EnErGie: Enteral Nutrition in Malnutrition due to Gastrointestinal Diseases

From Basic Understanding to Innovative Treatment Concepts

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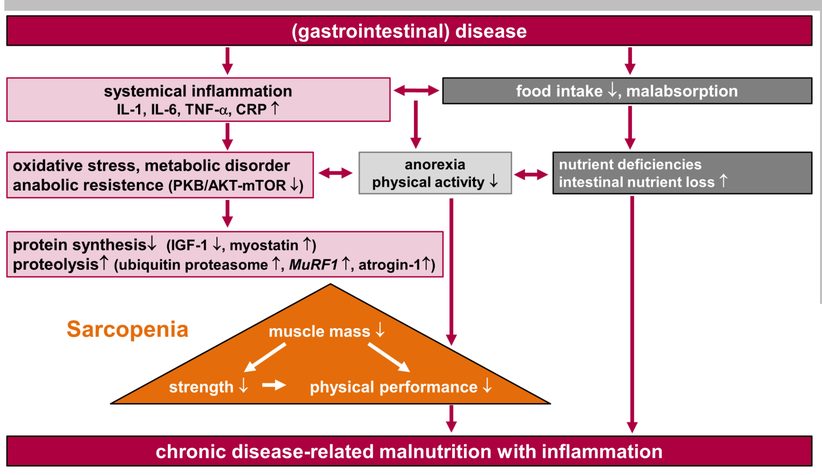
Introduction

Malnutrition and sarcopenia are key features in life threatening gastrointestinal diseases such as liver cirrhosis (LC), chronic pancreatitis (CP) or short bowel syndrome (SBS). Approximately 30% of gastrointestinal inpatients are malnourished. Disease-related malnutrition is associated with a reduced life expectancy, an increased risk of complications, an impaired quality of life and higher expenses. Pathophysiologically, disease-related malnutrition is linked to a low-grade systemic inflammation which in turn contributes to the reduction of muscle mass and subsequently sarcopenia (**Figure 1**).

In a multimodal approach, **EnErGie** addresses three project goals:

1. Understanding of the mechanistic interplay between malnutrition, sarcopenia and low-grade systemic inflammation in the different gastrointestinal diseases,



2. Developing a set of methods for diagnosis and follow-up of malnourished patients with gastrointestinal diseases and

3. Enabling a better care of malnourished patients.

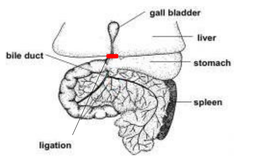
Figure 1: Pathophysiological mechanisms leading to sarcopenia and disease-related malnutrition.

I - Mouse models

- Experimental models of LC (bile duct ligation), CP (pancreatic duct ligation) and SBS (ileocecal resection) → all lead to malnutrition (**Figure 2**)
- Investigation of sarcopenia in all models
- Analyses and comparison throughout all models

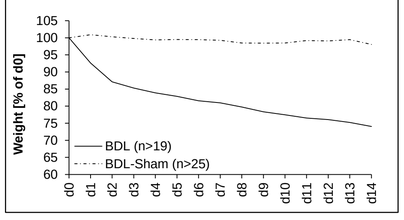
Bile duct ligation (BDL)

LC



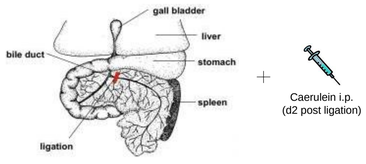
(modified according to Sendler et al. *Gastroenterology*. 2015)

- Cholestasis
- ➢Liver fibrosis
- ➢Malnutrition:



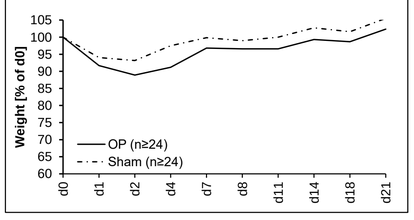
Pancreatic duct ligation

CP



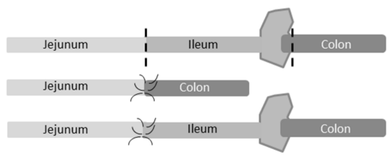
(Sendler et al. *Gastroenterology*. 2015)

- Loss of exocrine pancreatic tissue (fibrosis)
- ➢ Malnutrition:



Ileocecal resection (ICR)

SBS



(Berlin et al. *Am J Gastrointest Liver Physiol*, 2019)

- Malnutrition similar to SBS
- Adaptation possible
- ➢Malnutrition:

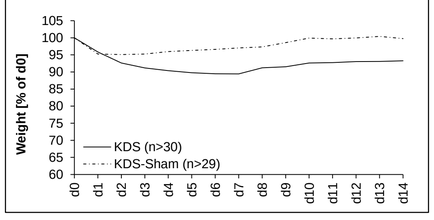


Figure 2: Experimental mouse models.

Methods

- Tissue collection of pancreas, bowel, liver, kidneys, muscles (histological studies (H&E-staining, immunohistochemistry, immunofluorescence), gene and protein analyses)
- Metabolic cages (energy expenditure/nitrogen balance)
- Collection of stool (stool water content, microbiomics)
- Clinical blood analyses and plasma metabolome
- Muscle strength measurements (grip strength)
- Fractional protein synthesis rate via measurements of stable isotopes ($^2H_5$-phenylalaine)

II - Cross-sectional study

- **Study design:** multicenter, prospective, controlled study
- **Study sites:** UMR, UMG and HSNB (FBN involved)
- **Period**: 10/2018 – 03/2022 (42 months)
- **Study population**:

Table 1: Participants in the cross-sectional study. Date: 16/10/2020.

	Reached	%
Total: 325 study participants	268	82,5
LC: 50 patients (50 % malnourished*)	57 (35)	114,0 (61,4)
CP: 50 patients (50 % malnourished*)	50 (22)	100,0 (44,0)
SBS: 50 patients (50 % malnourished*)	27 (17)	54,0 (63,0)
Control patients: 75 (malnourished)	40 (15)	53,3 (37,5)
Healthy controls: 100 (not malnourished)	94	94,0

* ESPEN or GLIM criteria

III - Longitudinal study

- **Study design:** multicenter interventional study
- **Study sites:** UMR and UMG together with HSNB (FBN involved)
- **Period**: 06/2019 – 11/2021 (30 months)
- **Study population**: 80 malnourished patients

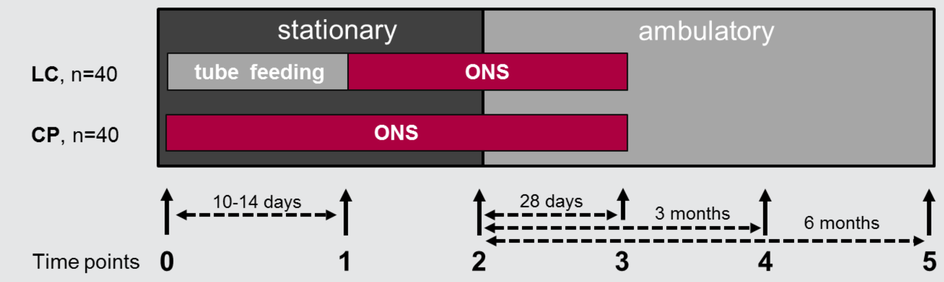
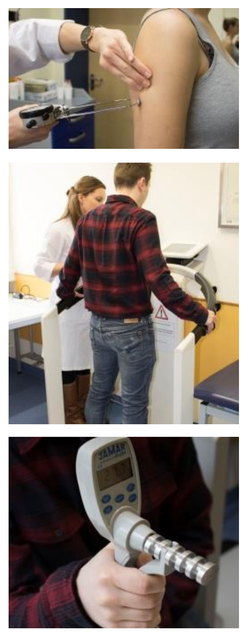


Figure 3: Study design of the longitudinal study. (ONS = oral nutritional supplements)

Methods

- Anthropometry (body weight, height, BMI, upper arm circumference, waist hip ratio, triceps skin fold thickness)
- Bioelectrical impedance analysis (FM(I), FFM(I), SMM(I), TBW, ECW, phase angle)
- Muscle strength and function (hand grip, walking speed)
- Questionnaires (food intake (SHIP-FFQ, DEGS-FFQ), physical activity (IPAQ) and mental health (depression, fatigue, loneliness))
- Clinical blood analyses and plasma metabolome
- Monocyte studies
- Intestinal barrier function (gene- and protein function of claudins and transporters, zonulin and lactulose/mannitol ratio)
- Transcriptomics
- Dietary counseling (G-NCP-based, face-to-face & by phone)



The joint project **EnErGie** combines expertise of five project partners from the fields of nutritional sciences, nutritional medicine, gastroenterology and basic, experimental research to study mechanisms of malnutrition and sarcopenia and to improve the medical care of malnourished patients.

Table 2: Project consortium.

Partner	Project Leader	Research Institution
P1	Prof Georg Lamprecht, Prof. Robert Jaster, Dr. Peggy Berlin	University Medical Center Rostock, Center for Internal Medicine, Clinic II, Department for Gastroenterology and Endocrinology
P2	Prof. Markus M. Lerch, Dr. Ali A. Aghdassi, Dr. Simone Gärtner	University Medical Center Greifswald, Clinic and Policlinic for Internal Medicine A, Department for Gastroenterology, Endocrinology and Nutritional Medicine
P3	Prof. Luzia Valentini	Hochschule Neubrandenburg, Division Agriculture and Food Sciences, In-Institute for Evidence-based Dietetics (NIED)
P4	Prof. Cornelia C. Metges	Leibniz-Institute for Farm Animal Biology Dummerstorf, Institute for Nutritional Physiology
P5	Prof. Leif-Alexander Garbe	Hochschule Neubrandenburg, Division Agriculture and Food Sciences, Food Technology

This joint project is funded by the European Union though the European Social Fund (ESF) within the framework of the qualification programme "Promotion of Young Scientists - Excellence Research Programme of the State of Mecklenburg-Western Pomerania".