https://doi.org/10.15360/1813-9779-2026-2-2687

Comparative Assessment of Equivalence of the Post-Operative Use of Two Amino Acid Solutions

Ionas S. Simutis[1,2]*, Alexey Yu. Yakovlev[3], Yurij V. Levadnev[2,4], Maria A. Saveleva[2]*, Kristina S. Blitsõn[2]*, Roman S. Perefilev[3], Andrey Yu. Smorkalov[3]

[1] Sokolov Northwestern District Research and Clinical Center, Federal Medico-Biological Agency of Russia, 4 Ave. Culture, 194291 Saint Petersburg, Russia
[2] I. I. Mechnikov North-Western State Medical University, Ministry of Health of Russia, 47 Piskarevskii prospect, 195067 St. Petersburg, Russia
[3] N. A. Semashko Nizhny Novgorod Regional Clinical Hospital, 190 Rodionova Str., 603126 Nizhny Novgorod, Russia
[4] Rauchfuss Children's City Multidisciplinary Clinical Center for High Medical Technologies 8 Ligovsky Ave., 190961 St. Petersburg, Russia

For citation: *Ionas S. Simutis, Alexey Yu. Yakovlev, Yurij V. Levadnev, Maria A. Saveleva, Kristina S. Blitsõn, Roman S. Perefilev, Andrey Yu. Smorkalov.* Comparative Assessment of Equivalence of the Post-Operative Use of Two Amino Acid Solutions. *Obshchaya Reanimatologiya = General Reanimatology.* 2026; 22 (2): 15–28. https://doi.org/10.15360/1813-9779-2026-2-2687 [In Russ. and Engl.]

***Correspondence to:** Ionas S. Simutis, simutis@mail.ru; Maria A. Saveleva, aritnnru@list.ru; Kristina S. Blitsõn, kblitzine@gmail.com

Summary

Objective: to compare the nutritional and metabolic effects of two amino acids-containing solutions, differed in amino acid profiles and sorbitol presence, when employed as a part of standardized combined post-operative nutritional support in patients undergoing surgery for abdominal cancer.

Materials and Methods. A prospective randomized study was conducted in two specialized hospitals. The study included 120 nutritionally stable patients aged 18–80 with stage I–III colorectal tumors and ASA class II–III anesthetic risk (mean BMI 25.3–27.6 kg/m²), who underwent elective abdominal surgeries and required parenteral administration of protein-carbohydrate nutrition solution (PCNS) for at least 5 days. Patients were randomly assigned into two groups for receiving PCNS formulations Amiparcenin or Aminoven formulated at 10-percent concentration (60 patients, each group). Both regimens involved administering an amino acid solution at 10 ml/kg/day in combination with a 10% dextrose solution at 10 ml/kg/day, alongside with early enteral feeding. The amino acid and nutritional profiles were assessed before initiation of nutritional support (T0), on the 2nd (T1), and 5th (T2) postoperative days. Key indicators included the sum of branched-chain amino acids (BCAA_sum), the sum of aromatic amino acids (AAA_sum), the ratio of BCAA/AAA, the integral indicator of amino acids in the urea cycle (UreaCycle_sum), and index ratios of ornithine to citrulline, arginine to ornithine, and arginine to citrulline. Additionally, total protein, albumin, nitrogen balance, bioimpedance indicator of active cellular mass (BCM), creatinine, liver function markers, and electrolyte profiles were analyzed. To evaluate clinical equivalence, a two one-sided tests (TOST) analysis was employed with pre-defined limits of clinically acceptable difference (△) for each parameter.

Results. By day 5, both groups showed statistically significant changes in total protein and albumin levels, reflecting the transition from the early catabolic phase and the impact of nutritional support; no intergroup differences were observed for these parameters, and the TOST analysis confirmed their equivalence within the predefined limits of △. The branched-chain amino acids (BCAA_sum) level increased from T0 to T1 and then stabilized at T2 in both groups; the factors «group» and the «group×period» interaction were not significant ($p = 0.285$ and $p = 0.362$, respectively), however, the equivalence of absolute BCAA_sum values at T2 with a narrow △ = 10 µmol/L was not confirmed (p-TOST > 0.05). For AAA_sum, differences were documented based on the «group» factor ($p = 0.035$) and the interaction «period×group» ($p = 0.0099$), with alignment of absolute values at T2. The ratio of BCAA/AAA and the index indicators of the urea cycle (Orn/Cit, Arg/Orn, Arg/Cit) remained stable, with no intergroup differences, and met the equivalence criteria throughout all observation periods. According to bio-impedance analysis, the Amiparcenin group showed a more significant increase in active cell mass (p by Friedman = 0.00001; intergroup p at T1 = 0.0048, at T2 = 0.00014), while the Aminoven group did not show significant dynamics; moreover, the TOST analysis with a wide △ showed formal equivalence in BCM. Creatinine, urea, transaminases, and electrolyte levels remained comparable between the groups and were within clinically acceptable ranges; equivalence for these parameters was confirmed.

Conclusion. In the early postoperative period, Amiparcenin and Aminoven 10% solutions provide comparable amino acid and nutritional supply, and biochemical effects as a part of standardized combined nutritional support in patients with abdominal cancers. The studied regimens met equivalence criteria for most essential amino acid indicators (including BCAA/AAA), markers of inflammation, protein metabolism, liver and kidney function, and electrolyte balance. The differences found in absolute values of BCAA_sum, AAA_sum, UreaCycle_sum, and malondialdehyde (MDA) do not translate into clinically significant shifts during the first 5 days post-surgery.

Keywords: amiparcenin; aminoven; parenteral nutritional support; amino acid solutions; abdominal cancer surgery; nitrogen balance; amino acid profile

Conflicts of Interest. The authors declare no conflicts of interest.

Financial Support. The study was conducted with the support of the manufacturer company LLC «Medical Leasing Consulting», which provided the studied drugs (Amiparcenin and Aminoven 10%) and offered financial support for organizing laboratory research and publishing the article. The sponsor did not participate in designing of the study protocol, data collection and statistical processing, analysis of the results, or manuscript writing.

Information about the authors:

Ionas S. Simutis: https://orcid.org/0000-0002-2537-0142
Alexey Yu. Yakovlev: https://orcid.org/0000-0002-4616-5711
Yurij V. Levadnev: https://orcid.org/0000-0003-4087-9462
Maria A. Saveleva: https://orcid.org/0009-0008-5667-115X
Kristina S. Blitsõn: https://orcid.org/0000-0002-2347-0123
Roman S. Perefilev: https://orcid.org/0000-0002-7059-7493
Andrey Yu. Smorkalov: https://orcid.org/0009-0009-4951-8533

Introduction

For most patients with gastrointestinal neoplasms, nutritional deficiency and cachexia at the time of hospitalization are not a theoretical risk but a reality. According to international and national studies, 30–70% of cancer patients experience weight loss, muscle tissue loss, and metabolic disorders, which are associated with an increased incidence of postoperative complications, prolonged hospital stays, and worsened prognosis [1–4].

ESPEN guidelines on nutrition for cancer patients, clinical nutrition in surgery, ESMO clinical recommendations, and domestic documents emphasize that assessing nutritional status and its correction should be considered a mandatory part of the standard management of patients with gastrointestinal neoplasms [1–3, 5–9]. They highlight the necessity of early initiation of nutrition, prioritizing the enteral route while adding a parenteral component when it is not possible to meet the target protein and energy intake solely through the gastrointestinal tract.

A combined approach (enteral + parenteral nutrition) is considered a rational strategy when it is expected that enteral nutrition alone in the initial days will not cover ⩾ 50–60% of protein and energy needs, or in the presence of high nutritional risk [5–9]. In such situations, the parenteral component provides the opportunity to «catch up» on amino acids and calories while the enteral route is limited.

A key component of the protocol parenteral part is the amino acid solution. It determines the specific set of amino acids that the patient actually receives, how the amino acid profile of the plasma changes, and how effectively the body can compensate for surgical stress. The composition of standard and specialized mixtures (including nitrogen content, the ratio of branched-chain and aromatic amino acids, the presence of arginine, histidine, sulfur-containing amino acids, etc.) and their potential impact on outcomes are discussed in detail in the ESPEN reviews and guidelines on parenteral nutrition and perioperative management [10–13].

A particular significance is given to the Fisher ratio — the ratio of branched-chain amino acids to aromatic amino acids (BCAA/AAA). It has been shown that a decrease in this ratio in liver cirrhosis is associated with the risk of hepatic encephalopathy and an unfavorable prognosis, while its normalization is considered a desirable outcome of nutritional therapy [14, 15]. In this regard, BCAA-enriched solutions are being actively introduced for patients with severe liver failure; however, for surgical patients without decompensated liver function, standard amino acid mixtures remain the cornerstone of therapy [5, 10–15].

Despite the large amount of data on nutrition for cancer patients in general, the question of how the choice of a specific standard amino acid solution affects the amino acid profile in plasma and nitrogen metabolism in surgical patients has been studied only to a limited extent. There are individual randomized studies that compared different amino acid compositions in critically ill patients (neurosurgery, bone marrow transplantation, neonatology) with an assessment of the amino acid profile, nitrogen balance, and clinical parameters [12–19]. However, most of these studies either focus on specialized formulas (BCAA or glutamine-enriched solutions) or are dedicated to comparing routes of administration and conventional protocols (enteral vs. parenteral, premixes vs. compounded mixtures) [5, 12, 13, 19–21]. Direct studies on comparability of the clinical and biochemical effects of standard amino acid solutions in the context of strictly standardized combined nutritional support f or surgical cancer patients are virtually nonexistent.

An additional issue is that in clinical practice, various standard amino acid solutions, differing in the number of amino acids, their ratios, and the presence or absence of non-protein calories (such as sorbitol), are often used interchangeably as components of parenteral nutrition [10–12, 22]. However, the evidence base supporting their equivalence in key amino acid and nutritional parameters is extremely limited. Modern reviews emphasize that the choice of amino acid formula for parenteral nutrition (PN) is largely based on theoretical conside-

rations and collateral data, with few well-designed equivalence (or non-inferiority) trials of different standard solutions conducted [14, 15, 21, 23].

In this regard, it is relevant to conduct a study that does not claim pharmacokinetic bioequivalence of two formulations, but rather assesses the equivalence of the clinical and biochemical effects of two standard amino acid solutions that differ in composition and the presence of an additional energy substrate, under conditions of strictly standardized combined nutritional support in a homogeneous group of patients with colorectal neoplasms.

The aim of this study is to evaluate, based on key amino acid, biochemical, and bioimpedance indicators, how comparable the nutritional and metabolic effects of the two amino acid solutions, which differ in their amino acid profiles and the presence of sorbitol, are when used as part of standardized combined postoperative nutritional support in patients undergoing surgery for abdominal cancer.

Materials and Methods

Study Design. A prospective, randomized, controlled study was conducted to assess the clinical and biochemical comparability of two amino acid solutions for parenteral nutrition. The study involved two specialized hospitals located in Saint Petersburg and Nizhny Novgorod. The enrollment period was from July to December 2025.

The study protocol was approved by the local ethics committee of the L. G. Sokolov Northwest District Scientific Clinical Center of the Federal Medical-Biological Agency of Russia (protocol No. 4 dated May 22, 2025) and was agreed upon at the inter-center level. The study complied with the principles of the Helsinki Declaration and Good Clinical Practice (GCP) guidelines. Written informed consent was obtained from all patients. The study protocol was not registered in publicly accessible clinical trial registries, which was considered a methodological limitation.

After screening and signing the informed consent, patients were randomized into two groups based on the assignment of either Aminoven 10% or Amiparcenin.

- Aminoven group (the control group);
- Amiparcenin group (the study group).

The ratio was 1:1. The random allocation sequence was generated by an independent statistician using a computer-generated list. To implement the randomization, sealed opaque numbered envelopes were used, which were opened only after the patient was finally included and provided informed consent.

The sample size (a minimum of 120 patients, with 60 in each group) was calculated in advance based on the primary endpoint — the BCAA/AAA ratio on the 5th day after surgery (T2). The planning assumed an expected mean BCAA/AAA ratio of around 3.0 in both groups, a standard deviation of approximately 0.5, and a clinically acceptable difference interval $\triangle = \pm 0.3$ (about ±10% of the mean). With a significance level of $\alpha = 0.05$ and a power of $1-\beta = 0.90$, the required sample size was at least 54 patients in each group; considering possible dropout from the per-protocol population, the target size was increased to 60 patients per group (a total of 120 patients).

The flowchart of patient screening, randomization, follow up, and inclusion in various analysis populations is presented in Fig. 1.

Inclusion Criteria. Patients were included if they met all of the following criteria:

1. Age between 18 and 80 years.
2. Confirmed stage I–III colorectal neoplasm.
3. Elective radical or debulking surgery on the gastrointestinal tract.
4. Anesthetic risk classified as II–III according to the American Society of Anesthesiologists (ASA) scale.
5. Surgical anesthetic risk according to the P POSSUM scale greater than 5%.
6. Expected duration of combined nutritional support of at least 5 days due to the inability or insufficient effectiveness of purely enteral nutrition (in accordance with current clinical guidelines for perioperative nutritional support [1–3,5–11]).
7. Signed informed consent.

Exclusion criteria. Patients were excluded from the study or from the per protocol analysis if they had:

- refractory cachexia (9–12 scores on the 2018 cachexia staging scale [2]);
- stage IV cancer;
- subcompensated or decompensated diabetes mellitus;
- significantly reduced glomerular filtration rate (< 60 mL/min);
- liver failure in a sub- or decompensated stage;
- congestive heart failure classified as NYHA functional class III–IV;
- implanted pacemaker;
- refusal to participate in the study.

During the follow-up period, patients were excluded from the per protocol analysis if they developed:

- pulmonary embolism, acute myocardial infarction, or acute cerebrovascular accident;
- acute gastrointestinal bleeding;
- pneumothorax;
- acute kidney injury;
- severe infectious complications occurring within the first 5 days post-surgery.

Randomized patients who initiated treatment but were excluded for the specified reasons were retained in the ITT population but were not included in the PP analysis.

Nutritional support and the intervention under investigation. All patients received combined nutritional support—a combination of enteral and parenteral nutrition—in accordance with the recommendations of the European Society for Clinical Nutrition and Metabolism and domestic clinical guidelines [1–3, 5–11]. The parenteral component was considered an adjunct to early enteral nutrition rather than as total parenteral nutrition.

Calculation of nutritional needs. Ideal body weight was calculated using the Broca formula (weight, kg = height, cm – 100). Daily requirement for amino acids: 1.2 g/kg of ideal body weight. Daily energy requirement: 25 kcal/kg of ideal body weight. Contribution of protein: 4 kcal per 1 g of amino acids.

The remaining energy was distributed between carbohydrates and fats, adhering to recommended infusion rates (for glucose — no more than 0.5 g/kg per hour, for fat emulsions — no more than 0.11 g/kg per hour) [1–3, 5–11].

Parenteral component. In the Amiparcenin group, patients received an amino acid solution (11 amino acids, amino acid concentration about 9.1%, additional energy source — sorbitol 50 g/L, =200 kcal/L) at a dose of 10 ml/kg/day (averaging 500–700 ml/day), which corresponded to approximately 1.0–1.1 g of amino acids/kg/day. The solution was primarily administered through a central venous catheter at a rate not exceeding 1 ml/min, simultaneously with a 10% dextrose solution at 10 ml/kg/day.

In the Aminoven 10% group, patients received a standard amino acid solution (15 amino acids, amino acid concentration 10%, without additional non-protein calories) at a dose of 10 ml/kg/day (also = 1.0–1.1 g of amino acids/kg/day) and a 10% dextrose solution at 10 ml/kg/day. Additional non-protein calories in both groups were primarily provided through enteral nutrition; when necessary, fat emulsions could be used at the discretion of the attending physician, but they were not the subject of comparative analysis in this study. This means that the use, dosage, and type of fat emulsions were not controlled by the protocol, which may be considered an additional uncontrolled factor that could affect energy balance, nitrogen metabolism, and dynamics of body cell mass.

Enteral component. Enteral nutrition (via nasointestinal tube) was generally initiated on the following day after surgery. The volume, concentration, and daily dose of the standard nutritional mixture were gradually increased until at least 70% of the calculated daily protein and energy requirements were met [1–3, 5–11].

Assessment of effectiveness. The following indicators were evaluated:

1. Amino acid profile:

- Total branched-chain amino acids (BCAA_sum: leucine, isoleucine, valine);
- Total aromatic amino acids (AAA_sum: phenylalanine, tyrosine, tryptophan);
- Ratio of BCAA to AAA (Fisher's ratio) [14,15];
- Indicators of the urea cycle amino acids: ornithine, citrulline, arginine; composite indicator UreaCycle_sum and index ratios of ornithine/citrulline, arginine/ornithine, arginine/citrulline.

These indices are traditionally used in cases of liver failure, but we considered them more broadly—as integral markers of amino acid balance and nitrogen metabolism, applicable in surgical patients without severe liver decompensation [14–16].

2. Nutritional status and body composition:

- Bioelectrical impedance analysis (DIAMANT device, Russia): body cell mass (BCM).

Among the various parameters of bioelectrical impedance analysis, we pre-selected body cell mass as the primary bioelectrical impedance endpoint, as BCM is most consistently associated with the risk of complications and survival in cancer patients [4,24]. This allowed us to prioritize the analysis and avoid excessive multiplicity of comparisons.

3. Laboratory and clinical parameters:

- total protein, albumin;
- creatinine, cystatin C;
- AST, ALT, De Ritis ratio, bilirubin;
- C-reactive protein;
- nitrogen balance based on daily nitrogen output with urea.

All parameters were collected at three reference time points: before initiation of nutritional support (T0), on the second (T1), and fifth (T2) postoperative days.

Primary endpoints:

1. BCAA_sum;
2. AAA_sum;
3. BCAA/AAA ratio;
4. C-reactive protein (CRP) concentration.

The primary endpoint selected for sample size calculation and formal equivalence analysis is the BCAA/AAA ratio at day 5 (T2).

Secondary endpoints: protein metabolism indicators (total protein, albumin), BCM, nitrogen balance, liver and kidney function markers, electrolytes, and composite and index indicators of the urea cycle.

Populations for analysis:

- Intention to treat (ITT): all 120 randomized patients were analyzed according to the initial randomization.
- Per protocol (PP): patients who completed the protocol without significant deviations and received the parenteral component of combined nutritional support for at least 5 days.

Equivalence and changes in indicators were primarily analyzed in the PP population; the ITT analysis was used to verify the robustness of the results and to reflect «real-world clinical practice».

Laboratory and instrumental methods used. The plasma amino acid profile was determined

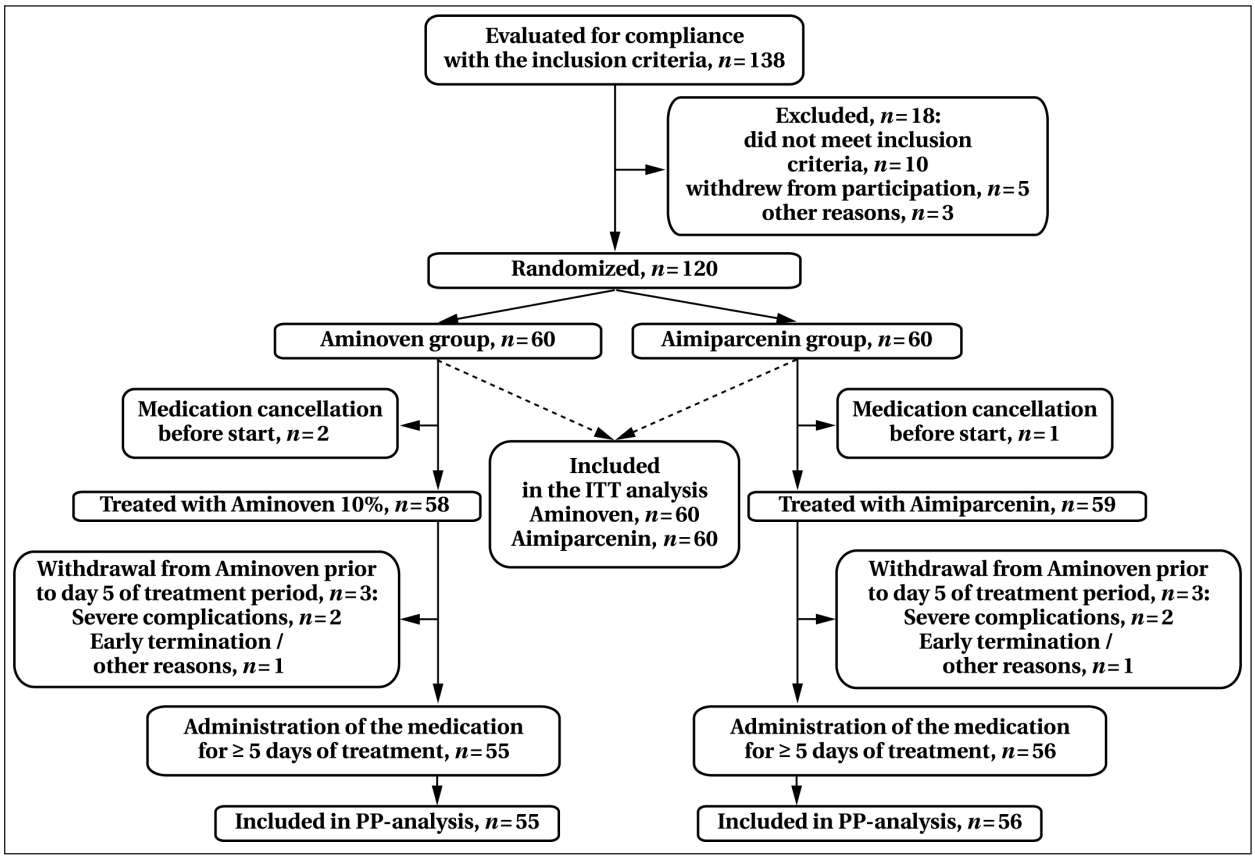


Fig. 1. Scheme for selecting and including patients in the study.

using high-performance liquid chromatography (Agilent 1260 Infinity analyzer, USA). Biochemical parameters (total protein, albumin, creatinine, urea, AST, ALT, bilirubin, CRP, electrolytes) were analyzed on the automated Cobas c702 analyzer (Roche). Cystatin C was measured by immunonephelometry (BN ProSpec, Siemens). Malondialdehyde (MDA) was assessed using a spectrophotometric method with thiobarbituric acid. Body cell mass was evaluated by bioimpedance analysis (DIAMANT, Russia). All methods are validated, with variability ⩽ 8%.

Statistical analysis. We used Statistica version 15 (StatSoft, USA). The normality of the distribution was assessed using the Kolmogorov–Smirnov tests (with Lilliefors correction) and the Shapiro–Wilk test. Normally distributed data were presented as *M*±*SD* with a 95% confidence interval; non-normally distributed data were presented as *Me* [*Q1*; *Q3*]. To compare independent groups, we used the Student's *t*-test or the Mann–Whitney *U* test; for paired measurements, we used the paired *t*-test or the Wilcoxon test.

For analyzing changes over time (T0, T1, T2), we applied repeated measures ANOVA or the Friedman test. When there was overall significance, we conducted pairwise comparisons between the reference time points using the paired t-test or the Wilcoxon test with the Holm-Bonferroni correction for multiple comparisons.

The influence of the «group» and «period» factors and their interaction («group×period») on BCAA_sum and AAA_sum indicators, the BCAA/AAA ratio, and the level of C-reactive protein was assessed using repeated measures ANOVA, calculating the partial eta squared (partial η^2).

To account for potential confounding factors (age, sex, baseline biochemical parameters), additional correction was performed in several models (ANCOVA/repeated measures models including covariates).

Analysis of equivalence (TOST). To assess the equivalence between groups regarding BCAA/AAA, index parameters of the urea cycle, nitrogen balance, creatinine, total protein, albumin, liver function tests, and electrolytes, a Two One-Sided Tests (TOST) approach was employed. For each parameter, a clinically acceptable range of difference [–△; +△] (zone of clinical insignificance) was established prior to the study. Equivalence was considered established if:

• The 90% confidence interval of the mean difference (or the ratio of geometric means for log-transformed parameters) was entirely within the range [–△; +△];

• Both one-sided TOST tests had $p < 0.05$.

For the composite amino acid parameters (BCAA_sum, AAA_sum, UreaCycle_sum), relative △expressed as percentages were used, while for

electrolytes, absolute △ were applied (Na^+ ±3 mmol/L, K^+ ±0.3 mmol/L, Cl^- ±3 mmol/L, Ca^{2+}±0.1–0.15 mmol/L). The results of the TOST analysis were compiled into a separate table (Table 3), indicating the effect, 90% CI, and the conclusion of «equivalent / not equivalent».

Missing data. Missing values for key indicators and reference time points were sporadic. ANOVA and the Friedman test were used only for patients with a complete set of data for the corresponding indicator. Multiple imputation was not applied. The potential impact of missing data was addressed in the «Study Limitations» section.

Differences were considered statistically significant at $p < 0.05$.

Results

Patients' baseline characteristics. A total of 120 patients were included, with 60 individuals in each group. Patients' nutritional status was preserved with average BMI in the Amiparcenin group of 27.64 ± 3.59 kg/m², and in the Aminoven group — of 25.34 ± 3.84 kg/m², signifying overweight. No significant changes in biochemistry panel parameters were recorded at baseline. The Amiparcenin and Aminoven groups were comparable in terms of age, sex, tumor location and stage, anesthetic risk level, as well as the extent and duration of surgery (Table 1).

At baseline (T0), the measurements of body weight, body mass index, bioimpedance parameters (including body cell mass), total protein levels, albumin, creatinine, and liver function showed no clinically significant differences between the groups (Table 1).

Based on the amino acid profile at baseline, no differences were found in the total amount of branched-chain amino acids (BCAAs) and the ratio of BCAA to aromatic amino acids (AAA); the total AAA in the Amiparcenin group was lower than in the Aminoven group, which subsequently affected the dynamics of this indicator (Table 2).

Amino acid profile. The overall dynamics of relative increases in amino acids plasma levels following the administration of various amino acid solutions are presented in heat maps (Fig. 2) and summary graphs (Fig. 3). This indicates a high degree of comparability of the amino acid effect between two regimens.

The total of branched-chain amino acids (BCAA_sum, Fig. 3, *a*). Following the initiation of combined nutritional support, BCAA_sum increased in both groups by T1, with a slight decrease or stabilization by T2, indicating a consistent trend in both groups.

Within-group analysis (Friedman test):

- Aminoven: $p = 0.2285$;
- Amiparcenin: $p = 0.0515$.

Intergroup differences in BCAA_sum at each reference time-point were not statistically significant (T0: $p = 0.110$; T1: $p = 0.379$; T2: $p = 0.740$). Repeated measures ANOVA confirmed the effect of time ($p = 0.0209$) with no significant «group» or «group × period» interaction effects.

The TOST analysis with a strict equivalence interval (△ = 10 μmol/L) did not confirm two regimens equivalence in terms of absolute BCAA_sum values at T2, despite the similar trends observed.

The total of aromatic amino acids (AAA_sum, Fig. 3, *b*). The dynamics of AAA_sum varied across groups. In the Amiparcenin group, a pronounced overall dynamic was recorded according to the Friedman test ($p = 0.00188$), showing a trend towards

Table 1. Patients' baseline characteristics.

Parameters	Parameter values in the groups		*p*
	Amiparcenin, *n* = 60	Aminoven, *n* = 60	
Age, years	66.8 ± 6.4	60.6 ± 13.8	0.002
Males, *n* (%)	37 (61.7)	24 (40.0)	0.028
BMI	27.64 ± 3.59	25.34 ± 3.84	0.34
Neoplastic site: benign tumor of the colon, *n* (%)	4 (6.7)	0 (0.0)	0.115
Neoplastic site: sigmoid and rectum, *n* (%)	14 (23.3)	13 (21.7)	0.115
Neoplastic site: colon (proximal), *n* (%)	42 (70.0)	47 (78.3)	0.115
Stage: I	19 (31.7)	19 (31.7)	0.976
Stage: II	22 (36.7)	23 (38.3)	0.976
Stage: III	19 (31.7)	18 (30.0)	0.976
ASA class: II	40 (66.7)	38 (63.3)	0.848
ASA class: III	20 (33.3)	22 (36.7)	0.848
Duration of surgery, min	195.6 ± 30.4	185.8 ± 42.4	0.151
Epidural analgesia, *n* (%)	42 (70.0)	40 (66.7)	0.844
Body cell mass (BCM) T0, kg	47.43 ± 2.88	48.05 ± 4.47	0.371
Total protein, g/L	56.77 ± 8.45	59.80 ± 5.35	0.221
Albumin, g/L	33.12 ± 5.32	31.80 ± 3.52	0.113
Creatinine, μmol/L	92.45 ± 29.26	102.83 ± 33.19	0.072
AST, U./L	32.38 ± 12.05	35.53 ± 17.92	0.261
ALT, U./L	37.27 ± 10.62	40.73 ± 17.47	0.192
Bilirubin, μmol/L	10.57 ± 4.55	16.04 ± 7.70	0.000
De Ritis Ratio, CU	0.87 ± 0.28	0.92 ± 0.34	0.371

Table 2. Baseline total amino acid values (T0) and p-values of intergroup differences (Mann–Whitney test).

Parameters	Parameter values in the groups, *M*±*SD*		*p* (T0)
	Aminoven	Amiparcenin	
BCAA_sum	384.8±103.7	327.0±108.8	0.1094
AAA_sum	138.3±42.0	103.0±31.2	0.208
BCAA_AAA_ratio	2.9±0.9	3.3±0.8	0.2599
UreaCycle_sum	139.7±35.8	152.3±67.3	0.9527

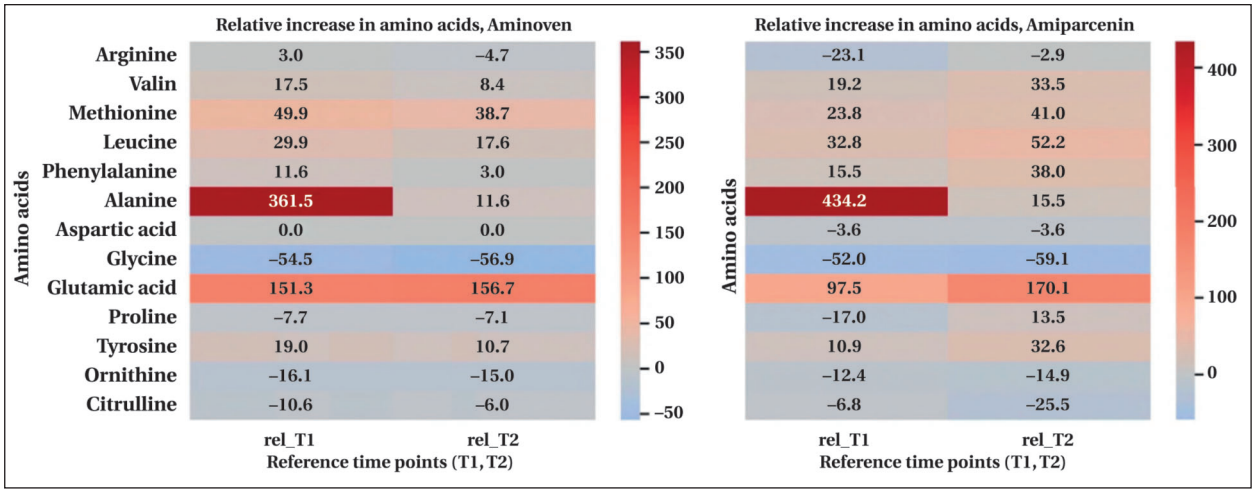


Fig. 2. Heat maps of average relative increases in amino acids (% from T0) in the Aminoven and Amiparcenin groups.

an increase at T1 and a significant rise at T2 compared to T0 and T1. In the Aminoven group, changes in AAA_sum were less obvious and did not reach statistical significance (p=0.09697).

Intergroup comparisons showed:

- At T0, AAA_sum was lower in the Amiparcenin group (p=0.019);
- At T1, the differences persisted (p=0.006);
- By T2, the values were closer together, and no statistically significant difference was observed (p=0.338).

Repeated measures ANOVA revealed a significant effect of the «group» and «period» factors and their interaction, reflecting different trajectories of AAA_sum changes, followed by the alignment of absolute values by the fifth day. The TOST analysis did not confirm the equivalence of absolute AAA_sum levels at early stages, but by T2, the differences diminished and were not accompanied by noticeable clinical effects (Table 3).

The ratio of branched-chain and aromatic amino acids (BCAA/AAA, Fig. 3, *c*). The BCAA/AAA

Table 3. Results of the Amiparcenin and Aminoven groups equivalence analysis (TOST) (PP population, *n*=120).

Parameters	Period	Δ*	Conclusion
BCAA_sum	T2	±10 μmol/L	Not confirmed
AAA_sum	T0, T1, T2	±15%	Not confirmed
BCAA/AAA ratio	T0, T1, T2	±15%	Confirmed
UreaCycle_sum	T2	±15%	Not confirmed
Orn/Cit, Arg/Orn, Arg/Cit	T2	±15%	Confirmed
C-reactive protein (CRP), GMR	T0, T1, T2	±25%	Confirmed
Total protein	T2	±10%	Confirmed
Albumin	T0, T1, T2	±10%	Confirmed
Creatinine	T2	±15%	Confirmed
Cystatin C	T0, T1	±20%	Confirmed
Urea	T2	±20%	Confirmed
Nitrogen balance(△T2–T0)	—	±20%	Confirmed
Body cell mass (BCM)	T1, T2	±10 CU	Confirmed
Na^+, K^+, Ca^{2+}, Cl^-	T2	±3 / ±0.3 / ±0.1 / ±3	Confirmed
Malondialdehyde (MDA)	T0, T1, T2	±20%	Not confirmed

Note. Orn/Cit, Arg/Orn, Arg/Cit — ornithine/citrulline, arginine/ornithine, arginine/citrulline. GMR — geometric mean ratio. * — Specific △ values for each measure were set prior to the study and are detailed in the «Statistical Analysis» section. All *p* values for TOST were reported according to the statistician's report; the TOST analysis was conducted on a combined sample of 120 patients (PP analysis — for the corresponding measure). For BCM, the report used a broad clinically acceptable △ limit of 10 arbitrary/conventional units, reflecting inter-device and inter-patient variability.

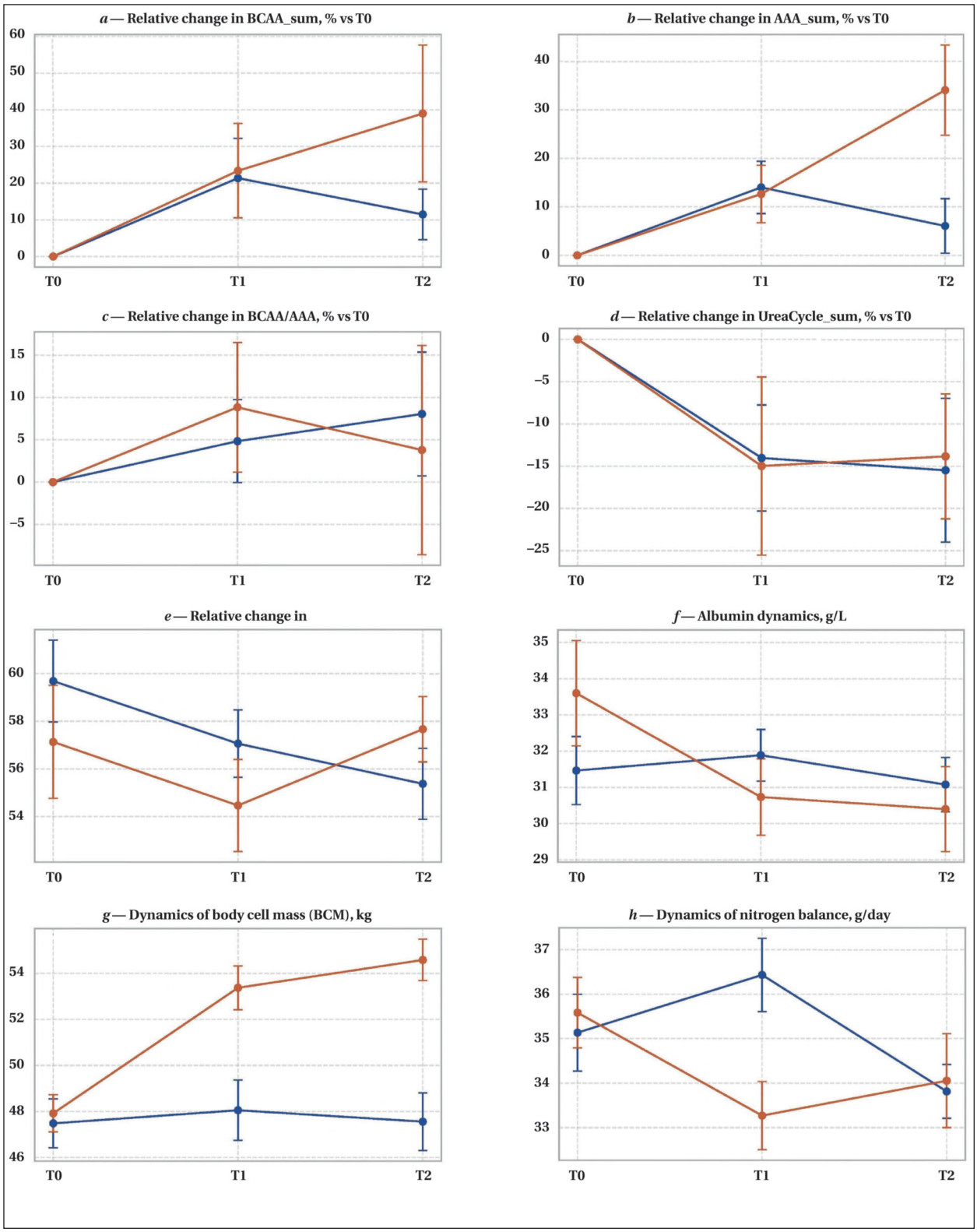
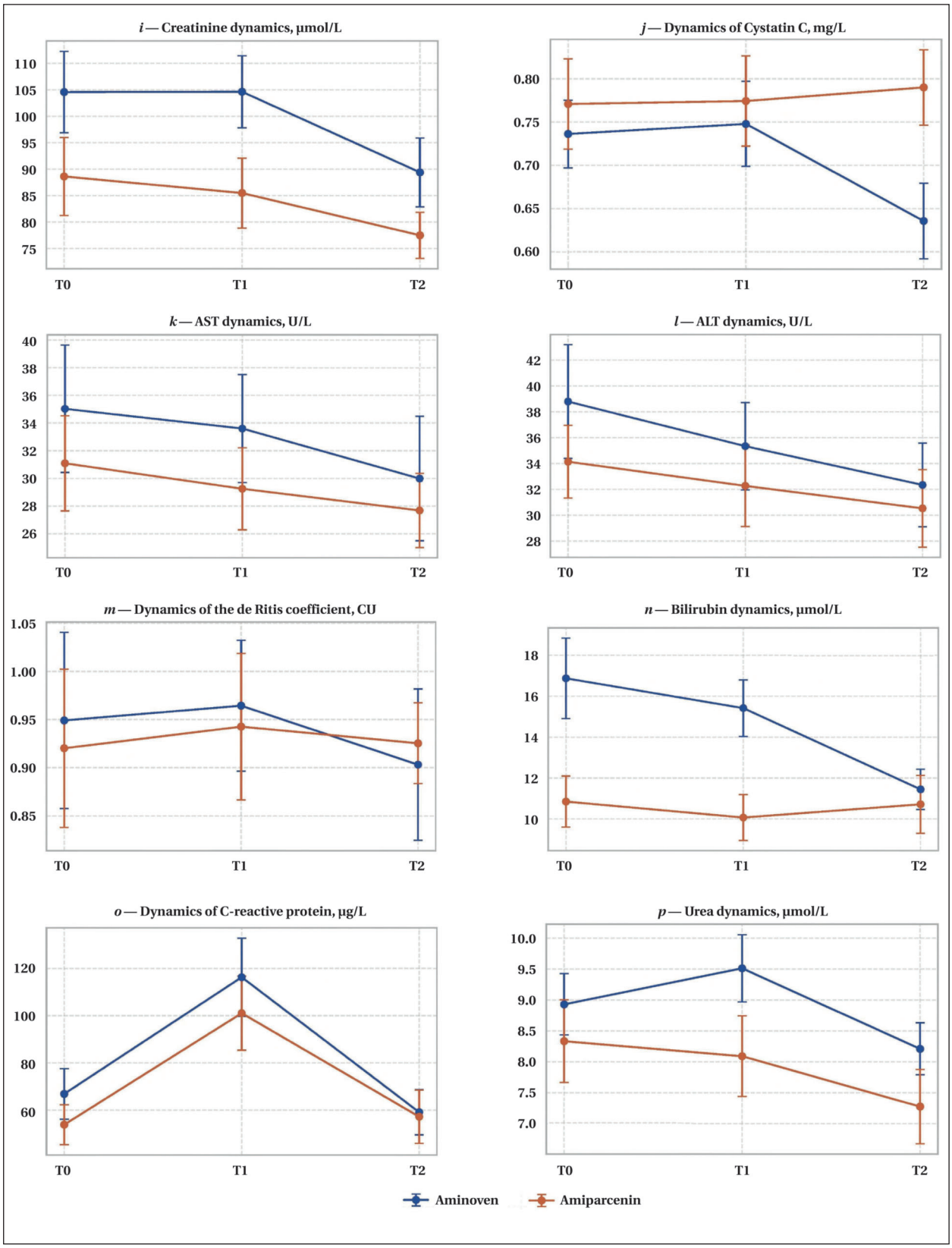


Fig. 3. Dynamics of indicators in the Aminoven and Amiparcenin groups.
Note. The X-axis represents the reference time points of the study. Indicators: amino acid profile — *a–d*; nutritional status and body composition — *g*; kidney function — *i, j*; liver function — *k–n*; other laboratory and clinical markers — *e, f, h, o, p*.

ratio (Fisher's coefficient) remained within the range typical for patients without severe liver failure at all reference time points. According to Friedman's criterion, no significant changes in the coefficient were observed in any group ($p > 0.3$); no intergroup differences were found either ($p > 0.2$ at each reference time point). Repeated measures ANOVA did not show a significant effect of the «group,» «period,» and «group × period» factors on Fisher's coefficient.



Continuation of Fig. 3.

The TOST analysis demonstrated that the BCAA/AAA ratio at all reference time points met the equivalence criteria for two regimens: 90% CI of the difference between groups completely fell within the pre-defined interval [−△; +△].

Urea cycle indicators (UreaCycle_sum, Fig. 3, *d*). The composite of UreaCycle_sum changed moderately in both groups, without a clear unidirectional trend according to Friedman's criterion. However, differences in absolute values of UreaCycle_sum

were observed between the groups, and the TOST analysis did not confirm equivalence for this composite measure.

The ratios of ornithine/citrulline, arginine/ornithine, and arginine/citrulline:

- did not change significantly according to Friedman's criterion;
- did not differ between groups at reference time points;
- met equivalence criteria according to TOST in all reference time points.

Considering comparable levels of creatinine and nitrogen balance, the differences in UreaCycle_sum were regarded as having no clinically significant impact on nitrogen utilization.

Nutritional indicators and body composition.

Total protein and albumin (Fig. 3, *e, f*). By the fifth postoperative day, the concentration of total protein and albumin significantly changed compared to baseline values in both groups.

In the Aminoven group, total protein and albumin increased across all pairs of reference time points (T0–T1, T1–T2, T0–T2), with $p<0.001$ for most comparisons. In the Amiparcenin group, the dynamics were comparable, with statistically significant increases between all pairs of reference time points.

No intergroup differences in absolute values of total protein and albumin were found at each reference time point. The TOST analysis indicated that the differences between the regimens for these indicators were within the pre-defined range of clinically acceptable differences, and equivalence was confirmed (Table 3).

Body cell mass according to bioimpedance analysis (Fig. 3, *g*). In the Amiparcenin group, bioimpedance analysis showed a clear positive trend in body cell mass:

- Friedman criterion: $p=0.00001$;
- Pairwise comparisons (Wilcoxon) confirmed the increase in BCM between T0 and T1, T1 and T2, and between T0 and T2 ($p<0.01$).

In the Aminoven group, the overall dynamics of BCM according to the Friedman criterion were less pronounced and did not reach statistical significance ($p=0.18435$), although there was a trend toward its increase.

When comparing between groups, the baseline BCM values were comparable ($p=0.770$), but on days 2 and 5, the values in the Amiparcenin group became significantly higher (T1: $p=0.004816$; T2: $p=0.000139$). Additionally, TOST analysis with a wide $\triangle$ showed formal equivalence in BCM between the groups, indicating that even the more significant BCM increase in the Amiparcenin group remained within the predefined range of clinically acceptable differences.

Nitrogen balance (Fig. 3, *h*). The nitrogen balance in the Amiparcenin group significantly improved over five days (Friedman criterion $p=0.00001$), while the Aminoven group showed a statistically insignificant trend ($p=0.20584$). In intergroup comparisons:

- At T0, no differences in nitrogen balance were observed ($p=0.6726$);
- At T1 and T2, significant differences were found ($p=0.0392$ and $p=0.001556$, respectively), with more favorable values in the Amiparcenin group. TOST analysis indicated that the difference in changes $\triangle$(T2–T0) between the groups remained within the predefined clinical range, and the equivalence in nitrogen balance was generally maintained (Table 3).

Kidney function. The concentrations of creatinine and cystatin C in both groups remained within reference values and did not show a trend toward significant increase by the fifth day of follow up (Figure 3, *i, j*). No intergroup differences were noted for these parameters. The TOST analysis confirmed the equivalence of the effects of both regimens on kidney function markers at each reference time point (Table 3).

Liver function and electrolytes. Liver function markers (AST, ALT, De Ritis ratio, bilirubin concentration, Figure 3, *k, l, m, n*) moderately changed in the early postoperative period, but overall remained within acceptable limits and did not differ between groups. The TOST analysis showed that the values of these markers in both regimens at all reference time points were within clinically acceptable ranges, indicating no significant hepatotoxic effect from either solution.

Equivalence was also statistically confirmed for sodium, potassium, calcium, and chloride concentrations at all reference time points within predefined clinically relevant limits $\triangle$ (TOST, $p<0.01$; Table 3).

Discussion

The main practical question in the context of this research is not so much identifying the fundamental differences between two specific formulations, but rather assessing whether different standard amino acid solutions (with variations in amino acid profiles and the presence or absence of sorbitol) can be regarded as comparable in terms of clinical and biochemical effects components of combined nutritional support for patients with abdominal cancers.

It's important to emphasize that the study predominantly included stable patients with excess body weight (average BMI of 25.3–27.6 kg/m²) and no significant biochemical abnormalities; therefore, the results obtained primarily apply to this category of patients. In a limited number of studies comparing different amino acid formulations (in patients with severe neurosurgical conditions, in post-bone mar-

row transplant patients, and in premature infants), the amino acid profile, nitrogen balance, and specific clinical indicators were analyzed [12, 14–19]. Most contemporary research on parenteral nutrition focuses on comparing routes and regimens (enteral vs. parenteral, premixed vs. compounded mixtures) or on specialized formulations (BCAAs, glutamine, omega-3 enriched formulas) [5, 12, 13, 20, 21]. There are virtually no studies originally designed as equivalence trials of standard amino acid solutions using the TOST approach and predefined clinical △s.

The results obtained are generally consistent with the current recommendations from ESPEN, ESMO, the Ministry of Health of the Russian Federation, and the Federation of Anesthesiologists and Reanimatologists [1–3,5–11], which emphasize that for cancer patients without severe liver failure, the key factors for outcomes are:

- Timely initiation of nutrition (preferably within the first 24 hours after surgery);
- Achieving the target protein and energy intake of nutrients;
- Prioritizing the enteral route with the addition of a parenteral component when it is not possible to meet needs solely through the gastrointestinal tract.

In our study, the amino acid profile and the Fisher ratio (the BCAA/AAA ratio) remained within clinically acceptable ranges and did not differ between groups. This aligns with the concept that, in the absence of liver function decompensation, standard amino acid solutions typically provide an adequate BCAA/AAA ratio, and specialized BCAA-enriched mixtures are primarily warranted for patients with severe liver failure [5, 10–13]. It is important to emphasize that the Fisher ratio was not used as a surrogate for hepatic encephalopathy but rather as an integral marker of amino acid balance and metabolic stress.

Differences in the absolute values of BCAA_sum and AAA_sum between solutions reflect the characteristics of their composition and the baseline amino acid levels, which is expected based on comparative studies [12, 14, 16–19], but did not lead to development of a clinically significant amino acid imbalance. This is supported by the equivalence of the BCAA/AAA ratio and the index indicators of the urea cycle (ornithine/citrulline, arginine/ornithine, arginine/citrulline), as well as comparable values for nitrogen balance and markers of liver and kidney function.

The composite indicator of UreaCycle_sum differed statistically between groups and did not meet the formal criteria for equivalence according to the TOST analysis. However, the index ratios of urea cycle metabolites remained stable and equivalent, while levels of creatinine, urea, and nitrogen balance were comparable. Therefore, this allows to conclude that the observed differences in UreaCycle_sum have no clinically significant impact on nitrogen utilization.

The use of both regimens was accompanied by expected changes in total protein and albumin, characteristic of the early postoperative period and the nutritional support provided, as well as by improvement in nitrogen balance. These data are consistent with the results of randomized studies and meta-analyses demonstrating that adequate perioperative nutritional support (enteral, parenteral, or combined) reduces the rate of complications and length of hospital stay in patients with gastrointestinal neoplasms [4, 5, 11, 21, 22]. Furthermore, the results clarify that within the same combined support protocol, the choice between two standard amino acid solutions differing in compositions and presence of sorbitol does not have a significant impact on clinical and biochemical parameters in patients without severe liver and kidney failure.

A more pronounced increase in body cell mass and a significant improvement in nitrogen balance in Amiparcenin (containing sorbitol) group may indicate a somewhat faster gain in functionally active lean mass and a reduction of catabolism rates in the early postoperative period. Considering that reduced body cell mass and unfavorable bioimpedance indicators are associated with an increased risk of complications and worse survival in patients undergoing cancer surgery [4, 24], this observation appears clinically promising. However, from the perspective of formal TOST analysis, even these differences remain within the pre-defined limits △ for body cell mass, allowing these regimens to be interpreted as clinically comparable regarding this indicator. More extensive and longer studies are needed to assess the impact on «solid/robust» outcomes (Clavien-Dindo complications, survival, quality of life).

The conducted study adds to the limited literature comparing various amino acid compositions and parenteral regimens, often in specialized populations (premature infants, severe neurosurgical patients, patients after bone marrow transplantation) [12, 14, 16–19]. Unlike the referenced studies, this study evaluated the comparability of clinical and biochemical effects of two standard amino acid solutions in a group of adult patients undergoing surgery for abdominal neoplasms, using strictly standardized combined nutritional support protocol and a formal TOST approach.

The limitations of the study include:

- A focus on intermediate biochemical and nutritional indicators over a short follow up period (the first five days post-surgery);
- Lack of direct assessment of long term clinical outcomes (mortality, severe complications according to Clavien-Dindo classification, survival, quality of life);

• Exclusion of certain patients from the per-protocol analysis after randomization due to development of severe complications in the early postoperative period, which may lead to systematic error (attrition bias) and skew the results towards a more favorable outcome, despite conducting an ITT- analysis;

• Absence of prospective registration of the protocol in publicly accessible clinical trial registries;

• Selection of a relatively homogeneous population (stage I–III of the neoplastic progression, without severe comorbid liver and kidney pathology), which limits the extrapolation of results to more severely affected patient categories.

These limitations must be taken into account when interpreting the results and planning further research.

In the absence of specific restrictions, the choice of a particular amino acid mixture will most likely be determined by availability, cost, and logistical factors. In special clinical situations (for example, in cases of severe liver failure, severe cachexia, or multiple comorbidities), it is advisable to tailor the approach and continue the accumulation of data.

Conclusion

In patients undergoing surgery for abdominal neoplasms, standardized combined nutritional support during the early postoperative period including amino acid solutions Amiparcenin and Aminoven 10% is associated with comparable amino acid indices (including the BCAA/AAA ratio) and nitrogen metabolism indicators.

Differences in absolute total concentrations of individual amino acids (BCAA_sum, AAA_sum) and composite metabolites of the urea cycle (Urea-Cycle_sum) do not lead to clinically significant amino acid imbalances or significant changes in liver and kidney function in the early postoperative period.

Both solutions can be considered as interchangeable components of the parenteral part of combined nutritional support for patients undergoing surgery for abdominal neoplasms in the early postoperative period. However, any final conclusion regarding complete clinical equivalence should be approached with caution following lack of control over the use of fat emulsions in this study, which could introduce additional variability in energy and metabolic balance.

References

1. *Arends J., Bachmann P., Baracos V., Barthelemy N., Bertz H., Bozzetti F., Fearon K., et al.* ESPEN guidelines on nutrition in cancer patients. *Clin Nutr.* 2017; 36 (1): 11–48. DOI: 10.1016/j.clnu.2016.07.015. PMID: 27637832.
2. *Arends J., Strasser F., Gonella S., Solheim T. S., Madeddu C., Ravasco P., Buonaccorso L., et al.* Cancer cachexia in adult patients: ESMO Clinical Practice Guidelines. *ESMO Open.* 2021; 6 (3): 100092. DOI: 10.1016/j.esmoop.2021.100092. PMID: 34144781.
3. *Cederholm T., Barazzoni R., Austin P., Ballmer P., Biolo G., Bischoff S.C., Compher C., et al.* ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr.* 2017; 36 (1): 49–64. DOI: 10.1016/j.clnu.2016.09.004. PMID: 27642056.
4. *Burden S.T., Todd C., Hill J., Lai S.* Perioperative nutrition support in patients undergoing gastrointestinal surgery. *Cochrane Database Syst Rev.* 2012; 11: CD008879. DOI: 10.1002/14651858.CD008879.pub2. PMID: 23152265.
5. *Weimann A., Braga M., Carli F., Higashiguchi T., Hübner M., Klek S., Laviano A., et al.* ESPEN guideline: clinical nutrition in surgery. *Clin Nutr.* 2017; 36 (3): 623–650. DOI: 10.1016/j.clnu.2017.02.013.
6. *Arends J., Baracos V., Bertz H., Bozzetti F., Calder P.C., Deutz N.E.P., Erickson N., et al.* ESPEN expert group recommendations for action against cancer-related malnutrition. *Clin Nutr.* 2017; 36 (5): 1187–1196. DOI: 10.1016/j.clnu.2017.06.017. PMID: 28689670.
7. *Singer P., Blaser A.R., Berger M.M.. Alhazzani W., Calder P.C., Casaer M.P., Hiesmayr M., et al.* ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr.* 2019; 38(1): 48–79. DOI: 10.1016/j.clnu.2018.08.037. PMID: 30348463.
8. Министерство здравоохранения Российской Федерации. Периоперационная нутритивная поддержка взрослых пациентов: клинические рекомендации. М.; 2021. Ministry of Health of the Russian Federation. Perioperative nutritional support for adult patients: clinical guidelines. Moscow; 2021. (in Russ.).
9. *Лейдерман И.Н., Грицан А.И., Заболотских И.Б., Мазурок В.А., Поляков И.В., Потапов А.Л., Сытов А.В. с соавт.* Периоперационная нутритивная поддержка. Методические рекомендации Федерации анестезиологов и реаниматологов. *Вестн интенсивн тер им А.И. Салтанова.* 2021; 4: 7–20. *Leiderman I.N., Gritsan A.I., Zabolotskikh I.B., Mazurok V.A., Polyakov I.V., Potapov A.L., Sytov A.V., et al.* Perioperative nutritional support. Clinical practice recommendations of the national «Federation of Anesthesiologists and Reanimatologists». *Ann Crit Care =Vestnik Intensivnoy Terapii im A.I. Saltanova.* 2021; 4: 7–20. (in Russ.). DOI: 10.21320/1818-474X-2021-4-7-20.
10. *Bozzetti F., Forbes A.* The ESPEN clinical practice guidelines on parenteral nutrition: present status and perspectives for future research. *Clin Nutr.* 2009; 28 (4): 359–364. DOI: 10.1016/j.clnu.2009.05.010. PMID: 1952372.
11. *Braga M., Ljungqvist O., Soeters P., Fearon K., Weimann A., Bozzetti F., EPSEN.* ESPEN Guidelines on parenteral nutrition: surgery. *Clin Nutr.* 2009; 28 (4): 378–386. DOI: 10.1016/j.clnu.2009.04.002. PMID: 19464088.
12. *Struijs M.-Ch., Schaible T., van Elburg R.M., Debauche C., te Beest H., Tibboel D.* Efficacy and safety of a parenteral amino acid solution containing alanyl-glutamine versus standard solution in infants: a first-in-man randomized double-blind trial. *Clin Nutr.* 2013; 32 (3): 331–337. DOI: 10.1016/j.clnu.2012.09.001. PMID: 23562219.
13. *Adamkin D.H., McClead R.E. Jr., Desai N.S., McCulloch K.M., Marchildon M.B.* Comparison of two neonatal intravenous amino acid formulations in preterm infants: a multicenter study. *J Perinatol.* 1991; 11 (4): 375–382. PMID: 1770397.
14. Holeček M. Branched-chain amino acids in health and disease: metabolism, alterations in blood plasma, and as supplements. *Nutr Metab (Lond).* 2018; 15: 33. DOI: 10.1186/s12986-018-0271-1. PMID: 29755574.
15. *Plauth M., Bernal W., Dasarathy S., Merli M., Plank L.D., Schütz T., Bischoff S.C.* ESPEN guideline on clinical nutrition in liver disease. *Clin Nutr.* 2019; 38 (2): 485–521. DOI: 10.1016/j.clnu.2018.12.022. PMID: 30712783.
16. *Sun L.-C., Shih Y.-L., Lu C.-Y.. Hsieh J.-S., Chuang J.-F., Chen F.-M., Ma C.-J., et al.* Randomized, controlled study of branched chain amino acid-enriched total parenteral nutrition in malnourished patients with gastrointestinal cancer undergoing surgery. *Am Surg.* 2008; 74 (3): 237–242. PMID: 1837669.
17. *Arvanitakis M., Ockenga J., Bezmarevic M., Gianotti L., Krznarić Ž., Lobo D.N., Löser C., et al.* ESPEN practical guideline on clinical nutrition in acute and chronic pancreatitis. *Clin Nutr.* 2024; 43 (2): 395–412. DOI: 10.1016/j.clnu.2023.12.019. PMID: 38169174.

18. *Hoffer L.J.* Parenteral nutrition: amino acids. *Nutrients*. 2017; 9 (3): 257.
DOI: 10.3390/nu9030257. PMID: 28287411.
19. *Hall J.W.* Safety, cost, and clinical considerations for the use of premixed parenteral nutrition. *Nutr Clin Pract*. 2015; 30 (3): 325–330.
DOI: 10.1177/0884533615578459.
PMID: 25862011.
20. *Tan G.H.C., Chia C.S., Wong J.S.M., Ong W.S., Zhu H.-Y., Ong C.-A.J., Teo M.C.C.* Randomized controlled trial investigating perioperative iimmunonutrition for patients undergoing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). *Ann Surg Oncol*. 2020; 30: 777–789.
DOI: 10.1245/s10434-022-12509-w.
PMID: 36180619.
21. *Yu H.M., Tang C.W., Feng W.M., Chen Q.Q., Xu Y.Q., Bao Y.* Early enteral nutrition versus parenteral nutrition after resection of esophageal cancer: a retrospective analysis. *Indian J Surg*. 2017; 79 (1): 13–18.
DOI: 10.1007/s12262-015-1420-7.
PMID: 28331260.
22. *Ionescu V.A., Gheorghe G., Oprita R., Stanllie M., Dascalu R.-I., Zaharia O., Jinga V., et al.* The outcomes of nutritional support techniques in patients with gastrointestinal cancers. *Gastroenterol Insights*. 2022; 13 (3): 245–257.
DOI: 10.3390/gastroent13030025.
23. *Matthews L., Bates A., Wootton S.A., Levett D.* The use of bioelectrical impedance analysis to predict post-operative complications in adult patients having surgery for cancer: a systematic review. *Clin Nutr*. 2021; 40 (5): 2914–2922.
DOI: 10.1016/j.clnu.2021.03.008.
PMID: 33962360.
24. *Lee G.H., Gho H.J., Lee G., Kim H.G., Wang H.J., Kim B.-W., Lee M.Y., et al.* Bioelectrical impedance analysis for predicting postoperative complications and survival after liver resection for hepatocellular carcinoma. *Ann Transl Med*. 2021; 9 (3): 190.
DOI: 10.21037/atm-20-5194. PMID: 33708817.

Received 25.02.2026
Accepted 24.04.2026