Nutrición Hospitalaria

SENPE

Análisis del nitrógeno ureico urinario en pacientes quirúrgicos críticamente enfermos: variabilidad clínica y utilidad para la estimación calórica

Analysis of urinary urea nitrogen in critically ill surgical patients: clinical variability and utility for caloric estimation

10.20960/nh.05784

09/15/2025

OR 5784

Analysis of urinary urea nitrogen in critically ill surgical patients: clinical variability and utility for caloric estimation

Análisis del nitrógeno ureico urinario en pacientes quirúrgicos críticamente enfermos: variabilidad clínica y utilidad para la estimación calórica

Noam Goder[1,2,3,4], Oded Sold[4], Noa Gosher[3,4], Amir Gal Oz[1,3], Dekel Stavi[1,3], Avner Leshem[3,4], Alex Barenboim[3,4], Yael Lichter[1,5]

[1]Division of Anesthesia, Pain Management and Intensive Care. Tel Aviv Sourasky Medical Center. Tel Aviv, Israel. [2]Adult Critical Care Program. Sunnybrook Health Sciences Centre. Temerty Faculty of Medicine. University of Toronto. Toronto, Canada. [3]Faculty of Medicine. Tel Aviv University. Tel Aviv, Israel. [4]Division of Surgery. Tel Aviv Sourasky Medical Center. Tel Aviv, Israel. [5]University College London Hospitals, NHS Foundation Trust. London, UK

Received: 12/02/2025

Accepted: 01/06/2025

Correspondence: Noam Goder. Adult Critical Care Program. Sunnybrook Health Sciences Centre. Temerty Faculty of Medicine. University of Toronto. 2075 Bayview Ave, North York. Toronto ON M4N 3M5, Canada

e-mail: noamgdr@gmail.com

Ethical approval: The ethics committee of the Medical Center approved the study, Institutional Review Board No. 0726-21.

AI usage statement: ChatGPT was used to review the proper use of English and Spanish without manipulation of data or assistance in writing.

Conflict of interest: The authors declare no conflict of interest.

Artificial intelligence: The authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

ABSTRACT

Background: critical illness is associated with loss of muscle mass, adversely affecting patient outcomes. The estimation of caloric and protein targets allows to tailor nutrition. This study explores the utility of weekly urinary urea nitrogen (UUN) measurements in critically-ill surgical patients for estimating nutritional needs.

Methods: in this retrospective study, we analyzed weekly UUN measurements in patients admitted to a surgical intensive care unit (SICU) at a tertiary medical center. We compared UUN-derived EE calculations (UEE) with measured EE (MEE) obtained from indirect calorimetry (IC) and the predictive EE (PEE) using the Harris-Benedict equation. We also explored factors influencing UUN levels, and developed a predictive model for EE using UUN.

Results: a total of 1,720 measurements from 892 patients were included in the final analysis. The study found significant variability in UUN levels, influenced primarily by urine output (R^2 = 0.1584). The NPC:N ratio that was found to correlate best between MEE and UEE was 98.65. A moderate correlation was observed between UUN and both MEE and PEE, however the addition of UUN to classical variables of predictive models resulted in a marginal 1.6 % increase in R^2 value. A statistically significant increase in UUN was observed between the first and second weeks of ICU admission (mean difference = -1.465, 95 % CI: -2.634 to -0.296, $p = 0.004$).

Conclusions: while routine collection of UUN can reflect energy expenditure to some extent, their utility is limited by significant variability and therefore offers little added benefit in adjusting nutritional support for critically-ill surgical patients.

Keywords: Urinary urea nitrogen. Energy expenditure. Indirect calorimetry. Critically-ill patients. Nutrition.

RESUMEN

Antecedentes: la enfermedad crítica se asocia a la pérdida de masa muscular, lo que afecta negativamente los resultados de los pacientes. La estimación de los requerimientos calóricos y proteicos permite adaptar la nutrición a las necesidades individuales. Este estudio explora la utilidad de las mediciones semanales de nitrógeno ureico urinario (UUN) en pacientes quirúrgicos críticamente enfermos para estimar sus necesidades nutricionales.

Métodos: en este estudio retrospectivo analizamos las mediciones semanales de UUN de pacientes ingresados en una unidad de cuidados intensivos quirúrgicos (SICU) de un centro médico terciario. Comparamos los cálculos de gasto energético derivados del UUN (UEE) con el gasto energético medido (MEE), obtenido mediante calorimetría indirecta (IC), y el gasto energético predictivo (PEE), calculado con la ecuación de Harris-Benedict. También exploramos los factores que influyen en los niveles de UUN y desarrollamos un modelo predictivo para el gasto energético basado en UUN.

Resultados: se incluyeron un total de 1720 mediciones de 892 pacientes en el análisis final. El estudio encontró una variabilidad significativa en los niveles de UUN, influenciada principalmente por el volumen de orina (R^2 = 0,1584). La proporción NPC:N que mostró la mejor correlación entre MEE y UEE fue de 98,65. Se observó una correlación moderada entre UUN y tanto MEE como PEE. Sin embargo, la adición de UUN a las variables clásicas de los modelos predictivos solo resultó en un aumento marginal del 1,6 % en el valor de R^2. Se observó un aumento estadísticamente significativo en los niveles de UUN entre la primera y la segunda semana de ingreso en la UCI (diferencia media = -1,465, IC 95 %: -2,634 a -0,296, *p* = 0,004).

Conclusiones: si bien la recolección rutinaria de UUN puede reflejar en cierta medida el gasto energético, su utilidad se ve limitada por una variabilidad significativa y, por lo tanto, ofrece un beneficio adicional mínimo para ajustar el soporte nutricional en pacientes quirúrgicos críticamente enfermos.

Palabras clave: Nitrógeno ureico urinario. Gasto energético. Calorimetría indirecta. Pacientes críticos. Nutrición.

INTRODUCTION

Critical illness has been linked with loss of lean body mass which can negatively affect outcomes such as mobility, respiratory function and mortality (1-3). As much as 6.4kg of skeletal muscle mass can be lost within the first 3 weeks of ICU admission, even when adequate nutrition is administered (4). Estimation of 24-hour energy expenditure (EE) can help tailor the amount of nutrition and choice of regimen and has been shown to improve short-term patient outcomes (5,6). Continuous indirect calorimetry (IC) is considered the gold standard measurement tool of EE for ventilated patients (7) and even a short 2-hour measurement can predict 24-hours EE (8). Calculation of EE using the Harris-Benedict predictive weight-based equation is still widely used in non-ventilated patients, or when IC is not available (9,10). In addition to assessing total caloric requirements, evaluating and replenishing protein needs, by calculation of nitrogen balance, can attenuate muscle mass loss and defray catabolism in critically-ill patients (11), and sufficient protein delivery was associated with substantially reduced mortality, independently of energy intake (12). Concomitantly, hyperalimentation proved to be non-beneficial and even harmful (13-19), which emphasizes the need to individualize protein targets. Protein requirements in critically-ill patients are proportionately higher than energy requirements and are not easily met by routine enteral formulations, which typically have a high non-protein-calorie to nitrogen (NPC:N) ratio (20). The use of nitrogen balance or NPC:N ratios of 70:1-100:1 has been suggested for guiding nutritional support in the ICU setting, although its value is limited (21).

Despite research efforts to identify and measure catabolism, there is still no standard blood marker for protein needs (22). Measuring 24-hour urinary urea nitrogen (UUN) excretion is inexpensive, simple and widely used to calculate nitrogen balance and adjust protein administration (23). This method is limited by variability in ureagenesis, losses of nitrogen as ammonia and creatinine or in stools, impaired excretion in renal failure, or alterations in urinary pH, but is considered reliable despite being slightly less accurate than direct measurement of total urine nitrogen (24-26). Nitrogen balance tends to improve when sick patients recover, however it is unclear whether a better nutritional state contributes to clinical improvement, or it is the patient's recovery that leads to improvement in nutritional status (27). In a single-center RCT assessing early goal-directed nutrition (EGDN), with the use of IC and UUN to guide nutritional care for critically-ill, mechanically ventilated patients, aiming to administer 100 % of requirements from admission day 1, did not result in any benefit or harm compared to standard nutrition care (28). Despite areas of uncertainty, IC became a guideline recommendation in critically-ill patients, while there is no specific recommendation to routinely measure UUN and nitrogen balance (21,29).

In this retrospective longitudinal study, we analyzed results of weekly UUN measurements in critically-ill patients admitted to a surgical intensive care unit (SICU) in a tertiary medical center. We aimed to: 1) describe the variability of UUN results; 2) analyze which factors influence the results; 3) compare UUN-derived calculation of EE (UEE) with measured EE by IC (MEE) and with predicted EE (PEE) calculated by a weight-based equation, thus exploring the feasibility of calculating UEE, rather than relying on PEE, for patients in which MEE is not available; 4) explore a predictive model of EE using UUN; 5) describe the weekly variations in UUN during ICU stay.

A previous study in the same SICU cohort examined substrate utilization, focusing on the oxidation of carbohydrates, fat, and protein based on IC and UUN measurements (25). While that study provided insights into metabolic substrate breakdown, the current analysis expands on these findings by incorporating a larger dataset of UUN measurements and specifically evaluating its utility in predicting energy expenditure (EE) and guiding nutritional support.

METHODS

This was a retrospective longitudinal study. Study data was routinely collected for clinical use in patients admitted to the SICU in a tertiary medical center. All patients who had a 24 hour urine collection for measurement of UUN were included in the study. Exclusion criteria were oliguria (urine output < 400 ml/d) and patients undergoing renal replacement therapy.

Urine was collected over a 24-hour period, from 8:00 AM to 8:00 AM the following day, on a routine weekly basis for all patients. Data collection included demographic and anthropometric information (age, gender, weight, and height at time of ICU admission), EE, and UUN levels. EE assessments were performed utilizing both indirect calorimetry when applicable, and the Harris-Benedict equation, adjusting the nitrogen to non-protein calorie (NPC:N) ratio to ensure alignment with indirect calorimetry values for enhanced precision. In ventilated patients, IC was acquired for a minimum of 24 hours using M-COVX, datex-ohmeda (Helsinki, Finland) module connected to a gas sampling line connector on the ventilatory circuit.

UEE was calculated based on UUN and the cohort-derived NPC:N ratio. The formula begins by estimating gastrointestinal protein loss, calculated as the product of the individual's weight and a constant nitrogen excretion rate (0.031 g/kg/day). This value is added to the measured urinary nitrogen excretion (UUN, in g/day) to provide an estimate of total nitrogen loss. Total nitrogen is then converted into protein calories by first multiplying by 6.25 (to convert nitrogen to protein grams) and then by 4 (calories per gram of protein). Non-protein calories are calculated using the cohort-derived NPC:N ratio, which is applied to the sum of UUN and nitrogen loss to determine total non-protein calorie expenditure. The UUN-based EE formula is as follows:

$\text{UEE} = \text{Nitrogen (N) derived calories} + \text{Non protein calories}$.

It can also be represented as:

$\text{UEE} = \text{N derived calories} + \text{NPC} : \text{N[cohort-derived]} \times \text{N}$, where:

$\text{N derived calories} = (\text{weight in kg} \times 0.031 + \text{UUN}) \times 6.25 \times 4$, and:

$\text{N} = (\text{weight in kg} \times 0.031 + \text{UUN})$.

Simplified, the UEE formula becomes:

$$UEE = (\text{weight in kg} \times 0.031 + UUN) \times (25 + NPC{:}N\ [\text{cohort-derived}]).$$

To determine the cohort-derived NPC:N ratio, we applied the UEE formula to a subset of measurements that included simultaneous urinary urea nitrogen (UUN) and measured energy expenditure (MEE) obtained via indirect calorimetry. The calculation was performed in the following steps:

1. We calculated the mean MEE across the paired measurements.
2. We applied the UEE formula to each individual measurement in the subset as follows:

   $$UEE\_patient = (weight\_patient \times 0.031 + UUN\_patient) \times (25 + NPC{:}N\_cohort)$$

3. We identified the single cohort-level NPC:N value that minimized the absolute difference between the calculated mean UEE and the observed mean MEE in the subset. This was done by solving the UEE equation iteratively across the dataset to find the NPC:N value for which the group mean UEE equaled the group mean MEE.
4. The resulting empirically derived cohort-level NPC:N ratio was then applied in all subsequent UEE calculations for the full study cohort.

Statistical analysis

Statistical analyses differentiated continuous variables into means ± SD for normally distributed data, and median with IQR for non-normally distributed variables. Categorical variables were described using frequency counts and percentages. Spearman correlation and linear regression analyses were conducted to examine the relationships between UUN levels, 24-hour urine output, protein enteral intake and EE as determined by both indirect calorimetry and the Harris-Benedict equation. The efficacy of these correlations and the predictive capacity of the models were evaluated. Repeated measures data were analyzed using a mixed linear model, focusing on the variation in UUN levels across the initial four weeks of the ICU stay to ascertain significant temporal changes in UUN levels. Statistical processes were carried out using IBM SPSS Statistics for Windows, version 29 (IBM Corp., Armonk, NY, USA).

Ethical compliance

The research protocol was approved by the ethics committee of the Medical Center (Institutional Review Board no. 0726-21).

RESULTS

Study population characteristics and demographics

A total of 1,804 urinary urea nitrogen (UUN) measurements were available in 970 patients, of which 63 measurements in 59 patients were excluded due to oliguria with urine output less than 400 ml/day on the day of collection. Further 21 cases in 19 patients were excluded due to the use of hemodialysis (HD) or continuous renal replacement therapy (CRRT) at the time of urinary collection. A total of 1,720 measurements from 892 patients were included in the final analysis (Fig. 1).

The average age of participants was 67.1 ± 17.1 years. The cohort's average body weight was 75.1 ± 17.1 kg, with an average height of 168 cm ± 13 cm. The median ICU length of stay for participants was 8.85 days [5.15, 18.57], with 59.8 % of patients (*n* = 533) being male. One-hundred and fifty-one patients (16.9 %) did not survive beyond 90 days post-admission. Within the population, 24.3 % (*n* = 216) were admitted without having operations, 21.6 % (*n* = 193) were admitted after elective general surgery, and 54.1 % (*n* = 483) were admitted after urgent surgery. Table I provides detailed characteristics of the study population.

Analysis of UUN levels: distribution and influencing factors

A histogram analyzing UUN levels was skewed to the right and reported a median value of 8.6 gr/day with an interquartile range (IQR) from 5.9 gr/day at the 25th percentile to 12.6 gr/day at the 75th percentile, indicating a non-normal distribution (Fig. 2).

For evaluation of the correlation between UUN levels and the volume of urine collected over a 24-hour period, a Spearman correlation analysis was conducted. The mean urine volume collected was 2075 ± 1119 ml. The Spearman correlation coefficient (r) between UUN levels and the 24-hour urine volume was 0.390, which was statistically significant with a two-tailed p-value of less than 0.001, showing a positive correlation between the two variables. The R-squared value of 0.1584 indicates that 15.8 % of the variance in UUN levels can be accounted for by the 24-hour urine volume.

Enteral protein intake matched to each UUN measurement day was available for all 1,720 cases. The distribution was right-skewed, with a median intake of 37.1 g/day and an interquartile range of 0.0 to 70.6 g/day. Intake was 0 g/day in 37.0 % (n = 637) of cases, indicating that a substantial proportion of surgical ICU patients were fasted on the collection day. Enteral protein intake demonstrated only a weak correlation with UUN levels (Spearman r = 0.108, $p < 0.001$), explaining approximately 1.16 % of the variance.

A linear regression model evaluating the factors that most significantly influence UUN levels yielded an R-squared value of 0.281. This model identified urine volume as the most significant predictor (importance: 0.42, $p < 0.001$), followed by height (importance: 0.22, $p < 0.001$), age (importance: 0.18, $p < 0.001$), BUN (blood urea nitrogen) with an importance of 0.17 ($p < 0.001$), and weight (importance: 0.02, p = 0.006).

Energy expenditure assessment using UUN (UEE)

Indirect calorimetry data, conducted simultaneously with the collection of urine, were available for 297 UUN measurements. MEE for this subset of patients, revealed a mean of 1,580 ± 462 kcal/day and a median of 1,538 kcal/day, with an IQR of 522 kcal/day. PEE calculated by the Harris-Benedict equation for the same patients showed a mean of 1,500 ± 271 kcal/day, with a median of 1469 kcal/day and an IQR of 397 kcal/day.

Simultaneously, the cohort-derived nitrogen to non-protein nitrogen (NPN:N) ratio was calculated to align the means of UEE (derived from UUN) and MEE (measured via indirect calorimetry), yielding a cohort-derived ratio of 98.65 based on the 297 measurements. The UEE was constructed to have a mean value of 1,580 kcal/day, identical to the mean MEE. Therefore, the more notable statistics include a UEE standard deviation of ± 782 kcal/day, a median of 1,406 kcal/day, and an interquartile range (IQR) of 911 kcal/day.

Across the 1,720 UUN measurements in the study, 1,423 did not have a corresponding MEE value. The predicted energy expenditure (PEE) calculated using the Harris-Benedict equation was 1,490 ± 294 kcal/day. Using the cohort-derived NPN:N ratio of 98.65, the UEE for all 1,720 measurements was calculated, yielding a mean of 1,532 ± 758 kcal/day, a median of 1,360 kcal/day, and an interquartile range (IQR) of 900 kcal/day.

Correlations between UUN and energy expenditure

Moderate, statistically significant linear correlation were identified among UUN, MEE and PEE. UUN and MEE had a moderate positive correlation of 0.431 (R^2 = 0.186, $p < 0.001$). UUN and PEE also had a moderate positive correlation of 0.390 (R^2 = 0.152, $p < 0.001$). The correlation between MEE and PEE was stronger, at 0.590 ($R^2 = 0.348$, $p < 0.001$). Scatter plots of correlated data are presented in figure 3.

Predictive modeling of energy expenditure using UUN

A linear regression model was developed to predict results of MEE, considered the "gold standard" for assessing caloric consumption, using the variables of UUN, gender, age, weight, and height. This model achieved an R-squared value of 0.409, indicating that approximately 40.9 % of the variance in caloric consumption can be accounted for by these variables. Among the predictors, age was found to be the most significant, with an importance score of 0.491 and a highly significant *p*-value (< 0.001), followed by weight with an importance of 0.300 and a similarly significant *p*-value (< 0.001). UUN also showed significance with an importance of 0.095 and a *p*-value of 0.004. Height and gender contributed less to the model, with importance scores of 0.018 ($p = 0.064$) and 0.037 ($p = 0.049$), respectively. Running the model without UUN yielded a slightly lower R-squared value of 0.393, highlighting age (importance 0.563, $p < 0.001$) and weight (importance 0.270, $p < 0.001$) as the most influential predictors in this configuration. A model designed to predict MEE, based on the PEE, achieved an R-squared value of 0.321.

Weekly variations in UUN during ICU stay

Mixed linear model analysis exploring the relationship between ICU LOS and UUN levels, revealed statistically significant variations in UUN levels over the first 4 weeks ($F = 4.578$, $p = 0.001$). The first week's average UUN level was 9.758 gr/day (95 % CI: 9.317 to 10.200 mg/dL). In the second week, there was an increase to an average of 11.224 gr/day (95 % CI: 10.538 to 11.910 mg/dL). The third week observed a slight decrease to an average of 10.831 gr/day (95 % CI: 9.945 to 11.717 mg/dL) and the fourth week presented an average UUN level of 9.993 gr/day (95 % CI: 8.969 to 11.018 mg/dL). There was a significant mean difference between week 1 and week 2 (mean difference = -1.465, 95 % CI: -2.634 to -0.296, p = 0.004). The rest of the pairwise comparisons did not reveal any significant differences.

DISCUSSION

In this retrospective longitudinal study, we explored the utility of weekly UUN measurements in critically-ill surgical patients. Our main findings are: 1) the main factor that significantly impacted UUN levels was urine output, while protein intake had only a minor influence; 2) the cohort-derived NPC:N ratio, which was found to correlate best between energy expenditure measured by indirect calorimetry (MEE) and energy expenditure calculated from UUN (UEE), was 98.65; 3) significant linear correlation was identified among UUN, MEE, and EE predicted by the Harris-Benedict equation (PEE); 4) the addition of UUN to classical variables in predictive modeling of EE resulted in a marginal 1.6 % increase in R^2 value; 5) there was a statistically significant increase in UUN between the first and second week of ICU admission, but not in weeks 3 or 4.

An international observational study highlighted that energy and protein prescriptions in ICU settings often fall short of recommendations, with an average of only 64.1 % of calories and 60.5 % of protein actually delivered. Importantly, the study found that delivering more than 80 % of the prescribed protein intake, irrespective of total calorie intake, was associated with reduced mortality and ICU LOS (12). Among methods for assessing protein needs, 24-hour UUN measurement stands out for its simplicity and accessibility. Despite this, it is not routinely recommended by critical care or nutrition scientific societies, resulting in a scarcity of large cohort studies. To the best of our knowledge, our study, which collected and analyzed 1,720 UUN measurements from 892 critically-ill surgical patients, represents the largest dataset of its kind to date.

We found a large variability of UUN levels and looked at factors that can influence UUN results. We discovered that urine volume accounts for 15.8 % of the variability in UUN levels, which has yet been specifically described. Impaired renal function can lead to reduced urinary excretion of nitrogen and its accumulation in the form of blood urea nitrogen (BUN) (30). For the purpose of calculating nitrogen balance, a mathematical adjustment can be used to account for the unfiltered nitrogen, which uses change in BUN and total body water (31). Surprisingly, protein intake had a very small effect on UUN, with around a 1 % effect on variance, suggesting that the amount of protein intake in the ICU setting has little impact on protein breakdown and secretion in urine.

IC is often unavailable, unreliable or simply cannot be done. Common examples are non-ventilated patients, ventilated patients on $FiO_2 > 0.6$ and patients on extracorporeal membrane oxygenation (ECMO). In such cases, predictive equations like the Harris-Benedict, serve as an alternative, but were shown to be inaccurate when compared to MEE (32). We were intrigued to find whether a UUN-based EE calculation could reliably reflect actual EE and therefore be used to adjust enteral feeding, in-lieu of predictive equations. Using data from 297 measurements of UUN simultaneously with IC in intubated patients, we attempted to construct a model to predict EE based on UUN. We found that in order for the calculation of UEE to match MEE that was simultaneously recorded by IC, an NPC:N ratio of 98.65 should be used. This is significantly lower than the historically suggested ratio of 150 (29), but aligns with more recent ICU literature recommendations of 70-100 (21). Eventually, although we succeeded in correlating this model with indirect calorimetry, it proved inferior to the correlation of the Harris-Benedict calculation with IC, rendering the UUN-based EE calculation impractical for use.

We then examined whether the addition of UUN to the calculation of PEE through baseline characteristics could predict MEE more accurately than the Harris-Benedict equation alone. We found that, although UUN could slightly enhance the accuracy of the model, this addition was negligible —accounting for only 1.6 % out of the 40.9 % of variance predicted in the model.

Our final analysis evaluated how UUN evolves during ICU stay. We observed a marginal elevation in UUN from week 1 to week 2 of the stay without further increase. These findings may suggest that muscle breakdown increases in the second week of ICU admission and remains constant thereafter, particularly in patients with long ICU stays, often due to ongoing complications. Several publications described the acute protein breakdown and a decrease in protein synthesis during the initial phase of critical illness, known as the "early acute phase" or "ebb phase", with hypercatabolism continuing into the later acute stage, known as the "flow phase" (29,34,35).

The strength of our study is in the large size of the cohort, our attempt to answer practical questions which could have clinical implementation and the methodology of the analysis. Some limitations still exist. First, our patient population is comprised of surgical patients with relatively prolonged ICU admission time, therefore our results cannot be generalizable to other groups of critically-ill patients. Second, we could not account for nitrogen loss through surgical drains which may have affected UUN results. Third, while we did demonstrate by linear regression that urine volume and BUN significantly influence UUN results, we did not include a mathematical correction for uremia.

In conclusion, our findings suggest that the routine collection of UUN exhibits large variance and offers little benefit in adjusting the nutritional support of patients in terms of total calories needed. Using UUN may still be beneficial in specific situations when protein underfeeding or overfeeding is a concern.

REFERENCES

1. Schweickert WD, Hall J. ICU-acquired weakness. Chest 2007;131(5):1541-9. DOI: 10.1007/s00134-020-05944-4
2. de Jonghe B, Lacherade JC, Sharshar T, Outin H. Intensive care unit-acquired weakness: risk factors and prevention. Crit Care Med 2009;37(10 Suppl):S3090-315. DOI: 10.1097/CCM.0b013e3181b6e64c
3. Hermans G, Van Mechelen H, Clerckx B, Vanhullebusch T, Mesotten D, Wilmer A, et al. Acute outcomes and 1-year mortality of intensive care unit-acquired weakness. A cohort study and propensity-matched analysis. Am J Respir Crit Care Med 2014;190(4):410-20. DOI: 10.1164/rccm.201312-2257OC
4. Monk DN, Plank LD, Franch-Arcas G, Finn PJ, Streat SJ, Hill GL. Sequential changes in the metabolic response in critically injured patients during the first 25 days after blunt trauma. Ann Surg 1996;223(4):395-405. DOI: 10.1097/00000658-199604000-00008
5. Zusman O, Kagan I, Bendavid I, Theilla M, Cohen J, Singer P. Predictive equations versus measured energy expenditure by indirect calorimetry: A retrospective validation. Clinical Nutrition 2019;38(3):1206-10. DOI: 10.1016/j.clnu.2018.04.020
6. Duan JY, Zheng WH, Zhou H, Xu Y, Huang HB. Energy delivery guided by indirect calorimetry in critically ill patients: a systematic review and meta-analysis. Crit Care 2021;25(1):88. DOI: 10.1186/s13054-021-03508-6
7. Cooney RN, Frankenfield DC. Determining energy needs in critically ill patients: equations or indirect calorimeters. Current Opinion in Critical Care 2012;18(2):174-7. DOI: 10.1097/MCC.0b013e3283514bbc
8. Lichter Y, Sold O, Angel Y, Nizri E, Gerstenhaber F, Gal Oz A, et al. Two-hour indirect calorimetry measurement as a predictor of 24-hour energy expenditure in critically ill surgical patients: A longitudinal

study. JPEN J Parenter Enteral Nutr 2023;47(7):896-903. DOI: 10.1002/jpen.2545
9. Walker RN, Heuberger RA. Predictive equations for energy needs for the critically ill. Respir Care 2009;54(4):509-21.
10. Frankenfield DC, Coleman A, Alam S, Cooney RN. Analysis of Estimation Methods for Resting Metabolic Rate in Critically Ill Adults. J Parenter Enteral Nutr 2009;33(1):27-36. DOI: 10.1177/0148607108322399
11. Wojnar MM, Hawkins WG, Lang CH. Nutritional support of the septic patient. Crit Care Clin 1995;11(3):717-33.
12. Nicolo M, Heyland DK, Chittams J, Sammarco T, Compher C. Clinical Outcomes Related to Protein Delivery in a Critically Ill Population: A Multicenter, Multinational Observation Study. J Parenter Enteral Nutr 2016;40(1):45-51. DOI: 10.1177/0148607115583675
13. Larsson J, Lennmarken C, Mårtensson J, Sandstedt S, Vinnars E. Nitrogen requirements in severely injured patients. Br J Surg 1990;77(4):413-6. DOI: 10.1002/bjs.1800770418
14. McNurlan MA, Garlick PJ. Protein and amino acids in nutritional support. Crit Care Clin 1995;11(3):635-50.
15. Detsky AS. Parenteral nutrition--is it helpful? N Engl J Med 1991;325(8):573-5. DOI: 10.1056/NEJM199108223250808
16. Schulman RC, Mechanick JI. Can Nutrition Support Interfere with Recovery from Acute Critical Illness? In: Singer P, editor. World Review of Nutrition and Dietetics [Internet]. S. Karger AG; 2013 [cited 2025 Apr 10]. *p.* 69-81. Available from: https://karger.com/books/book/273/chapter/5188439
17. Singer P, Blaser AR, Berger MM, Calder PC, Casaer M, Hiesmayr M, et al. ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit. Clinical Nutrition 2023;42(9):1671-89. DOI: 10.1016/j.clnu.2023.07.011

18. Heyland DK, Patel J, Compher C, Rice TW, Bear DE, Lee ZY, et al. The effect of higher protein dosing in critically ill patients with high nutritional risk (EFFORT Protein): an international, multicentre, pragmatic, registry-based randomised trial. The Lancet 2023;401(10376):568-76. DOI: 10.1016/S0140-6736(22)02469-2
19. Bels JLM, Thiessen S, Van Gassel RJJ, Beishuizen A, De Bie Dekker A, Fraipont V, et al. Effect of high versus standard protein provision on functional recovery in people with critical illness (PRECISe): an investigator-initiated, double-blinded, multicentre, parallel-group, randomised controlled trial in Belgium and the Netherlands. The Lancet 2024;404(10453):659-69. DOI: 10.1016/S0140-6736(24)01304-7
20. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). J Parenter Enteral Nutr 2016;40(2):159-211. DOI: 10.1177/0148607115621863
21. McClave SA, Martindale RG, Vanek VW, McCarthy M, Roberts P, Taylor B, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). J Parenter Enteral Nutr 2009;33(3):277-316. DOI: 10.1177/0148607109335234
22. Page A, Flower L, Prowle J, Puthucheary Z. Novel methods to identify and measure catabolism. Curr Opin Crit Care 2021;27(4):361-6. DOI: 10.1097/MCC.0000000000000842
23. Milner EA, Cioffi WG, Mason AD, Mcmanus WF, Pruitt BA. Accuracy of Urinary Urea Nitrogen for Predicting Total Urinary Nitrogen in Thermally Injured Patients. J Parenter Enteral Nutr 1993;17(5):414-6. DOI: 10.1177/0148607193017005414

24. Konstantinides FN, Konstantinides NN, Li JC, Myaya ME, Cerra FB. Urinary Urea Nitrogen: Too Insensitive for Calculating Nitrogen Balance Studies in Surgical Clinical Nutrition. J Parenter Enteral Nutr 1991;15(2):189-93. DOI: 10.1177/0148607191015002189
25. Blackburn GL, Bistrian BR, Maini BS, Schlamm HT, Smith MF. Nutritional and metabolic assessment of the hospitalized patient. J Parenter Enteral Nutr 1977;1(1):11-21. DOI: 10.1177/014860717700100101
26. Berger MM, Pichard C. Feeding should be individualized in the critically ill patients. Curr Opin Crit Care 2019;25(4):307-13. DOI: 10.1097/MCC.0000000000000625
27. Manning EM, Shenkin A. Nutritional assessment in the critically ill. Crit Care Clin 1995;11(3):603-34.
28. Allingstrup MJ, Kondrup J, Wiis J, Claudius C, Pedersen UG, Hein-Rasmussen R, et al. Early goal-directed nutrition versus standard of care in adult intensive care patients: the single-centre, randomised, outcome assessor-blinded EAT-ICU trial. Intensive Care Med 2017;43(11):1637-47. DOI: 10.1007/s00134-017-4880-3
29. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clinical Nutrition 2019;38(1):48-79. DOI: 10.1016/j.clnu.2018.08.037
30. Druml W. Protein Metabolism in Acute Renal Failure. Mineral Electrolyte Metab 1998;24(1):47-54. DOI: 10.1159/000057350
31. Irwin RS, Rippe JM, editors. Irwin and Rippe's intensive care medicine. 8. edition. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2018. 2164 *p*.
32. Kolpek JH, Ott LG, Record KE, Rapp RP, Dempsey R, Tibbs P, et al. Comparison of Urinary Urea Nitrogen Excretion and Measured Energy Expenditure in Spinal Cord Injury and Nansteroid-Treated Severe Head Trauma Patients. J Parenter Enteral Nutr 1989;13(3):277-80. DOI: 10.1177/0148607189013003277

33. Long CL, Schaffel N, Geiger JW, Schiller WR, Blakemore WS. Metabolic Response to Injury and Illness: Estimation of Energy and Protein Needs from Indirect Calorimetry and Nitrogen Balance. J Parenter Enteral Nutr 1979;3(6):452-6. DOI: 10.1177/014860717900300609
34. Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, et al. Acute Skeletal Muscle Wasting in Critical Illness. JAMA 2013;310(15):1591. DOI: 10.1001/jama.2013.278481
35. Sakurai Y. Protein Metabolism in Critical Illness: Methodologies and Their Problems Underlying in Kinetic Studies Using Isotope Tracers In Vivo. Keio j med 1999;48(2):69-78. DOI: 10.2302/kjm.48.69

Table I. Baseline characteristics and admission diagnoses of patients

Variable	**Number**	**Mean/ (Median)**	**Std. deviation / %**	**IQR**
UUN measurement number	1720			
Patient number	892			
Age (years)		67.1	17.1	
Gender (male)	533/892 (59.80 %)			
Body weight (kg)		75.1	17.1	
Height (cm)		168	13	
Length of stay (days)		(8.85)		[5.2, 18.6]
90-day mortality	151/892 (16.90 %)			
UUN (g/day)	1720	(8.6)		[5.9, 12.6]
24-hour urine volume (ml)		2075	1119	
Harris-Benedict EE (kcal/day)	1720	1490	294	
NPN:N ratio EE (kcal/day)	1720	1532/(1360)	758	[998, 1896]
Indirect calorimetry	297	1580/(1538)	462	[129

EE (kcal/day)				6, 1817]
Creatinine (mg/dl)		(0.69)		[0.4 6, 1.15]
BUN		(23)		[15, 36]
Surgery				
No surgery	217		24.30 %	
Vascular procedures (angiography)	11		1.23 %	
Bowel resections	96		10.75 %	
Cholecystectomies	28		3.14 %	
Debridements	19		2.13 %	
Exploratory laparotomies	79		8.85 %	
Hernia repairs	9		1.01 %	
HIPEC	11		1.23 %	
Esophagectomies	27		3.02 %	
Gastrectomies	17		1.90 %	
Hepatectomies	21		2.35 %	
Pancreatectomies	45		5.04 %	
Transplant surgeries	13		1.46 %	
Sarcoma resections	21		2.35 %	

Small bowel resections	65		7.28 %	
Other surgery	213		23.85 %	
Diagnosis				
Trauma	96		10.76 %	
Gastrointestinal bleeding	80		8.97 %	
Colon perforation	57		6.39 %	
Post-op abdominal sepsis	51		5.72 %	
Cancer of pancreas	46		5.16 %	
Small bowel obstruction	46		5.16 %	
Cholecystitis and cholangitis	39		4.37 %	
Upper GI perforation	33		3.70 %	
Mesenteric event	31		3.48 %	
Pancreatitis	26		2.91 %	
Esophageal tumor	25		2.80 %	
Postoperative bleeding	21		2.35 %	
Sarcoma	21		2.35 %	
Large bowel obstruction	20		2.24 %	
Liver tumor	19		2.13 %	
Ischemic colitis	18		2.02 %	
Colon tumor	16		1.79 %	
Aspiration	14		1.57 %	

Kidney transplant	13		1.46 %	
Fournier gangrene	12		1.35 %	
Gastric tumor	12		1.35 %	
Small bowel perforation	12		1.35 %	
Appendicitis	10		1.12 %	
Other	174		19.51 %	

UUN: urine urea nitrogen; EE: energy expenditure; NPN: non-protein nitrogen; N: nitrogen; BUN: blood urea nitrogen; HIPEC: hyperthermic intraperitoneal chemotherapy; GI: gastrointestinal.

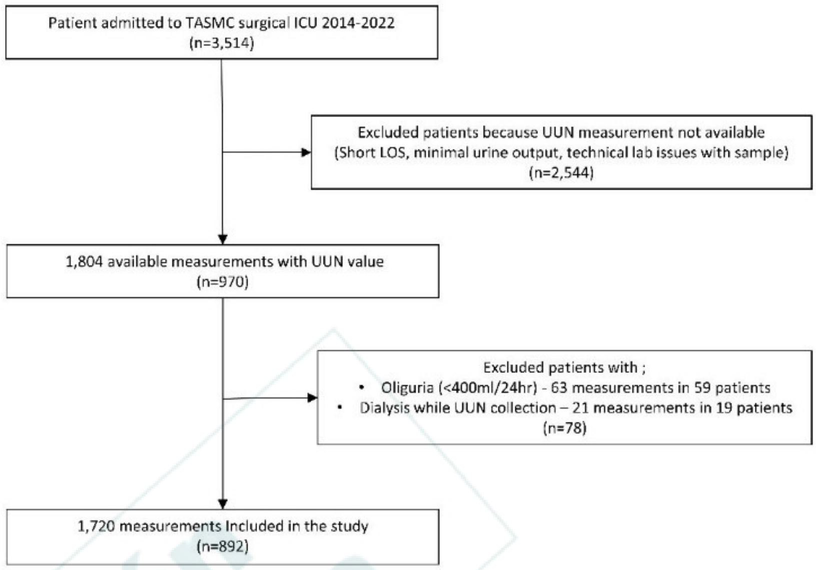

Figure 1. Flow diagram of included patients.

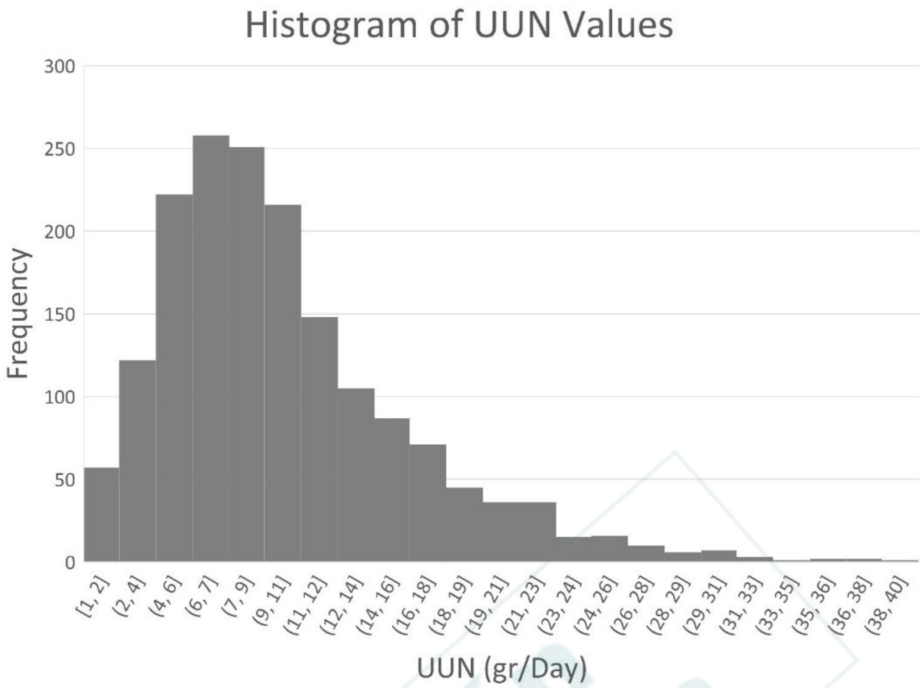

Figure 2. Distribution of 1,720 UUN value measurements among the 892 patients included.

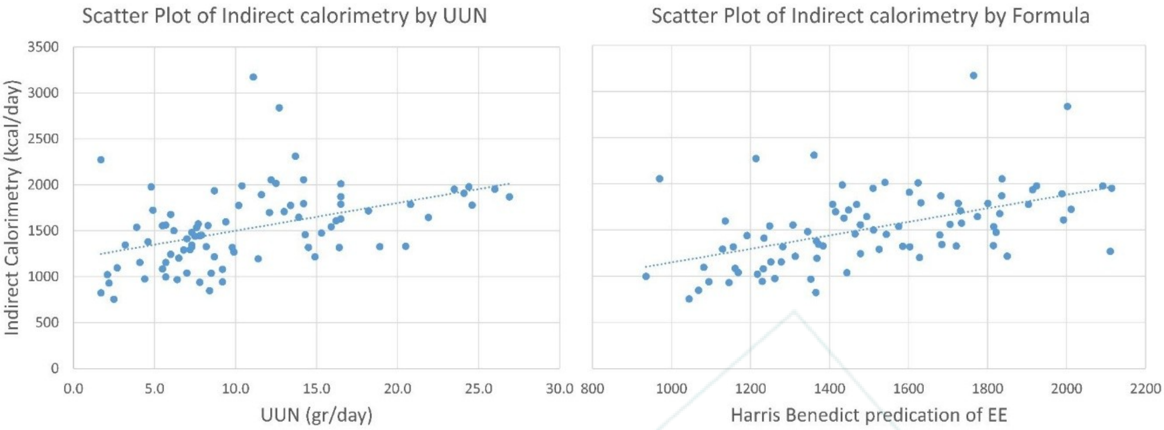

Figure 3. Scatter plots of correlation of indirect calorimetry by UUN collected in this study and by the Harris Benedict formula for energy expenditure.