.

**Conclusions:** According to most recent recommendations nitrogen has been provided in higher amounts than previously, especially in critical care patients with RRT.

**Key words:**

Nitrogen. Protein. Parenteral nutrition. Critical care. Renal replacement therapies. Individualized diets.

## Resumen

**Introducción:** algunos estudios recientes sugieren que se ha dado gran importancia al aporte calórico en la nutrición parenteral (NP) del paciente adulto, infraestimando su contenido proteico. Sin embargo, se ha demostrado su relación con los resultados clínicos. Con este objetivo se ha estudiado el contenido en nitrógeno (N) de las NP administradas en un hospital terciario a lo largo de cuatro años.

**Material y métodos:** se recogieron datos de la NP de pacientes hospitalizados en planta, así como en la Unidad de Cuidados Intensivos (UCI). El peso del paciente, su índice de masa corporal (IMC), el contenido en nitrógeno (total y por peso), el aporte calórico no proteico y la duración de la NP fueron algunas de las variables estudiadas. Se compararon en 2013 los aportes en la planta general, en UCI y en aquellos que recibieron algún tipo de terapia renal sustitutiva (TRS). Se utilizó el análisis de varianza (ANOVA) de un factor, previa comprobación de la normalidad y homocedasticidad.

**Resultados:** se ha observado un aumento progresivo en aporte nitrogenado medio diario cada año ($p < 0,01$) de 14 a 15,05 g, con descenso del contenido calórico no proteico ($p < 0,001$) de 111,6 a 101,8 kcal /g N. El rango de N en bolsa fue de 4,1 a 32,6 g. Aumentó el porcentaje de bolsas con ≥ 18 g N (12,8 en 2010 *vs.* 19,6 en 2013). También hubo diferencias entre grupos de pacientes en g N/estancia ($p < 0,0001$): 13,5 plantas de hospitalización *vs.* 15,9 UCI *vs.* 17,6 UCI con TRS, igualmente si referidos a peso ajustado.

**Conclusiones:** En consonancia con las recomendaciones más recientes, el contenido en nitrógenos ha aumentado con los años, en especial en la NP del paciente crítico, siendo aún mayor en los sometidos a TRS.

**Palabras clave:**

Nitrógeno. Proteína. Nutrición parenteral. Cuidados intensivos. Técnicas de depuración extrarrenal. Dietas individualizadas.

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## INTRODUCTION

There have been several recent studies focusing on caloric intake in parenteral nutrition (PN) while protein content relevance has been underestimated. Protein deficiency has also an impact on patient outcomes (1,2).

There is a clear need to identify safe amounts of nutrients for each acute disease stage in order to avoid under or overfeeding (3). In critically ill patients, undernourishment has been correlated with a higher number of infections, respiratory and immunology function impairment, as well as an increase in hospital length of stay and mortality (4). The results of a European study in 2012 including 102 patients showed a higher mortality rate on those patients who received a lower protein load, less than 1.2-1.5 g/kg/day (5). Other recent trials have shown that most critically ill patients do not reach nutritional requirements, being a low protein intake the most remarkable one (5-9), although there are some exceptions (10).

Based on our experience, we wanted to design a study to quantify the nitrogenous content in parenteral nutrition (PN) during 2010-2013 periods, comparing patients in the general ward and in the Intensive Care Unit. At the same time, we recorded the number of standardized/tailored solutions as well as insulin and glutamine addition.

## MATERIAL AND METHODS

A retrospective descriptive study was performed. The pharmacist recorded daily, clinical, anthropometric and analytical information using the Nutridata® program. PN composition was also recorded. This program offers the possibility to explore data through SPSS®. Some content parameters, considered as targets, were obtained to estimate differences among different groups of patients.

Some of the analyzed variables were current weight, present weight, ideal weight (IW) and the % of weight loss/time. Body mass index (BMI) was calculated after exporting weight and height information to Excel, as well as the adjusted weight (AW = IW ± 25% of the excess or defect in weight). Current weight data are the result of the analysis done through the Process Infornut® (11), when a nutritional risk alarm arises in the filter FILNUT (12,13), during the hospital stay. If there was no opportunity to record the patient's weight, it was obtained through digital clinical records (Diraya specialized care - DAE - oncology pharmacy - Farmis Oncofarm®, reports from preanesthesia, hemodynamics, etc.). In any case, it is mandatory to fulfill patient's weight and height into the justification sheets for PN (14). Any missing information would be obtained through the visit done by a member of the nutritional team. When a new weight is recorded into Nutridata® from a patient on long-term PN, the mean weight is used as the calculator for global weight/case. When it is not feasible to get patient's height, it can be estimated from the ulna bone length. Variables such as g N/kg or the non-protein kcal/g N are calculated by the program on a daily basis. The percentage and number of PN diets and their distribution as per the different target variables were calculated using the Nutridata® database per case and day. The information regarding g N/kg is referred to the current weight in the four-year period. Enteral nutrition intake was not considered.

Three groups of patients were established: general ward, ICU, and ICU requiring renal replacement therapy (RRT). Patients on RRT are those who received PN at any time during the RRT therapy, even if it was for a short period of time.

In 2011, the Nutritional Support Team proposed a new PN protocol. It included 27 different diets ranging from standard, fat-free, cholestasis, renal o liver failure and sepsis mixtures with different nutrient content. As a novelty, it also included diets with 18 and 20 g N with a low non-protein kcal/g N ratio (highly stressed patients) (Smofkaviben® and Olimel® triple chamber bags); glutamine dipeptide (Dipeptiven®) was added in certain cases, mainly in critically ill patients. A personalized diet was defined as the one with different macronutrients and/or volume composition when compared with those in the protocol, but not different in terms of electrolytes, insulin addition or glutamine composition.

The one-way analysis of variance (ANOVA) test was used after checking data for normality and homoscedasticity.

## RESULTS

Table I shows results in the three groups. The most severe and the longer the stay, the longer the length of PN use, and the higher the nitrogen load. The number of tailored formulations was higher in ICU patients requiring RRT. Table II shows yearly evolution in the study period. The number of PN bags remains similar, with a trend to higher nitrogen content and lower nitrogen/non-protein calorie ratio.

Figure 1 shows the evolution of the nitrogen intake as per weight, in the four-year period and other indicators fixed as targets. Figure 2 shows average values/stay (day) and 95% CI for nitrogen (g), non-protein kcal/g N, adjusted weight (AW) and g N/Kg AW in the three groups of patients. Patients in the ICU requiring RRT received a significantly higher nitrogen load as well as a lower N/non-protein kcal ratio.

## DISCUSSION

Standard PN solutions are widely used in most hospitals. There is also the possibility of designing standardized formulations based on standard patient profiles, including different stress situations, sepsis, cholestasis, and renal or hepatic impairment. Individualized formulations could be of interest in those patients with a complex clinical situation (up to 25-40% of the cases) (15). The ready-to-use bags (triple chamber bags) have dramatically reduced the need for manual compounding, by significantly reducing manipulation and liquid transfer (16). Martínez Romero et al. (17) demonstrated that 75% of their metabolically stable patients had their needs addressed by only three standardized formulations they had designed according to case-mix. Schoenenberger

**Table I.** Comparison of nitrogen content in patients according to their location

| 2013<br>Total patients 365[1] | Hospitalization wards | ICUs | ICUs with RRT[2] |
|---|---|---|---|
| Cases | 251 | 168 | 53 |
| Administered bags | 2,973 | 2,178 | 1,015 |
| *PN days/case* | *11.84* | *12.97* | *19.15* |
| *BMI/case* | 25.19 ± 5.28 | 27.06 ± 6.23 | 28.58 ± 6.6 |
| Current weight/case (kg) | 69.46 ± 15.82 | 75.89 ± 17.74 | 81.81 ± 15.33 |
| Current weight/stay | 68.68 ± 16.19 | 79.60 ± 18.20 | 85.13 ± 17.19 |
| Ideal weight/stay | 58.83 ± 7.87 | 61.67 ± 7.76 | 61.96 ± 8.64 |
| Adjusted weight/stay | 61.37 ± 8.28 | 66.32 ± 8.25 | 67.99 ± 8.13 |
| *g N/ stay (mean ± σ)* | *13.56 ± 3.13* | *15.87 ± 4.19* | *17.60 ± 4.28* |
| % ≤ 18 | 94.8 | 72.4 | 52.7 |
| % 18.1-22 | 4.4 | 20.4 | 33.8 |
| % > 22 | 0.8 | 7.2 | 13.5 |
| *Non-prot kcal/g N/stay (mean ± σ)* | *112.2 ± 20.1* | *97.3 ± 22.6* | *89.68 ± 18.4* |
| % ≤ 80 | 2.9 | 14.9 | 27.5 |
| % 80.1-95 | 14.5 | 44.5 | 44.7 |
| % > 95 | 82.6 | 40.6 | 27.8 |
| *g N/kg*/stay (mean ± σ)* | | | |
| **/adjusted weight* | *0.223 ± 0.046* | *0.240 ± 0.059* | *0.260 ± 0.060* |
| Protein g equivalent | 1.39 | 1.5 | 1.63 |
| */current weight | 0.204 ± 0.052 | 0.205 ± 0.056 | 0.211 ± 0.056 |
| */ideal weight | 0.233 ± 0.055 | 0.260 ± 0.068 | 0.288 ± 0.070 |
| % ≥ 0.26-current- | 15.6 | 20.4 | 22.8 |
| % personalized diets | 17.1 | 25 | 41.3 |
| % protocol (% triple chamber bags) | 82.9 (38) | 75 (36.7) | 58.7 (25.7) |
| PN bags with insulin (%) | 8.6 | 22.5 | 31.3 |
| Glutamine g/bag [3] | 0.8 | 4.83 | 7.43 |

*[1]Fifty-four patients stayed both in ICUs and wards; 731 bags were excluded (five homecare patients). [2]Critically ill patients requiring RRT at any time. It includes all bags with or without RRT. [3]Equivalent to 6.1; 36.6 and 56.3 ml of Dipeptiven®/bag.*

et al. showed that a standardized protocol which included 20 diets helped to prepare 6,300 formulations; up to 30% of the cases were prepared from different macronutrients, although only 8% of the formulations were really individualized (18).

As our own program allowed collecting data on prescription, elaboration and dispensation, we were able to assess the protein load in our PN solutions in all three scenarios: general ward, ICU patients, and those in the ICU requiring RRT. There was an increase in the g N/stay year after year ($p < 0.01$) except from 2012 and 2013 ($p = 0.181$). The range was established from 4.1 to 32.6. PN (%) diets with ≥ 18 g N have increased every year, ranging from 12.8% (2010) to 19.6% (2013). Data from 2014 show the same trend (21.3% ≥ 18 g N). There were no yearly significant differences for mean weight or BMI per case. Nevertheless, the mean weight/stay on PN in 2013 was significantly higher ($p < 0.001$) than in the three previous years.

In Weijs paper, including 886 patients, an optimal caloric and protein intake (between 1.2 and 1.5 g/kg/day) was associated with a decrease in mortality, while only reaching the caloric targets was not sufficient to establish that association (19). In agreement with this, in a pilot study including 2,772 ICU patients a higher caloric and protein intake was associated with better clinical outcomes, especially if BMI was < 25 o ≥ 35 on admission (20). Other studies confirm these findings (21,22), suggesting that classically recommended protein intake (ESPEN) may not be sufficient.

Regarding the use of glutamine, most published studies in critically ill patients have shown beneficial effects (23), leading to diverse scientific societies to recommend glutamine use (24,25). Heyland described that very high doses administered through enteral and parenteral route (> 0.5 g/kg/day) and during the acute phase in patients with multiple organ dysfunction and shock increased mortality (26).

According to recent recommendations, we have increased the g N/stay in our PN from 14 to 15.05, with a decrease in the non-protein caloric content, from 112 to 102. This nitrogen increase has happened despite the increase on PN average duration (two days) and partly due to the increase in the number of complementary PN, but also as a result of an improvement on

**Table II.** Nitrogen content evolution between 2010 a 2013

| Year | 2010 | 2011 | 2012 | 2013 |
|---|---|---|---|---|
| *PN cases*[(1)] | *411* | *419* | *409* | *365* |
| Mean age/case | 61 | 61.5 | 62.7 | 59.7 |
| Males % | 62 | 60.6 | 62.1 | 61.4 |
| *Stays (bags)* | *5,738* | *6,142* | *6,141* | *5,882* |
| Days/case | 14.2 | 14.9 | 15.2 | 16.6 |
| *BMI* | *25.82 ± 5.38* | *25.77 ± 5.97* | *25.91 ± 5.66* | *25.86 ± 5.49* |
| Current weight/case | 71.28 ± 14.9 | 71.24 ± 16.44 | 71.88 ± 16.82 | 71.98 ± 16.37 |
| Current weight/stay | 72.44 ± 17.51 | 71.82 ± 18.58 | 71.63 ± 20.11 | 74.25 ± 19.56 |
| *g N/stay (mean ± σ)* | 14.00 ± 3.28 | 14.62 ± 4.21 | 14.89 ± 4.08 | 15.05 ± 4.24 |
| % ≥ 16 g N | 29.65 | 37.87 | 43.09 | 43.9 |
| % ≥ 18 g N | 12.8 | 17.2 | 17.4 | 19.6 (2014: 21.3) |
| % ≥ 22 g N | 1.73 | 5.37 | 5.06 | 7.6 |
| *g N/kg-current-/stay (mean ± σ)* | *0.201 ± 0.057* | *0.211 ± 0.066* | *0.218 ± 0.070* | *0.210 ± 0.059* |
| Protein g equivalent | 1.256 | 1.319 | 1.363 | 1.313 |
| % ≥ 0.26 g N/kg | 15.9 | 21.7 | 25 | 21.3 |
| % ≥ 0.3 g N/kg | 4.7 | 6.9 | 12.2 | 10.1 |
| *Non-prot kcal/g N/stay (mean ± σ)* | *111.6 ± 22.2* | *107.6 ± 25.1* | *106.1 ± 20.3* | *101.8 ± 25.4* |
| % ≤ 95 non-prot kcal/g N | 24.8 | 36.8 | 37.2 | 41.4 |
| % ≤ 110 non-prot kcal/g N | 36.8 | 48.5 | 48.6 | 56.4 |
| % >110 non-prot kcal/g N | 63.2 | 51.5 | 51.4 | 42.9 |
| % Personalized diets [(2)] | 7 | 15.5 | 20.7 | 26.5 |
| % Protocol (% triple chambre bags) | 93 (46.5) | 86.5 (44.7) | 79.3 (33.7) | 73.5 (31.5) |
| % bags with insulin | 11.1 | 11.1 | 16.8 | 15 |

*[1]Hospitalization wards, ICUs and homecare patients included. [2]Personalized: those different from the protocol in terms of macronutrients and/or volume, not those with added electrolytes and/or insulin or glutamine dipeptide.*

the way PN is gradually initiated in patients at risk of refeeding syndrome. There was a yearly significant increase in g N/kg/stay from 0.20 to 0.22 until 2012 ($p < 0.001$). In 2013 there was a significant decrease when compared with 2012. The value reached was similar to 2011 value (0.21) and higher than 2010 value. This could be explained by the higher current weight/stay in 2013. Its equivalent in g prot/kg/d varied between 1.26 and 1.38, in accordance with ESPEN guidelines for PN (27).

The reduction in non-protein kcal/g of N turns out to be significant ($p < 0.001$ year by year, excepting 2011-2012, $p < 0.05$). An important reduction appeared in this ratio, lowered from 111.6 (2010) to 101.8 (2013). The need for personalized diets was more necessary (26.5% in 2013) when the nitrogenous content increased.

We also found a significant difference among groups when comparing the variable g N/stay (13.5 *vs* 15.9 *vs* 17.6, $p < 0.0001$). The same significance was reached for the difference in non-protein kcal/g N/stay (112 *vs* 97 *vs* 90). The increase in g N/kg/stay in ICU did not reach statistical significance when compared with hospitalization wards; however, those on RRT did ($p < 0.01$). These differences were statistically significant among the three groups when the variable g N/kg considered the IW or AW/stay ($p < 0.0001$). Patients on the general wards received 0.22 by average, while the ICU ones received 0.24. Those on RRT received 0.26 g N/kg AW, raising up to 0.29 g N when referred to the IW.

Critically ill patients, and those requiring RRT, had higher weight than those in hospital wards, received PN for a longer period, and also received higher nitrogenous content, in absolute terms and with regards to weight kg, and less non-protein calories per gram. Finally, glutamine dipeptide, as a PN component, was mainly used in these patients.

If a clinical pharmacist is fully integrated in the interdisciplinary nutrition support team, as it was in our case, in close collaboration with the Intensive Care Unit as a reference consultant, it is more feasible to adjust nutrient supplies to patient needs and, therefore, to favor quality of care in patients requiring PN.

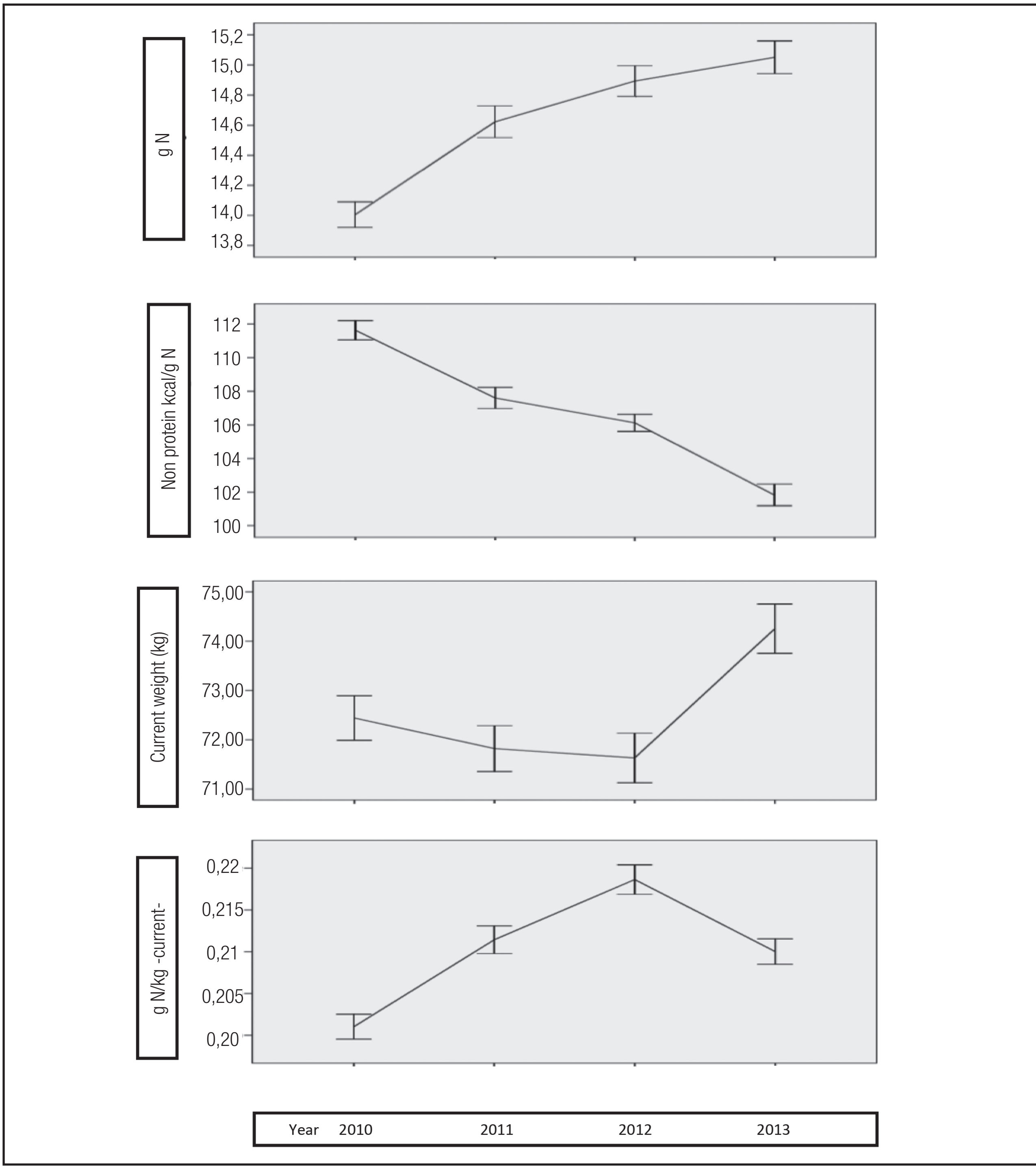


**Figure 1.**

Four-year evolution 2010-2013 (mean/stay with PN, CI 95%).

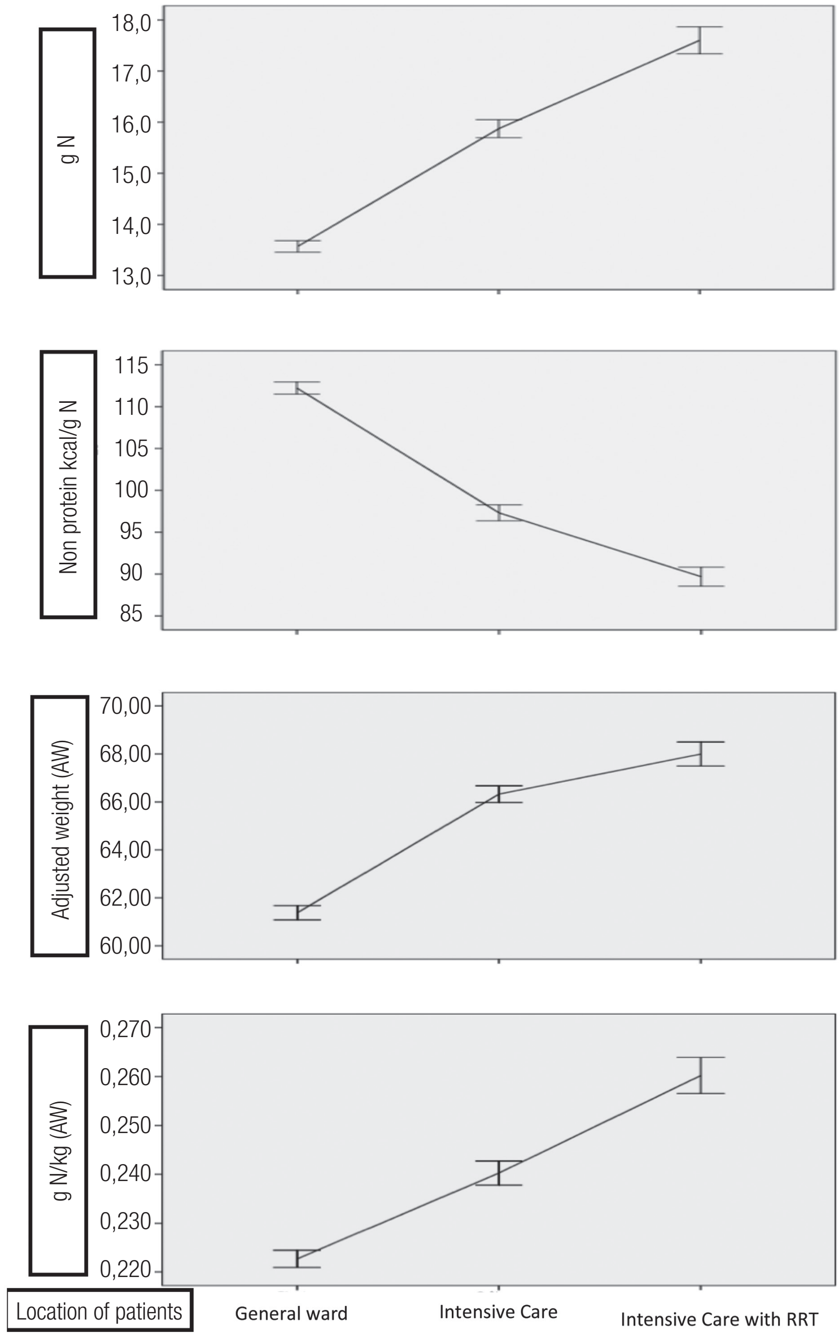


**Figure 2.**

Comparison during 2013: Wards/ICUs/ICUs with RRT (mean/stay with PN, CI 95%).

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