VER
Vascular & Endovascular Review

Impact of Personalized Nutritional Intervention on Inflammatory Markers in Hospitalized Patients with Multiple Comorbidities

Vanessa Paulina Vargas Olalla[1], Manuel Fernando Vargas Vargas[2], Valeria Guadalupe De La Cajiga Torres[3]

[1]Universidad Estatal de Milagro (UNEMI), Milagro, Ecuador
Email: vvargaso@unemi.edu.ec
ORCID: https://orcid.org/0000-0002-2116-2004
[2]Universidad de Aquino Bolivia
Email: vargas.psi.empre@gmail.com
ORCID: https://orcid.org/0009-0008-9732-3493
[3]Valeria Guadalupe De La Cajiga Torres
Universidad Autónoma del Estado de Hidalgo
Email: valeriacajiga@gmail.com
ORCID: https://orcid.org/0009-0005-0223-0955

ABSTRACT

Introduction: Disease-related malnutrition is common in hospitalized patients with multimorbidity and is associated with increased morbidity, mortality, and hospital stay. Systemic inflammation, as assessed by C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), modulates the response to nutritional therapy (Wunderle et al., 2025a). The ESPEN guidelines recommend individualized nutritional support in polymorbid patients (Wunderle et al., 2023).

Objective: To evaluate the impact of a personalized nutritional intervention on changes in CRP, IL-6, and TNF-α in hospitalized patients with multiple comorbidities, compared to standard nutritional care.

Methodology: Quasi-experimental study with random assignment by blocks (1:1) in a tertiary hospital. A total of 120 adult patients (≥ 18 years) with ≥ 2 chronic comorbidities and nutritional risk were included (NRS-2002 ≥ 3). The intervention group (IG) received personalized nutritional support guided by the Nutritional Care Process and the ESPEN guidelines; the control group (CG) received the usual nutritional care. CRP, IL-6 and TNF-α were measured at admission (day 0) and at day 7.

Results: The mean age was 72.3 ± 10.7 years; the median number of comorbidities was 4 (IQR 3–5). At day 7, the IG showed greater relative reductions in CRP (−36.8% vs. −17.9%; p = 0.006) and IL-6 (−23.9% vs. −9.8%; p = 0.022) compared to the CG. The reduction in TNF-α was greater in the IG (−11.5% vs. −4.9%; p = 0.09). 72% of the IG reached ≥75% of the energy and protein requirements compared to 45% of the CG (p = 0.003). Fewer infectious complications were observed in the IG (23.3% vs. 38.3%; p = 0.048).

Conclusions: Personalized nutritional intervention was associated with a greater reduction in CRP and IL-6 and with better coverage of nutritional requirements in hospitalized patients with multimorbidity. These findings support the systematic incorporation of personalized nutrition models guided by inflammatory biomarkers in the comprehensive management of disease-related malnutrition.

KEYWORDS: Personalized nutrition; multimorbidity; hospitalized patients; C-reactive protein; interleukin-6; TNF-α; systemic inflammation

How to Cite: Vanessa Paulina Vargas Olalla, Manuel Fernando Vargas Vargas, Valeria Guadalupe De La Cajiga Torres., (2025) Impact of Personalized Nutritional Intervention on Inflammatory Markers in Hospitalized Patients with Multiple Comorbidities, Vascular and Endovascular Review, Vol.8, No.19s, 83-91

INTRODUCTION

Multimorbidity – defined as the coexistence of two or more chronic diseases – represents one of the main challenges for contemporary health systems, especially in elderly populations. Recent epidemiological studies indicate that more than 65% of hospitalized older adults have multimorbidity, a condition associated with greater frailty, functional impairment, reduced risk of longevity, and intensive use of health resources (Deelen et al., 2023; Maier et al., 2022). This complex clinical profile is often accompanied by disease-related malnutrition, which is recognized as an independent factor of mortality, prolonged hospital stay, and increased complications during hospitalization (Maier et al., 2022; Wunderle et al., 2025b).

In these patients, malnutrition is not only the result of insufficient intake, but the result of an interaction between systemic inflammation, metabolic stress, and accelerated loss of muscle mass and function. Recent scientific literature highlights that chronic low-grade inflammation constitutes a central pathophysiological axis in the progression of multimorbidity and plays a

determining role in the response to nutritional support (Koelman et al., 2022; Deelen et al., 2023). Inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) reflect the intensity of this inflammatory response and independently predict adverse clinical outcomes, including functional impairment, hospital-acquired infections, and mortality (Gadhavi et al., 2025; Koelman et al., 2022).

Recent evidence from the secondary analysis of the EFFORT trial demonstrated that elevated IL-6 levels and CRP are associated with lower effectiveness of standard nutritional support, suggesting that the degree of inflammation acts as a critical modulator of the response to nutritional intervention (Wunderle et al., 2025a). In this context, the identification and monitoring of inflammatory biomarkers acquires strategic relevance for clinical decision-making and to guide more precise nutritional support plans adapted to individual needs.

Personalized nutrition—also called precision nutrition—has emerged as an innovative approach that integrates clinical, metabolic, genetic, and biomarker-based information to optimize nutritional intervention. This approach aims to overcome traditional models of generalized nutritional support by explicitly considering the metabolic and clinical heterogeneity of patients (Livingstone et al., 2022). Recent reviews highlight the usefulness of inflammatory and nutritional biomarkers to individualize therapy, identify subgroups of patients at higher risk, and monitor the effectiveness of nutritional support in real time (Wunderle et al., 2025b; Pokushalov et al., 2024).

Likewise, the updated ESPEN guidelines on nutritional support in polymorbid patients emphasize the need for individualized interventions that incorporate both energy and protein requirements and the assessment of inflammatory status to optimize nutritional treatment (Wunderle et al., 2023). These guidelines recommend applying specific dietary strategies—including anti-inflammatory dietary patterns—and, in selected cases, targeted supplementation based on documented deficiencies or persistent inflammatory activity (Koelman et al., 2022; Pokushalov et al., 2024).

However, despite the growing interest in precision nutrition, there is a gap in evidence directly assessing the impact of a structured model of personalized nutritional intervention on inflammatory markers in hospitalized patients with multimorbidity. Most of the available studies have focused on specific populations (obesity, diabetes, cardiovascular disease) or isolated dietary interventions, rather than on comprehensive nutritional support strategies designed for a complex hospital setting.

Based on this need, the present study aims to evaluate whether a personalized nutritional intervention —based on the integration of nutritional status, inflammatory profile and multiple comorbidities— is capable of significantly modulating key inflammatory markers (CRP, IL-6 and TNF-α) in hospitalized patients, compared to standard nutritional care. This approach not only responds to an emerging clinical demand, but also aims to provide operational evidence to design more efficient models of nutritional support in highly vulnerable populations.

Theoretical Framework

Nutritional intervention in hospitalized patients with multiple comorbidities is based on a series of interrelated theoretical constructs that cover the pathophysiology of malnutrition, the biology of systemic inflammation, the role of biomarkers, and the development of contemporary models of personalized nutrition. This theoretical framework integrates recent scientific evidence to provide a solid basis for the study.

1. Disease-Related Malnutrition and Multimorbidity

Disease-related malnutrition (DREM) is a multifactorial condition characterized by an imbalance between nutritional requirements, intake, and functional capacity of the body, frequently exacerbated by the presence of systemic inflammation (Maier et al., 2022). Multimorbidity, defined as the coexistence of two or more chronic diseases, alters energy and protein metabolism, increasing the risk of sarcopenia, frailty, and clinical complications (Deelen et al., 2023).

Recent studies have shown that between 40% and 60% of hospitalized patients with multiple comorbidities have some degree of MRE at the time of admission, which is directly associated with longer hospital stay, nosocomial infections, and mortality (Wunderle et al., 2025b).

Table 1. Interaction between multimorbidity and disease-related malnutrition

Pathophysiological component	Clinical involvement	Recent Evidence
Chronic systemic inflammation	Increased protein catabolism and loss of muscle mass	Deelen et al. (2023)
Decreased intake	Anorexia and appetite alteration due to inflammatory mediators	Koelman et al. (2022)
Metabolic alterations	Anabolic stamina, increased basal energy expenditure	Maier et al. (2022)
Reduced functionality	Frailty, risk of falls, dependence	Wunderle et al. (2025b)

2. Systemic inflammation: role of PCR, IL-6 and TNF-α biomarkers

Systemic inflammation is a central mechanism in both the genesis and perpetuation of MRE. The production of inflammatory cytokines such as IL-6 and TNF-α activates catabolic metabolic pathways, reduces appetite, promotes insulin resistance, and increases muscle protein degradation (Gadhavi et al., 2025).

CRP is an acute-phase reactant synthesized in the liver in response to IL-6, and is used as a clinical marker of acute and systemic inflammation. Its elevation has been linked to a worse prognosis in chronic diseases, hospital infections, and mortality (Koelman

et al., 2022).

Table 2. Physiological function and clinical relevance of inflammatory biomarkers

Biomarker	Physiological function	Role in malnutrition	Evidence
PCR	Acute phase reactant produced by IL-6	Predicts severity of inflammation and complications	Koelman et al. (2022)
IL-6	Key cytokine in immune activation and catabolism	Reduces appetite, increases proteolysis, is associated with mortality	Wunderle et al. (2025a)
TNF-α	Central Mediator of Systemic Inflammation	Induces anorexia and protein degradation	Gadhavi et al. (2025)

Secondary analysis of the EFFORT trial showed that patients with elevated IL-6 levels derived less clinical benefit from standard nutritional support, suggesting that inflammation modulates the response to nutritional intervention (Wunderle et al., 2025a).

3. Personalized nutrition in the hospital context

Personalized or precision nutrition is defined as a nutritional intervention tailored to individual patient characteristics, integrating clinical, dietary, metabolic data, and biomarkers to optimize therapeutic response (Livingstone et al., 2022). This approach recognizes that multimorbid patients have significant metabolic heterogeneity and that a uniform model of nutritional support is insufficient.

Wunderle et al. (2025b) highlight that the integration of inflammatory biomarkers (CRP, IL-6, TNF-α) in decision-making makes it possible to personalize the intensity of nutritional support, adjust energy and protein requirements, and identify subgroups of patients with severe inflammatory malnutrition.

Table 3. Components of the Personalized Inpatient Nutrition Model

Dimension evaluated	Indicators	Involvement in the intervention
Nutritional status	NRS-2002, GLIM, anthropometry, muscle mass	Determines requirements and feeding route
Inflammatory state	PCR, IL-6, TNF-α	Adjusts protein-energy density and supplementation
Comorbidities	Cardiovascular, renal, respiratory, metabolic	Determine dietary restrictions and accommodations
Functionality	Grip strength, mobility	Influences recovery and rehabilitation goals
Preferences and tolerance	Dietary acceptance, GI symptoms	Modifies texture, frequency and composition of the diet

The use of personalized nutrition has been shown to improve energy and protein intake, reduce hospital complications, and modulate inflammatory biomarkers in specific patient subgroups (Pokushalov et al., 2024).

4. Anti-inflammatory dietary patterns and targeted supplementation

Recent meta-analyses demonstrate that healthy dietary patterns—particularly the Mediterranean diet and low-inflammatory index diets—reduce CRP and IL-6 in populations with cardiometabolic diseases (Koelman et al., 2022). This suggests that the qualitative composition of the diet directly influences systemic inflammation.

On the other hand, biomarker-targeted supplementation—for example, with antioxidant micronutrients or omega-3 fatty acids—may improve inflammatory parameters, especially in patients with documented deficiencies (Pokushalov et al., 2024).

Table 4. Recent evidence on nutritional interventions with anti-inflammatory effect

Dietary intervention	Effects on biomarkers	Recent Evidence
Mediterranean diet	Reduction of PCR and IL-6	Koelman et al. (2022)
Omega-3 supplementation	Decrease in TNF-α	Gholizadeh et al. (2023)
Increased high-quality protein	Reduction of IL-6 and improvement in muscle mass	Nogueira et al. (2021)
Biomarker-Targeted Supplementation	Selective improvement of inflammation and nutritional status	Pokushalov et al. (2024)

5. Theoretical justification of the study

The convergence of three factors—multimorbidity, systemic inflammation, and malnutrition—creates a complex clinical scenario that requires individualized nutritional interventions. Recent findings from the EFFORT trial, as well as ESPEN guidelines, indicate that nutritional therapy should be adjusted according to the inflammatory profile of the patient (Wunderle et al., 2023; 2025a).

Despite conceptual advances, there is still a scarcity of studies that directly evaluate the impact of a personalized nutritional intervention on inflammatory biomarkers in polymorbid hospitalized patients, which justifies the relevance and originality of the present work.

Methodology

The methodology used in this study was designed in accordance with contemporary recommendations for research in clinical nutrition and polymorbid patients, following ESPEN guidelines (Wunderle et al., 2023), as well as good practices in quasi-experimental studies recently reported in the literature (Maier et al., 2022).

1. Study design

A quasi-experimental, prospective, longitudinal study **was carried out**, with **random assignment by blocks** (1:1) to two parallel groups:

- **Intervention Group (IG):** received personalized nutrition.
- **Control Group (CG):** received standard hospital nutritional care.

This design was chosen due to its applicability in hospital settings and its effectiveness in evaluating clinical modifications in short periods, especially in studies where absolute individual randomization may be limited by logistical or ethical aspects (Maier et al., 2022; Pokushalov et al., 2024).

Table 1. Characteristics of the methodological design

Design Element	Description
Type of study	Quasi-experimental, prospective, longitudinal
Allocation	Block Randomization (1:1)
Groups	Personalized Intervention vs. Standard Care
Duration	7 days or until hospital discharge
Unit of analysis	Adult Inpatient
Primary Variables	Cambios in PCR, IL-6, TNF-α
Secondary Variables	Nutritional intake, length of stay, complications

2. Population and selection criteria

The study included patients hospitalized in **internal medicine, cardiology, pulmonology, and nephrology** services, specialties with a high prevalence of multimorbidity and nutritional risk (Deelen et al., 2023).

2.1. Inclusion criteria

- Age ≥ 18 years.
- Presence of ≥ 2 documented chronic comorbidities (e.g., heart failure, COPD, type 2 diabetes, CKD, stable cancer).
- Nutritional risk determined by **NRS-2002 ≥ 3**, according to ESPEN guidelines (Wunderle et al., 2023).
- Expected hospital stay ≥ 5 days.

2.2. Exclusion criteria

- Admission to the ICU in the first 24 hours.
- Terminal illness with life expectancy < 3 months.
- Pregnancy or breastfeeding.
- Inability to give informed consent.

Table 2. Summary of selection criteria

Guy	Criteria
Inclusion	≥18 years, ≥2 comorbidities, NRS-2002 ≥3, stay ≥5 days
Exclusion	Early ICU, terminal illness, pregnancy, without consent

3. Assignment procedure and study flow

Eligible patients were randomly assigned by blocks to ensure proportionality between groups, a technique recommended in heterogeneous populations with variable nutritional risk (Livingstone et al., 2022).

Process Flow:

1. Nutritional Risk Screening (NRS-2002).
2. Informed consent.
3. Baseline data collection (anthropometry, functionality, biomarkers).
4. Assignment to GI or GC.
5. Intervention application for 7 days.
6. Reevaluation and measurement of biomarkers at day 7.

4. Personalized Nutritional Intervention (GI)

The intervention was designed following the ESPEN guidelines for polymorbid patients (Wunderle et al., 2023) and personalized nutrition principles described in recent literature (Livingstone et al., 2022; Pokushalov et al., 2024).

4.1. Initial comprehensive nutritional assessment

Included:

- Anthropometry: BMI, weight loss, arm circumference.
- Functionality: hand grip strength (Wunderle et al., 2025b).
- Dietary history and gastrointestinal symptoms.
- Comorbidities and polypharmacy.

4.2. Biomarkers panel (day 0 and day 7)

According to evidence supporting its prognostic value in malnutrition and inflammation (Koelman et al., 2022; Gadhavi et al., 2025):

- CRP (mg/L).
- IL-6 (pg/mL).
- TNF-α (pg/mL).
- Albumin and basic metabolic parameters.

4.3. Individualised calculation of requirements

Following recognized nutritional formulas and ESPEN recommendations:

- **Energy:** 25–30 kcal/kg/day.
- **Protein:** 1.2–1.5 g/kg/day; up to 1.8 g/kg/day in elevated inflammation or sarcopenia, provided renal function permits (Wunderle et al., 2023).
- **Lipids and carbohydrates:** adjusted according to metabolic pathologies (diabetes, CVD, CKD).

4.4. Design of the personalized nutritional plan

Included:

- Adaptation of texture and energy density.
- Hyperprotein oral nutritional supplements.
- Enteral/parenteral nutrition if intake < 60% of requirements.
- Qualitative modification towards evidence-based anti-inflammatory diet (Koelman et al., 2022).
- Biomarker-targeted supplementation (Pokushalov et al., 2024).

Table 3. Components of Personalized Nutrition Intervention

Component	Description	References
Comprehensive assessment	Anthropometry, functionality, diet	Wunderle et al. (2023)
Biomarkers	PCR, IL-6, TNF-α	Koelman et al. (2022)
Requirements Calculation	25–30 kcal/kg/day; 1.2–1.5 g/kg/day protein	Wunderle et al. (2023)
Qualitative adjustments	Anti-inflammatory diet, low in trans fats	Pokushalov et al. (2024)
Targeted supplementation	According to deficiencies or persistent inflammation	Pokushalov et al. (2024)

5. Standard Nutritional Care (CG)

The CG received the usual hospital practice, consisting of:

- Nutritional screening on admission.
- Standard diet or modified due to illness.
- Occasional oral supplementation according to medical criteria.
- Without systematic evaluation of biomarkers to guide decisions (Maier et al., 2022).

6. Study variables

6.1. Primary variables

- Relative changes (%) between day 0 and day 7 in:
  - PCR.
  - IL-6.
  - TNF-α.

6.2. Secondary variables

- Percentage of energy and protein requirements achieved.
- Hospital stay (days).
- Infectious complications.
- Functional evolution (manual grip strength).

7. Collection Procedures and Quality Control

Standardized measurement protocols recommended in recent multicenter studies were used (Wunderle et al., 2025b). Blood collection was performed by trained personnel, and the samples were analyzed by high-sensitivity immunoassay.

8. Statistical analysis

- Student's t-test or Mann-Whitney U test to compare continuous variables.

- χ^2 or Fisher's exact test for categorical variables.
- ANCOVA tuned to analyze changes in biomarkers, controlling:
  - baseline values,
  - age
  - gender
  - number of comorbidities.

This procedure is recommended when analyzing the clinical response to personalized interventions (Livingstone et al., 2022; Wunderle et al., 2025a).

Table 4. Statistical techniques used

Objective	Statistical technique	Justification
Baseline comparison between groups	t de Student / Mann-Whitney	Independent groups
Comparison of proportions	χ^2 / Fisher	Categorical variables
Evaluate changes in biomarkers	ANCOVA	Control of clinical covariates
Level of significance	$p < 0.05$	Standard in Life Sciences

RESULTS

A total of 120 patients were analyzed, equally distributed between the **intervention group (IG)** and the **control group (CG).** The mean age was 72.3 ± 10.7 years, with a predominance of males (52%). No statistically significant differences were observed between groups in baseline variables, confirming the initial comparability of the cohorts (Wunderle et al., 2025a; Maier et al., 2022).

1. Basal characteristics of the sample

Table 1 presents the baseline anthropometric, functional, and inflammatory data of the patients. Baseline CRP, IL-6, and TNF-α values were elevated in both cohorts, consistent with the literature on systemic inflammation in patients with multimorbidity (Deelen et al., 2023; Koelman et al., 2022).

Table 1. Baseline characteristics of the patients included

Variable	GI (n=60)	GC (n=60)	p-value
Age (years, mean ± SD)	72,0 ± 11,0	72,6 ± 10,4	0,78
Male gender (%)	51,7 %	53,3 %	0,84
Number of comorbidities (median, IQR)	4 (3–5)	4 (3–5)	0,91
BMI (kg/m²)	25,4 ± 4,2	25,7 ± 4,1	0,72
Grip strength (kg)	18,9 ± 6,1	19,4 ± 5,9	0,65
PCR basal (mg/L)	6,9 ± 3,4	7,1 ± 3,2	0,74
IL-6 basal (pg/mL)	18,2 ± 9,1	17,8 ± 8,6	0,82
TNF-α basal (pg/mL)	13,5 ± 6,5	13,2 ± 6,2	0,79

The baseline levels observed are consistent with a moderate inflammatory state, typical in hospitalized polymorbid patients (Wunderle et al., 2025a; Gadhavi et al., 2025).

2. Changes in inflammatory biomarkers (Day 0 vs. Day 7)

The **intervention group (IG)** showed a significantly greater reduction in **CRP** and **IL-6** compared to CG, which is consistent with recent evidence on the usefulness of individualized nutritional interventions to modulate systemic inflammation (Pokushalov et al., 2024; Wunderle et al., 2025b).

Table 2. Changes in PCR, IL-6 and TNF-α between day 0 and day 7

Biomarker	GI, Half ± OF	GC, average ± OF	Adjusted difference	p-value
PCR (% change)	−36,8 % ± 21,5	−17,9 % ± 19,0	−17,5 p.p.	**0,006**
IL-6 (% exchange rate)	−23,9 % ± 20,1	−9,8 % ± 18,2	−13,0 p.p.	**0,022**
TNF-α (% change)	−11,5 % ± 16,7	−4,9 % ± 15,3	−5,8 p.p.	0,09

The more marked reduction in CRP and IL-6 in the IG supports the hypothesis that **personalized nutrition mitigates the inflammatory response**, an effect also described by contemporary studies (Koelman et al., 2022; Wunderle et al., 2025b).

Descriptive Graphic (Explanatory Text)

- The drop in CRP in the IG was approximately **twice as high** as in the CG.
- The reduction in IL-6 was almost **2.5 times greater** in the IG.
- TNF-α showed a favorable trend, although without reaching statistical significance, as is often the case in short-term interventions (Gholizadeh et al., 2023).

3. Coverage of nutritional requirements

Evidence indicates that the degree of coverage of energy and protein requirements largely determines the clinical evolution of the

hospitalized patient (Maier et al., 2022; Wunderle et al., 2023).
The IG achieved significantly higher caloric-protein intake than the CG.

Table 3. Coverage of nutritional requirements at day 7

Variable	GI	GC	p-value
% Energy Requirement Covered	82,5 % ± 12,4	63,4 % ± 14,1	**0,001**
% Protein Requirement Covered	85,1 % ± 11,2	59,9 % ± 15,0	**0,001**
Patients with ≥ 75% requirements covered	72 %	45 %	**0,003**

These results are consistent with recent analyses showing that **personalized nutrition improves actual intake** compared to standard regimens (Livingstone et al., 2022; Pokushalov et al., 2024).

4. Hospital complications
Personalized nutritional intervention was associated with a **lower incidence of infectious complications**, which coincides with research indicating that adequate protein-energy intake strengthens immunocompetence (Wunderle et al., 2025a).

Table 4. Complications during hospitalization

Complication	GI (%)	GC (%)	P-Value
Nosocomial infections	23,3 %	38,3 %	**0,048**
Metabolic decompensations	11,6 %	18,3 %	0,21
ICU Requirement	5,0 %	10,0 %	0,19

The significant difference in infections suggests that **nutritional optimization reduces immune vulnerability**, in accordance with the literature on inflammatory response and malnutrition (Deelen et al., 2023).

5. Hospital stay
A **non-significant trend** towards a shorter hospital stay was observed in the IG.

Table 5. Hospital stay

Group	Median (RIC)	P-Value
GI	9 days (7–12)	
GC	11 days (8–15)	**0,07**

Although the difference did not reach statistical significance, the trend is clinically relevant and consistent with previous results from the EFFORT trial, where individualized nutritional support reduced complications and stays (Wunderle et al., 2025a).

6. General interpretation of the results
The findings of the present study show:

1. **Significant reductions in CRP and IL-6** in the GI → evidence of decreased inflammation.
2. **Better coverage of nutritional requirements**, key to modulating catabolism in patients influenced by chronic inflammation.
3. **Significant reduction in hospital infections**, associated with better immune integrity.
4. **Trend towards shorter hospital stays**, a clinically relevant result.

These results are consistent with the contemporary literature supporting the use of **personalized nutrition** to improve inflammatory biomarkers and clinical outcomes in hospitalized patients (Livingstone et al., 2022; Pokushalov et al., 2024; Wunderle et al., 2025b).

CONCLUSIONS

The results of this study provide strong evidence on the key role of **personalized nutritional intervention** in modulating systemic inflammation and improving clinical outcomes in hospitalized patients with **multiple comorbidities**. The magnitude of the benefit observed in inflammatory and functional variables is consistent with the contemporary literature on precision nutrition and advanced nutritional support (Livingstone et al., 2022; Pokushalov et al., 2024).

First, it was shown that the personalized intervention produced **significantly greater reductions in CRP and IL-6 levels**, two biomarkers validated as predictors of adverse clinical progression and mortality in hospitalized patients (Wunderle et al., 2025a; Koelman et al., 2022). The observed reduction in these markers supports the hypothesis that nutrition adapted to individual requirements, inflammatory status, and clinical profile has the ability to modulate metabolic pathways involved in protein catabolism, inflammation-induced anorexia, and anabolic resistance (Gadhavi et al., 2025).

Second, the greater **coverage of energy and protein requirements** in the intervention group underscores the effectiveness of the personalized model in overcoming nutritional barriers typical of polymorbid patients, such as low intake, fatigue, gastrointestinal symptoms, and dietary restrictions derived from comorbidities (Maier et al., 2022; Wunderle et al., 2025b). This improvement in actual intake is clinically relevant, as the literature consistently shows that meeting at least 75% of nutritional requirements is associated with lower morbidity and better functional recovery in hospitalized patients (Wunderle et al., 2023).

Third, the finding of **a lower incidence of nosocomial infections** in the intervention group suggests that personalized nutrition not only influences systemic inflammation, but also the body's immune competence and ability to cope with hospital stress. Recent studies have confirmed that disease-related malnutrition and chronic inflammation increase the risk of nosocomial infections and systemic complications (Deelen et al., 2023), so this reduction represents a clinically significant outcome.

Fourth, although the **reduction in hospital stay** did not reach statistical significance, the trend observed in the intervention group coincides with previous trials, such as EFFORT, where individualized nutrition contributed to reducing hospitalization days, complications, and mortality (Wunderle et al., 2025a). This trend suggests that longer-term interventions or interventions applied systematically and early could yield even greater benefits.

Together, the findings strengthen the perspective that **personalized nutrition based on biomarkers** constitutes an effective, cost-effective and necessary strategy for the comprehensive clinical management of hospitalized patients with multimorbidity. This approach goes beyond traditional models of nutritional support by integrating biological, functional, and clinical dimensions that allow therapy to be tailored to the individual inflammatory and metabolic profile (Livingstone et al., 2022).

Clinical implications

1. **The routine implementation of inflammatory biomarkers** (CRP, IL-6, TNF-α) should be incorporated into hospital nutritional support protocols to stratify risk and personalize interventions, as proposed by Wunderle et al. (2025b).
2. Hospitals could benefit from **standardized personalized nutrition protocols**, based on ESPEN guidelines, that integrate nutritional requirements, comorbidities, functional status, and inflammatory profile (Wunderle et al., 2023).
3. The health care team should consider nutritional support as a **therapeutic mainstay** and not as a complementary intervention, especially in complex patients with active inflammation.

Limitations of the study

While the results are encouraging, there are limitations:

- The intervention period was relatively short (7 days), which could limit the magnitude of the changes observed in TNF-α and functional variables.
- The sample was of moderate size and came from a single hospital, which could affect the generalizability of the results.
- Omics biomarkers (metabolomics, microbiota), which could enrich future models of personalized nutrition, were not incorporated (Livingstone et al., 2022).

Recommendations for future research

- Extend the duration of nutritional interventions and post-discharge follow-up.
- Integrate advanced analytics technologies, such as artificial intelligence and personalized medicine, to improve nutrition response prediction (Tsihrintzis & Virvou, 2024).
- To evaluate hospital costs associated with the reduction of complications and stays, to strengthen the evidence of cost-effectiveness.

Final conclusion

This study demonstrates that **personalized nutritional intervention**, designed based on a comprehensive assessment and guided by inflammatory biomarkers, **significantly improves the inflammatory response and clinical outcomes** in hospitalized patients with multiple comorbidities. The evidence fully supports their systematic incorporation into modern hospital practice.

REFERENCES

1. Deelen, J., Slagboom, P. E., & others. (2023). Biomarkers of the ageing immune system and their association with frailty: A systematic review. *Experimental Gerontology, 175*, 112142. https://doi.org/10.1016/j.exger.2023.112142
2. Erickson, N., Sullivan, E. S., Kalliostra, M., Laviano, A., & Wesseling, J. (2023). Nutrition care is an integral part of patient-centred medical care: A European consensus. *Medical Oncology, 40*, 112. https://doi.org/10.1007/s12032-023-02008-9
3. Gadhavi, D. N., Ghantiya, U. V., & Gondaliya, T. K. (2025). Correlation of inflammatory biomarkers (IL-6, CRP, and TNF-α) with severity and outcomes in patients with STEMI: A prospective cohort study. *Journal of Heart Valve Disease, 30*(5), 15–19.
4. Galazzo, M., van Baar, H., Oshima, T., & others. (2024). Personalized nutrition strategies for patients in the intensive care unit. *Nutrients, 17*(10), 1659. https://doi.org/10.3390/nu17101659
5. Gholizadeh, M., Khalili, A., Roodi, P. B., Saeedy, S. A. G., Najafi, S., Keshavarz Mohammadian, M., & Djafarian, K. (2023). Selenium supplementation decreases CRP and IL-6 and increases TNF-alpha: A systematic review and meta-analysis of randomized controlled trials. *Journal of Trace Elements in Medicine and Biology, 76*, 127199. https://doi.org/10.1016/j.jtemb.2022.127199
6. Hariri, M., Amirkalali, B., Baradaran, H. R., & Gholami, A. (2024). The effect of parenteral selenium therapy on serum concentration of inflammatory mediators: A systematic review and dose-response meta-analysis of randomized clinical trials. *Biological Trace Element Research, 202*, 1910–1925. https://doi.org/10.1007/s12011-023-03751-3
7. Keller, H. (2019). Nutritional laboratory markers in malnutrition. *Clinical Nutrition*. (Methodological reference used in the section on biomarkers.)
8. Koelman, L., Rodrigues, C. E., & Aleksandrova, K. (2022). Effects of dietary patterns on biomarkers of inflammation

and immune responses: A systematic review and meta-analysis of randomized controlled trials. *Advances in Nutrition, 13*(1), 101–115. https://doi.org/10.1093/advances/nmab086

9. Livingstone, K. M., Ramos-López, O., Pérusse, L., Kato, H., Ordovas, J. M., & Martínez, J. A. (2022). Precision nutrition: A review of current approaches and future endeavors. *Trends in Food Science & Technology, 129*, 390–401. https://doi.org/10.1016/j.tifs.2022.08.017
10. Luo, S., et al. (2024). Effects of dietary interventions on systemic inflammation: A systematic review. *Nutrition Reviews*, 82(4), 512–528.
11. Maier, A. B., van der Velde, B., & others. (2022). Individualised nutritional care for disease-related malnutrition: A review of current practice and recommendations. *Nutrients, 14*(17), 3534. https://doi.org/10.3390/nu14173534
12. Nogueira, A. C., et al. (2021). Effect of whey protein consumption on IL-6 and TNF-alpha: A systematic review and meta-analysis of randomized controlled trials. *Nutrition, Metabolism & Cardiovascular Diseases, 31*(12), 3394–3404. https://doi.org/10.1016/j.numecd.2021.08.028
13. Pokushalov, E., Ponomarenko, A., Shrainer, E., Kudlay, D., & Miller, R. (2024). Biomarker-guided dietary supplementation: A narrative review of precision in personalized nutrition. *Nutrients, 16*(23), 4033. https://doi.org/10.3390/nu16234033
14. Sungur, S., et al. (2023). The effect of diets with different inflammatory scores on inflammation-related biomarkers and anthropometric indices among obese individuals: A randomized controlled trial. *Revista da Associação Médica Brasileira, 69*(4), 1–10.
15. Tsihrintzis, G. A., & Virvou, M. (2024). Personalized nutrition applications using nutritional biomarkers and artificial intelligence. En G. A. Tsihrintzis & M. Virvou (Eds.), *Personalized Medicine and Intelligent Systems* (pp. 25–48). Springer. https://doi.org/10.1007/978-3-031-15707-3_2
16. Volkert, D., Beck, A. M., Cederholm, T., Cruz-Jentoft, A., Hooper, L., Kiesswetter, E., … Bischoff, S. C. (2022). ESPEN practical guideline: Clinical nutrition and hydration in geriatrics. *Clinical Nutrition, 41*(5), 958–989.
17. Wunderle, C., Gomes, F., Schuetz, P., Stumpf, F., Austin, P., Ballesteros-Pomar, M. D., … Bischoff, S. C. (2023). ESPEN guideline on nutritional support for polymorbid medical inpatients. *Clinical Nutrition, 42*(6), 1545–1568. https://doi.org/10.1016/j.clnu.2023.06.023
18. Wunderle, C., Martin, E., Wittig, A., Tribolet, P., Lutz, T. A., Köster-Hegmann, C., … Schuetz, P. (2025a). Comparison of the inflammatory biomarkers IL-6, TNF-alpha, and CRP to predict the effect of nutritional therapy on mortality in medical patients at risk of malnutrition: A secondary analysis of the EFFORT trial. *Journal of Inflammation, 22*, 16. https://doi.org/10.1186/s12950-025-00442-0
19. Wunderle, C., Urbach, K., Buchmueller, L., Randegger, S., Kaegi-Braun, N., Laviano, A., van Zanten, A. R. H., Seres, D. S., & Schuetz, P. (2025b). Biomarkers for individualized nutritional therapy in disease-related malnutrition: A narrative review. *The American Journal of Clinical Nutrition, 122*(3), 671–679. https://doi.org/10.1016/j.ajcnut.2025.07.009