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Interpretation of data in patients with enteral and parenteral nutrition

Research Article

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Abstract: Multivariate statistical analysis is performed using clinical data characterizing the state of patients subject to early enteral (EEN) and pareneteral (PN) nutrition after major gastrointestinal surgery. Several patterns of linkage, between the clinical parameters for both groups of observed patients (with mixed (EEN+PN) and with parenteral nutrition only (TPN)), were found and interpreted. Discriminating indices for the internal grouping of patients were found related to the type of nutrition and the clinical status of the patients. It was found that the mixed (enteral and parenteral) nutrition offers better options for the overcoming of the metabolic stress after the surgery.

Keywords: *Early enteral nutrition • Parenteral nutrition • Multivariate statistics*

1. Introduction

Malnutrition is a clinical syndrome with high frequency (30–60%) among hospitalized patients. It is due to a reduced food intake or to increased food needs, provoked by metabolic stress caused by sepsis, trauma, burns, surgery or malignity. Malnutrition leads to severe deterioration of physiological functions, increased morbidity, mortality, prolonged recovery, and hospital stay and higher associated health care costs.

The main types of nutritional support applied in clinical practice are parenteral nutrition (PN), enteral nutrition (EN) or a combination of both of them [1-3].

Adequate nutritional support in patients with malnutrition or nutrition risk is an important component in the complex treatment. It improves the immune response, accelerates health processes, shortens the time of rehabilitation and hospital expenses and improves the quality of life. The main types of nutrition support applied in the clinical practice are PN, EN and the combination of the two – mixed feeding [1-3].

It is accepted that this is one of the most significant breakthroughs in the field of medicine in the twentieth century due to vastly improved survival rates and quality of life in patients with gastrointestinal malfunctioning as a result of peritonitis, bowel obstruction, short bowel syndrome, and inflammatory bowel disease.

In the 1950s, the first protein hydrolysates and fat emulsions for intravenous application were introduced. Later, a further rapid development of the method took place with an introduction of central total parenteral nutrition (TPN), synthetic α-amino acid solutions, new generations of lipid emulsions and the concept of "all

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in one", accordingly all nutrients were mixed together and infused into one system. Unfortunately, TPN also has several disadvantages. Prolonged application leads to severe trophic changes of the gastrointestinal mucosa associated with bacterial translocation, septic complications and higher hospital costs. All these side effects of TPN can be prevented with early enteral nutritional intervention.

Many clinical investigations show that early postoperative EN improves the postoperative course of treatment. In contemporary practice, early EN (EEN) is a preferable technique of clinical nutrition. The frequency of infectious complications is lower with EEN due to the smaller risk of bacterial translocation and preservation of structural and functional integrity of the gastrointestinal tract. It is tolerated very well by most patients. EEN encounters faster overcome of stressed metabolic response, better immune status and improved quality of life [4-6].

Many formulae with optimal composition are developed for different categories of patients. EN formulae are administered orally or nasal or with percutaneous feeding tubes. Type of nutrition: PN, EN or a combination between both is selected according to the conditions of the digestive and resorptive capacity of the gastrointestinal tract. If this capacity is preserved effectively and there are no contraindications, EN is the method of choice.

Absolute contraindications for EN are any state of shock, acute abdomen, intestinal perforation, mechanical obstruction, and acute gastrointestinal bleeding. Relative contraindications include gastrointestinal atony, and enterocutaneous fistula with high secretion rate [7,8].

According to the previous research, EN appears to be much more beneficial than PN. It is less expensive and offers a lot of advantages: improved intestinal perfusion and maintenance of the mucosal barrier, stimulation of peristalsis and production of gastrointestinal hormones with trophic effects, improvement of immunocompetence as a prophylaxis against infection and sepsis [9].

The aims of the present study are as follows:

1. to evaluate statistically the influence of the nutritional status and postoperative nutritional support on recovery of patients with elective major gastrointestinal surgery;
2. to find relationships between the clinical parameters of the patients subject to different nutritional treatment;
3. to classify the various groups of patients;
4. to offer discriminating factors explaining the classification patterns.

2. Experimental

2.1. Data set

2.1.1. Patients

Sixty five patients with major gastrointestinal surgery and indications for postoperative nutritional support are included in the study. They are randomized into 2 groups: EEN and TPN. The following inclusion criteria are used:

1. Major elective gastrointestinal surgery – stomach and intestinal resections
2. Indications for nutritional support in the post operative period
3. Informed consent of the patient and the operator for participation and following of the protocol of nutrition support
4. Intraoperatively placed special feeding tube: nasogastric or nasojejunal tube in the group with EEN.
5. Central venous line for delivery of PN

The excluding criteria were as follows:

1. Haemodynamic instability (shock)
2. Liver and kidney insufficiency
3. Lethal exit before tenth post operative day (POD)
4. Refusal of the operator or the patient to follow the protocol and the scheme for EEN.

All patients included in the study were subject to nutritional support in the postoperative period as a component of the complex treatment.

The patients are randomized into two groups: mixed nutrition – 33 with EEN and PN and 32 with TPN after the respective operative interventions (Table 1):

Table 1. Operative interventions for the group of patients

Type of Surgery	Gr.1 (EEN+PN)	Gr. 2 (TPN)	All
Gastric resections	18	11	29
Colon resections	10	11	21
Rectal resections	4	7	11
Pancreatic resections	1	3	4

2.1.2. Determination of Nutritional Risk Index (NRI)

All patients receive preoperative evaluation of the nutritional risk through the formula of the NRI and the protocol Nutritional Risk Screening, ESPEN-2002 (European Society of Parenteral and Enteral Nutrition) [10-13]. According to this protocol the screening is made on the basis of BMI, loss of body mass, reduced food intake, evaluation of the severity of the disease and the metabolic stress. At ages over 70, the final mark must

be added 1. The patients with values ≥ 3 have nutritional risk and are indicated for nutritional support.

2.1.3. Patients on EEN

The enteral formulae are given via intra operative feeding tube: nasogastric (NG) or nasojejunal (NJ). The type of the feeding tube depends on the type of surgical intervention. For patients with gastrectomies, one lumen jejunal tube was introduced after partial gastric resections – combined Freka-Trelumina (Fresenius Kabi). After intestinal resections one lumen stomach tube was used. EEN began on 1 POD at 9 a.m., but not later than 12-16 hours after the operation. The enteral formulae were introduced by means of a standard infusion pump in gradually increasing doses according a preliminary scheme observing the tolerance to EEN. Enteral formulae with similar characteristics were applied (osmolarity, content of nutrients and calories/mL) – "Ensure" of Abbott Laboratories and "Fresubin" of Fresenius Kabi. For the full supplying of the caloric-energy needs during the first six days the patients of EEN group received additional PN. The next scheme of EEN was followed (Table 2).

Table 2. Feeding formulae

Feeding formula	NG bolus/30 min	NJ infusion
1 POD Osmolite/Reconvan 200 mL + PN	4 x 50 mL	10 mL/h/20 h
2 POD Osmolite/Reconvan 400 mL + PN	4 x 100 mL	20 mL/h/20 h
3 POD Osmolite/Reconvan 600 mL + PN	4 x 150 mL	30 mL/h/20 h
4 POD Ensure/Fresubin 1000 mL + PN	5 x 200 mL	50 mL/h/20 h
5 POD Ensure/Fresubin 1200 mL + PN	6 x 200 mL	60 mL/h/20 h
6 POD Ensure/Fresubin 1200 mL	6 x 250 mL	75 mL/h/20 h
7 POD Ensure/Fresubin 1800 mL	6 x 300 mL	90 mL/h/20 h
8-10 POD Ensure/ Fresubin 1800-2000 mL	6 x 300-350 mL	120 mL/h/16 h

2.1.4. Patients on TPN

TPN began on 1 POD at 9 a.m. and lasted at least 7 days up to restoring an adequate oral food intake (60% of the energy needs). Usually the EN in this group began with clear liquids after 4 PODs according to the decision of the medical team to restore the gastro-intestinal functions and tolerance. It lengthened with strained mixtures.

The TPN is carried out through intraoperative central venous source. The next parenteral solutions are infused: 10-20 % Sol. Glucosae of Balkanpharma, 10 % Lipofundin MCT/LCT of B.Braun and amino acids solution – 10 % Aminoplasmal of B. Braun.

Patients to whom it applied received a normocaloric feeding regimen of 20 ÷ 25 kcal/kg weight, respectively: carbohydrates 3 ÷ 4 g/kg, lipids 0.8 ÷ 1.0 g/kg, proteins 1.5 g/kg.

On the second, fifth and tenth POD the serum levels of albumin, prealbumin, acute-phase protein or C-reactive protein (CRP), blood glucose, triglycerides, urea, creatinine, liver enzymes, electrolytes are assayed, and the number of lymphocytes – on the second and on the tenth POD.

The infectious complications, the length of hospital stay (LOS) and the postoperative stay are also considered parameters.

Finally, the anthropometric, biochemical, immunological, and screening indicators used for multivariate statistical data interpretation of the patients groups includes:

2.1.5. Anthropometric indices

1. Age
2. BMI – body mass index

2.1.6. Biochemical indices

3. S-alb – serum albumin (ALB), a transport protein which regulates the osmotic pressure of the blood. Albumin is one of the proteins with a longer half-life (17 ÷ 23 days). It has a delayed reaction to sudden changes in feeding. Albumin used for initial diagnostics.
4. S-prealb (transthyretin) – prealbumin (PREAL), one of the functional proteins with a short half-life (anabolic proteins), which are the first affected by absolute or relative alimentary deficit. Prealbumin has a half-life of 11 ÷ 50 h. It transports the thyroid hormone thyroxine (T4) and retinol.
5. CRP – C-reactive protein, or acute-phase protein. Its level increases with inflammatory diseases, thus suppressing the microbial growth. CRP provides insight on the severity of the diseases leading to malnutrition.

2.1.7. Immunological indices

6. Ly – number of lymphocytes in peripheral blood. They are given as a number of Ly x 10^9/L. The number of Ly correlates with the effectiveness of the organism's defense against severe diseases. The patient is considered to be in a state of malnutrition if the number of Ly falls below 2.2 x 10^9/L.

S-prealb, CRP, S-alb and Ly are followed up to four times:

- On the preoperative day at which the corresponding data is marked as 0.
- On the second POD at which the corresponding data is marked as 2.
- On the fifth POD at which the corresponding data is marked as 5.

• On the tenth POD at which the corresponding data is marked as 10.

2.1.8. Screening indices

7. ASA (American Society of Anaesthesiologists) – classification of the ASA for the determination of the preoperative status of the patient.

8. NRI – index for the risk of feeding. It is calculated according to the formula:

NRI = 1.519 alb (g / l) + 4.17(BW / UBW), where BW – body weight, UBW – usual body weight

At NRI > 100 – no state of malnutrition; 97.5 ÷ 100 – light malnutrition; 83.5 ÷ 97.5 – moderate malnutrition; < 83.5 – acute malnutrition.

9. SP2 (Screening protocol No. 2, ESPEN-2002) – for the nutritional risk of hospitalized patients (NRS – nutritional risk screening), accepted in 2002 by ESPEN.

It gives an evaluation of the presence of nutritional risk, **which is a sum of the evaluation of the nutritive status and the evaluation of the severity of the illness** (metabolic stress).

2.1.9. Types of Nutrition Support

10. LOS – length of hospital stay.

2.2. Multivariate statistics

Cluster analysis (CA) is an exploratory data analysis tool for solving classification problems, based on unsupervised learning [14]. CA enables objects stepwise aggregation according to the similarity of their features. As a result hierarchically or non-hierarchically ordered clusters are formed. A single cluster describes a group of objects that are more similar to each other than to objects outside the group. Similarity understood in those terms, CA measures how similar two cases are. While the term similarity has no unique definitions, it is common to refer to all similarity measures as "distance in multi-features space" measures since the same function is served. A similarity between two objects *i* and *i'* is a distance if:

$$(D_{i'i} = D_{ii'}) \leq 0 \;\; where \;\; D_{ii'} = 1 \;\; if \;\; x_i = x_{i'} \quad (1)$$

(where x_i and $x_{i'}$ are the row-vectors of the data table **X** with the features measurements describing objects *i* and *i'*). When two or more features are used to define their similarity, the one with the largest magnitude will dominate. Because of this primary standardization of features becomes necessary. The most popular way of determining how similar interval measured objects are to each other is: *Euclidean distance* – the distance between two objects x_i and $x_{i'}$ is defined by formula 2 where *j* presents repetition of measurements:

$$d_{x_i x_{i'}} = \sqrt{\sum_{j=1}^{J} (x_{ij} - x_{i'j})^2} \quad (2)$$

Squared Euclidean distance removes the sign and places greater emphasis on objects further apart, thus increasing the effect of outliers (Eq. 3).

$$d_{(x_i, x_{i'})} = \sum_{j=1}^{J} (x_{ij} - x_{i'j})^2 \quad (3)$$

In case of CA one task is related with determination of similarity between measured objects, but an equally important task is to define how objects or clusters are combined at each step of similarity assessment procedure. One possibility for clustering objects is their hierarchical aggregation. In this case the objects are combined according to their distances from or similarities to each other.. A few of the most popular linkage algorithms are: *Nearest neighbor (single linkage)*, *Furthest neighbor (complete linkage)*, *Average linkage* , *Ward's method.*

In hierarchical agglomerative clustering the graphical output of the analysis is usually a dendrogram – a tree-like graphics, which indicates the linkage between the clustered objects with respect to their similarity (distance measure). Decision about the number of statistically significant clusters could be made for different reasons. Often a fixed number of clusters is to be assumed. For practical reasons the Sneath index of cluster significance is widely used. It represents this significance on two levels of distance measure D/D_{max} relation: $1/3\ D_{max}$ and $2/3D_{max}$ where D_{max} is the maximal distance in the similarity matrix. Only clusters remaining compact after breaking the linkage at these two distances are considered significant and are subject to interpretation.

In principle, the data set could be considered as a matrix consisting of rows (the objects) and columns (the variables describing the objects). CA makes it possible to classify both the objects and variables.

Principal Component Analysis (PCA) seems to be the most widespread multivariate chemometric technique and is a typical display method (also known as eigenvector analysis, eigenvector decomposition or Karhunen-Loéve expansion). It enables revealing the "hidden" structure of the data set and helps to explain the influence of latent factors on the data distribution [15]. PCA is done on a covariance matrix when the data are centered or on correlation matrix when the data are standardized. PCA transforms the original data matrix into a product of two matrices, one of which contains the information about the objects and the other about the features. The matrix characterizing objects contains the scores (understood as projection) of objects on principal components (PCs). The other one, characterizing features is a square matrix and contains the set of eigenvectors (understood as weights, in PCA terminology

called “loadings”) of the original features in each PC. In matrix terms, this can be expressed as:

$$X = S \bullet L + E \quad (4)$$

where:

X – is the original data matrix (features as columns, cases as rows),

S – is a scores matrix (has as many rows as the original data matrix),

L – is a loadings matrix (has as many columns as the original data matrix),

E – is an error matrix.

Some important features of PCA could be summarized as follows. The principal components axes (the axes of the hidden variables) are orthogonal to each other. Most of the variance of the data is contained in the first principal component. In the second component there is more information than in the third one etc. For interpretation of the projected data both the score and the loading vectors are plotted. In the score plots, the grouping of objects can be recognized. A loading plot reveals the importance of the individual variables with respect to the principal component model.

A very important task in PCA is the estimating the number of principal components necessary for a particular PC model. Several criteria exist in determining the number of components in the PCA model: percentage of explained variance, eigenvalue – one criterion, Scree – test.

Interpretation of the results of PCA is usually carried out by visualization of the component scores and loadings. In the score plot, the linear projection of objects is found, representing the main part of the total variance of the data (in the plot PC 1 vs. PC2). Other projection plots are also available (e.g. PC 1 vs. PC 3 or PC2 vs. PC3) but they represent less percentage of explained total variance of the system in consideration. Correlation and importance of feature variables is to be decided from the factor loading plots.

3. Results and Discussion

In Tables 3 and 4 the basic statistics of the experimental data for both groups of patients is presented.

In Figure 1 the hierarchical dendrogram as an output of the cluster analysis of the parameters describing the feeding pattern of group 1 of 33 patients (mixed nutrition EEN+PN) is presented.

Three major clusters are formed as follows (the cluster significance is checked by the Sneath’s criterion):

K1 (PREAL5, PREAL2, PREAL0, ALB10, ALB5, ALB2, LY2, PREAL10, ALB0 and NRI)

In K1 predominantly serum albumin and pre-albumin estimators are included, indicating the role of initial diagnostics of the patients. These important biochemical indices are closely related to NRI (nutrition risk index) and form the “*albumin pattern”* of the indicator list.

K2 (CRP5, CRP2, LY10, CRP0, BMI)

Table 3. Basic statistics for group of 33 patients (EEN +PN nutrition)

Variable	Valid N	Mean	Median	Min	Max	Variance	Std.Dev.
AGE	33	60.58	62.00	32.00	84.00	162.9	12.762
ASA	33	2.39	2.00	1.00	4.00	0.5	0.704
BMI	33	22.88	22.00	14.00	32.00	25.5	5.048
NRI	33	91.00	91.00	76.00	113.00	92.6	9.624
SP2	33	4.42	5.00	3.00	6.00	0.7	0.830
ALB0	33	35.46	35.00	28.00	47.10	23.9	4.891
ALB2	33	28.08	28.00	17.00	36.00	17.2	4.152
ALB5	33	29.24	29.00	19.00	40.00	25.0	5.000
ALB10	33	33.70	33.30	26.70	42.50	18.4	4.284
PREAL0	33	0.16	0.14	0.030	0.30	0.01	0.069
PREAL2	33	0.12	0.12	0.040	0.24	0.01	0.044
PREAL5	33	0.13	0.12	0.060	0.27	0.01	0.050
PREAL10	33	0.19	0.16	0.070	1.21	0.01	0.191
CRP0	33	15.79	4.59	0.154	122.00	714.0	26.720
CRP2	33	110.63	112.0	5.00	258.00	2976.2	54.555
CRP5	33	40.63	35.00	7.83	158.00	1002.0	31.655
CRP10	33	23.33	15.00	0.625	188.00	1106.9	33.270
LY2	33	1.32	1.20	0.13	3.50	0.6	0.745
LY10	33	1.94	1.80	0.44	3.90	0.7	0.864
LOS	33	10.15	11.00	7.00	14.00	3.6	1.906

Table 4. Basic statistics for group of 32 patients (TPN nutrition only)

Variable	Valid N	Mean	Median	Minimum	Maximum	Variance	Std.Dev.
AGE	32	58.91	59.00	35.00	80.00	135.12	11.62
ASA	32	2.34	2.00	2.00	3.00	0.23	0.48
BMI	32	23.66	24.50	16.00	32.00	17.20	4.14
NRI	32	91.31	90.50	68.00	113.00	96.61	9.82
SP2	32	4.13	4.00	3.00	6.00	0.56	0.75
ALB0	32	35.78	35.45	17.10	49.30	40.64	6.37
ALB2	32	27.96	29.00	15.50	42.00	34.56	5.87
ALB5	32	29.14	29.50	20.00	37.00	18.53	4.30
ALB10	32	31.48	32.45	19.00	41.00	25.16	5.01
PREAL0	32	0.19	0.14	0.070	1.52	0.06	0.24
PREAL2	32	0.15	0.11	0.060	1.12	0.03	0.18
PREAL5	32	0.17	0.12	0.050	1.42	0.06	0.23
PREAL10	32	0.20	0.15	0.090	1.64	0.07	0.26
CRP0	32	29.42	5.75	0.540	187.60	2697.58	51.93
CRP2	32	120.57	125.50	6.520	191.10	2077.20	45.57
CRP5	32	85.18	48.30	3.110	368.00	6577.82	81.10
CRP10	32	43.35	16.60	1.980	193.00	2880.67	53.67
LY2	32	1.52	1.40	0.040	3.30	0.54	0.73
LY10	32	1.76	1.75	0.140	3.50	0.49	0.69
LOS	32	13.06	12.00	8.00	32.00	30.06	5.48

Figure 1. Hierarchical dendrogram for clinical parameters (mixed mode of nutrition)

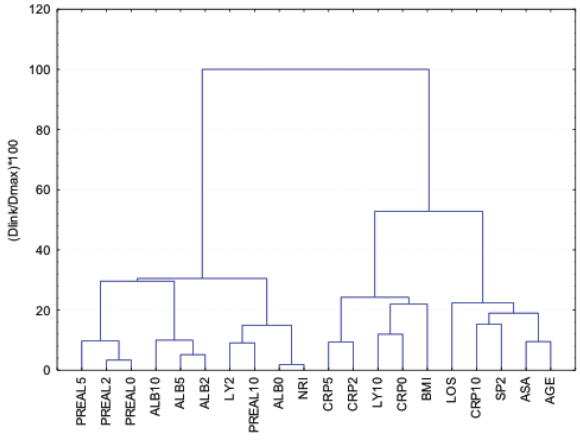
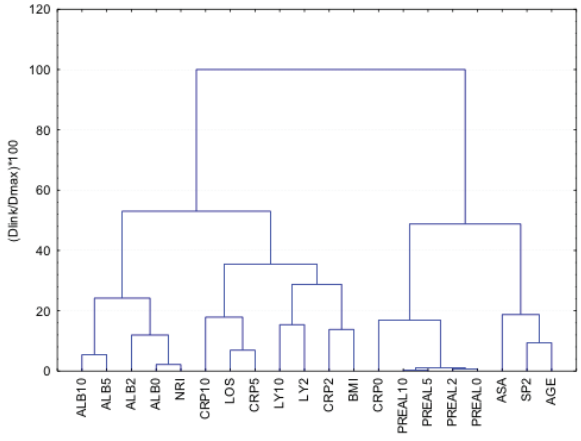


Figure 2. Hierarchical dendrogram for clinical parameters (TPN mode of nutrition)



K2 cluster informs on the significant role of the C-reactive protein values as indicator for the microbial growth and malnutrition effects, especially with its initial levels measured shortly after surgery. Logically, this set of indicators is strongly related to BMI and numbers of lymphocytes determined at later stages of the post-operative period. In this way a "*nutrition quality indicator pattern*" is formed.

K3 (LOS, CRP10, SP2, ASA and AGE)

The third cluster K3 is related mainly to anthropometric screening indices which are correlated to the values of the C – reactive protein at late stages of the treatment, i.e. when their level is in equilibrium. Thus, an "*anthropometric screening pattern*" among the indicator collection is offered.

It was of substantial interest to compare this way of linkage between the indicators for the patients subject to mixed (EEN+ PN) nutrition with the patterns formed in the second group of 32 patients subject to TPN nutrition. In Figure 2 the hierarchical dendrogram showing the linkage between the 20 indicators for patients with TPN nutrition mode is given.

In this case five different clusters are formed as follows (checked for significance by the Sneath's criterion):

K1 (ALB10, ALB5, ALB2, ALB0, NRI)

K4 (CRP0, PREAL10, PREAL5, PREAL2, PREAL0)

It is easily seen that the cluster structure in this situation differs from that described above. The major difference is the separation of the pre-albumin (PREAL) from the albumin (ALB) indicators. They form by their

Table 5. Factor loadings (EEN + PN);statistically significant loadings are marked

Variable	PC 1	PC 2	PC -3	PC 4	PC 5
AGE	-0.20	-0.27	-0.13	**-0.79**	-0.16
ASA	0.08	0.06	-0.21	**-0.85**	0.23
BMI	0.05	0.08	0.34	-0.27	**-0.66**
NRI	0.48	0.06	**0.76**	-0.16	-0.30
SP2	-0.07	0.23	-0.51	-0.32	**0.60**
ALB0	0.56	0.09	**0.71**	-0.14	-0.08
ALB2	**0.83**	0.04	0.03	0.02	-0.37
ALB5	**0.67**	0.24	0.04	0.02	-0.45
ALB10	**0.47**	0.12	0.33	0.22	-0.44
PREAL0	**0.73**	-0.34	0.29	0.33	0.07
PREAL2	**0.76**	-0.37	0.19	0.19	0.14
PREAL5	**0.73**	-0.12	0.16	0.06	0.01
PREAL10	0.04	-0.17	**0.72**	0.38	0.01
CRP0	-0.09	**0.81**	0.21	-0.01	0.22
CRP2	-0.03	**0.76**	-0.08	-0.05	-0.22
CRP5	-0.09	**0.59**	-0.08	0.01	-0.13
CRP10	-0.28	0.28	-0.02	**-0.52**	0.10
LY2	0.16	-0.13	**0.77**	0.30	-0.07
LY10	0.07	0.43	**0.62**	0.06	0.05
LOS	-0.15	-0.16	0.21	-0.23	**0.64**
Expl.Var%	*18.7*	*12.1*	*17.0*	*11.6*	*10.3*

Table 6. Factor loadings (TPN nutrition); statistically significant loadings are marked

Variable	PC1	PC 2	PC 3	PC 4	PC 5
AGE	-0.05	-0.47	0.10	**-0.59**	-0.01
ASA	0.24	-0.06	0.01	**-0.50**	0.14
BMI	0.17	-0.07	-0.20	**0.72**	0.04
NRI	-0.09	**0.81**	-0.20	0.22	-0.18
SP2	0.13	-0.25	0.01	**-0.78**	-0.25
ALB0	-0.01	**0.81**	-0.17	0.08	-0.33
ALB2	-0.01	**0.86**	0.01	-0.08	0.12
ALB5	0.03	**0.73**	0.42	0.18	0.30
ALB10	0.15	**0.53**	0.37	0.45	0.31
PREAL0	**0.97**	0.04	-0.06	-0.09	0.07
PREAL2	**0.96**	0.07	0.01	-0.04	0.08
PREAL5	**0.98**	-0.01	0.08	-0.08	0.06
PREAL10	**0.98**	0.00	0.07	-0.05	0.05
CRP0	**0.60**	-0.37	0.27	0.10	-0.00
CRP2	0.07	-0.13	-0.13	0.44	**0.76**
CRP5	-0.06	0.19	**-0.84**	0.15	0.14
CRP10	-0.15	-0.12	**-0.61**	-0.12	0.38
LY2	-0.31	-0.08	-0.02	0.27	**-0.48**
LY10	-0.38	0.02	0.42	**0.55**	-0.15
LOS	-0.04	0.04	**-0.76**	0.19	-0.29
Expl.Var%	*22.9*	*16.9*	*11.9*	*13.5*	*7.7*

dominant presence two clusters (K1 and K4). The NRI index is clearly linked to the serum albumin estimators. Therefore, one could assume not one, but two "albumin patterns" for the patients fed by TPN mode.

K2 (CRP10, LOS, CRP5)

K3 (LY10, LY2, CRP2, BMI)

K5 (ASA, SP2, AGE)

The linkage between the other indices is similar to the previous one (with the mixed mode of nutrition): K2 and K3 clusters inform on "nutrition quality pattern", and K5 – on the "anthropometric screening pattern". It seems that the TPN mode of nutrition leads to higher stress in patients after surgery due to, on the one hand, the delayed reaction to sudden changes in feeding (separate grouping of the serum albumin values as indicator), and, on the other, to the specific transport of the thyroid hormone thyroxine (T4) and retinol (indicated by the separate grouping of the pre-albumin parameters).

These findings are directly proven by carrying out principal component analysis of the data from both groups of patients. In Tables 4 and 5 the factor loadings for the identified latent factors are presented.

In Table 5 the latent factors for the group of patients with the mixed mode of nutrition are shown. Five principal components explain over 70 % of the total variance. The most important output of the PCA is that the ALB and PREAL indicators are dominantly presented together in PC1 (the first principal component) with nearly 19 % explanation of the total variance. Again, as in cluster analysis, the conditional name of this factor could be "*albumin factor*". The rest of the factors indicate correlations between CRP values (PC2), LY values (PC3), anthropometric and screening indices (PC4 and PC5).

As indicated in Table 6, the structure of the identified latent factors for the second group of patients (subject only to TPN nutrition mode) is slightly different. Again, five principal components explain over 70 % of the total variance. The significant point is that the latent factors PC1 and PC2 (explaining together almost 40 % of the total variance) show the distinct separation of two biochemical indices, namely ALB and PREAL. The rest of the latent factors (PC3 – PC5) are related to correlations between CRP, LY, anthropometric and screening characteristics.

In Figures 3 and 4 the biplots of the PC1 vs. PC2 for both groups of patients (factor loadings) convincingly prove the difference in both modes of nutrition.

It was interesting to additionally analyse the groups of patients with different modes of nutrition after major surgery by case (patient) clustering. In Figures 5 and 6 the hierarchical dendrograms for both modes are shown.

For patients with the mixed mode of nutrition (Figure 5) three clusters are visible: K1 with 10 patients (conditional numbers 2, 23, 26, 24, 30, 8, 18, 32, 33 and 17), K2 with 8 patients (29, 11, 13, 15, 14, 10, 16, 6) and K3 with 15 patients (20, 28, 21, 12, 5, 27, 19, 22, 4, 7, 3, 9, 31, 25, 1). In order to find discriminating parameters for each one of the identified clusters, the average values

Figure 3. Biplot factor 1 vs. factor 2 (mixed mode of nutrition, factor loadings)

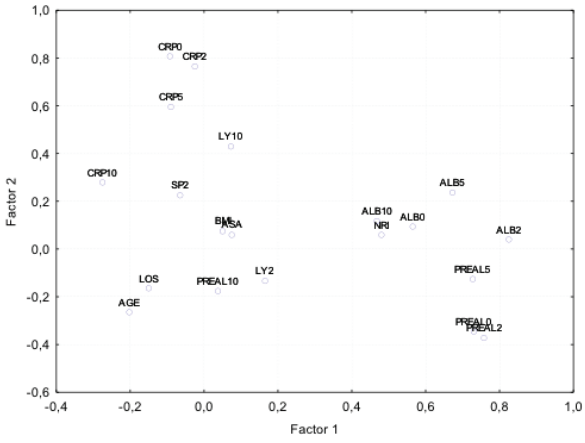


Figure 4. Biplot factor 1 vs. factor 2 (TPN mode of nutrition, factor loadings)

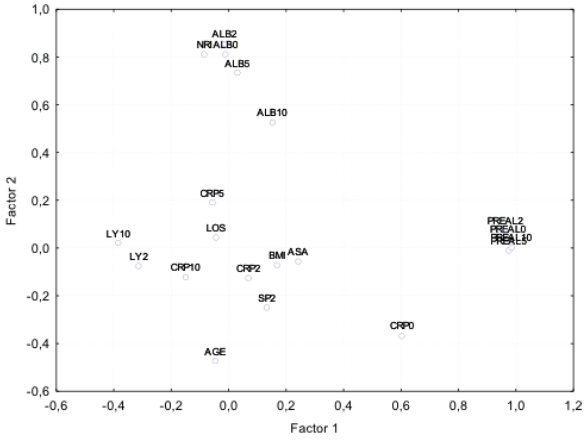


Figure 5. Hierarchical dendrogram for patients (mixed mode of nutrition)

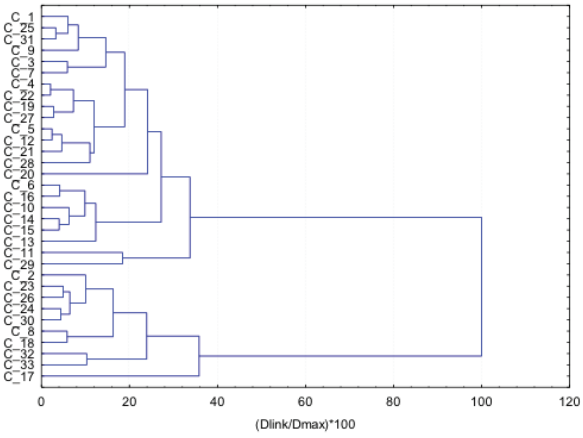
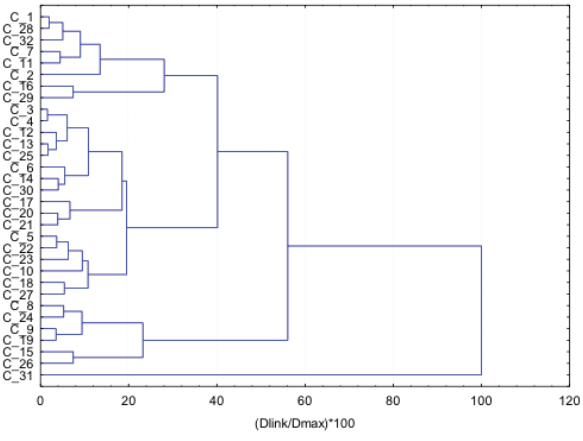


Figure 6. Hierarchical dendrogram for patients(TPN mode of nutrition)



of all indicators for the cases included in each cluster were calculated.

For K1 the highest values of BMI, NRI, all ALB and PREAL values are observed. Probably, these are patients responding to a specific “albumin pattern” having high levels of BMI I nutritional risk.

K2 is the group of younger patients with lower level of risky anthropometric indices and lower values of albumin indicators. They form a “low risk” pattern of patients subject to mixed mode of post-operational nutrition.

Finally, K3 includes elderly patients (highest average age) with lowest levels of pre-albumin but increased levels of CRP. They could be attributed to the pattern of “higher risk” cases.

The same discrimination was performed for the group of patients subject to TPN nutrition mode. As seen in Figure 6 three distinctive clusters are formed. One typical outlier is present in the dendrogram (case 31). Cases 8, 24, 9, 19, 15, 26 belong to K1, K2 includes cases 27, 18, 10, 23, 22, 5, 21, 20, 17, 30, 14, 6, 25, 13, 12, 4, 3. The rest of cases (29, 16, 2, 11, 7, 32, 28, 1) are members of cluster K3.

Concerning the discriminating variables following could be mentioned. The outlier case is characterized by highest levels of prealbumins and CRP and by lowest levels of LY and LOS. This isolated case probably suggests a specific pattern of fast food transportation and malnutrition risks.

The first cluster K1 unifies elderly patents but with low BMI and NRI, lowest levels of albumin and CRP5 which is an indication for a reliable nutrition pattern. K2 is the cluster of the younger patients, but with highest NRI values. The albumin values are the highest ones as well the LY values which is an indication for active and effective immune system response. Finally, K3 cases are characterized mainly by the highest levels of CRP (2, 5, and 10 day’s period of monitoring). This group could be representative for a malnutrition pattern.

4. Conclusion

The conclusions from the study carried out are as follows:

1. The mixed nutrition creates a better metabolic stability for the patients. This is shown by the grouping of the all ALB and PREAL factors to one group.
2. The condition of the patient depends on realtively few factors.
3. The mixed type of nutrition hardly differentiates the patients as oppose to the mixed mode of nutrition.
4. In the diagram of the parenteral nutrition, there is a strong split of the ALB and PREAL factors from the CRP and LY factors.
5. The factors which have the greatest influence upon the patient's conditions reveal the more severe metabolic stress of the organism at parenteral feeding. The stress catabolic response is more slowly to the effects provoked by the severe illness and the surgical intervention.

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