Klinik für Hämatologie und Stammzelltransplantation
Universitätsmedizin Essen
Westdeutsches Tumorzentrum

Universitätsmedizin Essen
Universitätsklinikum

Mangelernährung bei Patienten mit chronischer GvHD

Chronische GvHD – Prophylaxe, Therapie und Supportive Care

Jahrestagung der DGHO – Basel 12.10.2024

Christina Rautenberg

Conflicts of Interest

1. Employment or Leadership Position: -
2. Advisory Role or Speaker Honoraria: Pfizer, JAZZ Pharmaceuticals, BMS
3. Stock Ownership: -
4. Patent, Copyright, Licensing: -
5. Financing of Scientific Research: JAZZ Pharmaceuticals
6. Travel support: BMS, JAZZ Pharmaceuticals, MEDAC

Malnutrition and chronic GvHD

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Review > Biol Blood Marrow Transplant. 2020 Nov;26(11):e265-e270.
doi: 10.1016/j.bbmt.2020.08.004. Epub 2020 Aug 9.

Challenging and Practical Aspects of Nutrition in Chronic Graft-versus-Host Disease

Andrea Z Pereira [1], Sandra Elisa Adami Gonçalves [2], Morgani Rodrigues [3], Nelson Hamerschlak [3], Mary E Flowers [4]

Affiliations + expand

PMID: 32784069 DOI: 10.1016/j.bbmt.2020.08.004

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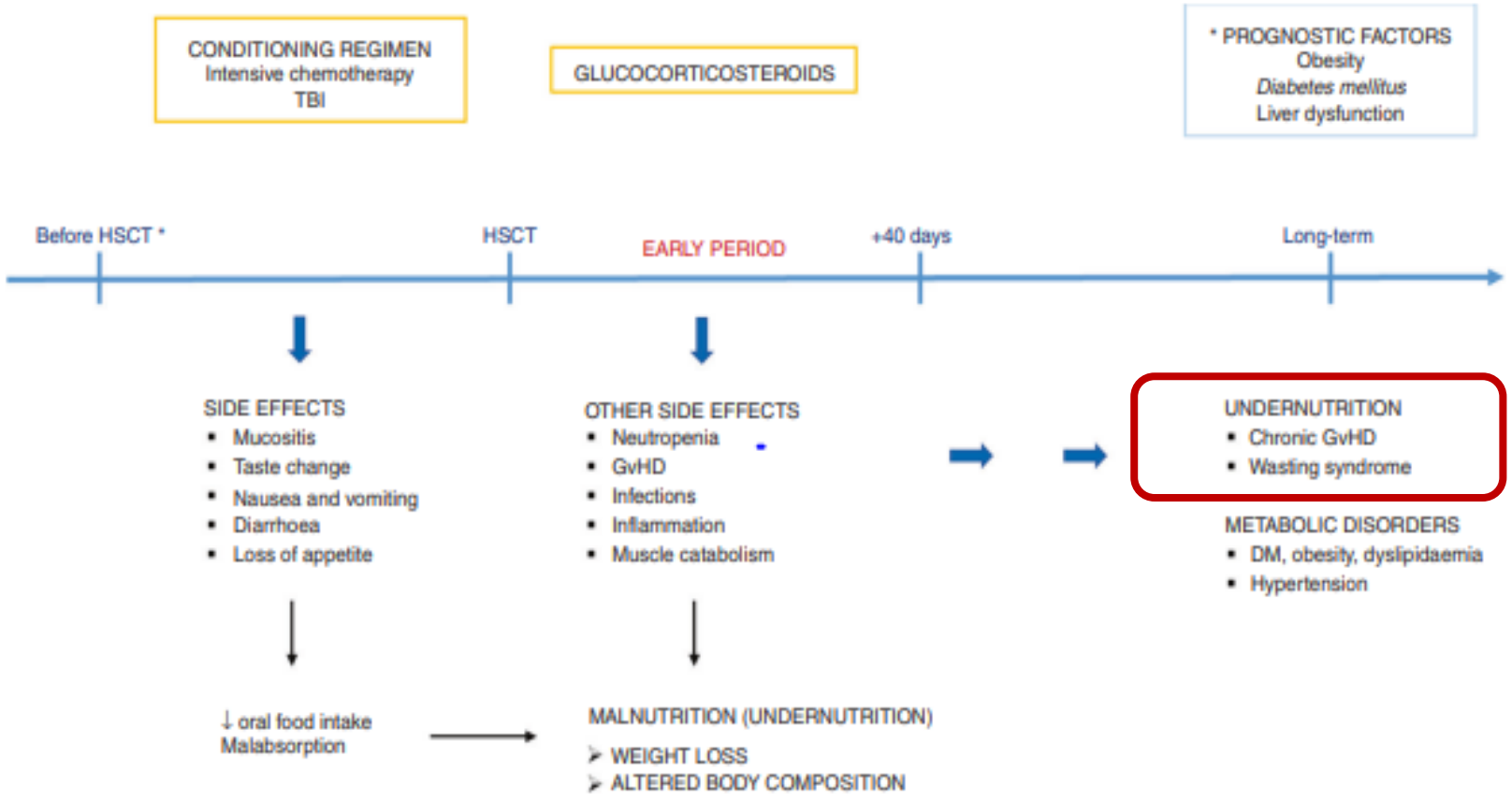
Agenda Malnutrition and chronic GvHD

- **Epidemiology, Etiology, Prognosis**
- **Screening Approaches**
- **Nutritional Strategies**
- **VitD and GvHD**
- **Outlook and Conclusion**

Although malnutrition occurs frequently during allo-SCT…



Casirati et al. BMT 2023

....it is not assessed regularly and/or in a standardized manner

Bone Marrow Transplantation

Variability of nutritional practices in peritransplant period after allogeneic hematopoietic stem cell transplantation: a survey by the Complications and Quality of Life Working Party of the EBMT

Zinaida Peric ✉, Stefano Botti, Jacqui Stringer, Joanna Krawczyk, Steffie van der Werf, Anja van Biezen, Mahmoud Aljurf, John Murray, Sarah Liptrott, Diana M. Greenfield, Rafael F. Duarte, Tapani Ruutu & Grzegorz W. Basak

all transplant centers reporting to the EBMT were invited → 19% (!) response

Table 2 Assessment and monitoring for malnutrition

Topic (question)	Results	Percentage
In your center, is there a guideline, protocol, or procedure that specifies how to monitor the nutritional status of transplant patients?	Yes	56%
	No	44%
In your center, is nutritional status assessed pre-transplant?	Yes	57%
	No	43%
In your center, is nutritional counseling performed during inpatient stay?	Yes, as routine	57%
	No	2%
	Only if necessary	41%
After discharge, is the nutritional status of patients evaluated?	Yes	49%
	No	7%
	Only for patients that have had some nutritional difficulty	43%
	Other (only weight is monitored)	1%
In centers where screening took place, who performed the screening:	Physicians	65%
	Nurses	22%
	Nutritionists	18%
	Dieticians	35%
In centers where screening took place, how did this take place (more than one response possible):	Part of history taking (social and dietary)	61%
	Anthropometric parameters	80%
	Blood chemistry parameters	78%
	Specific nutritional indices	53%
	Specific nutritional tools	16%

Malnutrition occurs frequently and correlates with cGvHD activity

2014 NIH Consensus Criteria for cGvHD of the GI Tract

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
GI Tract ***Check all that apply:*** ☐ Esophageal web/ proximal stricture or ring ☐ Dysphagia ☐ Anorexia ☐ Nausea ☐ Vomiting ☐ Diarrhea ☐ Weight loss ≥5%* ☐ Failure to thrive ☐ *Abnormality present but explained entirely by non-GVHD documented cause (specify):*_____	☐ No symptoms	☐ Symptoms without significant weight loss* (<5%)	☐ Symptoms associated with mild to moderate weight loss* (5-15%) **OR** moderate diarrhea without significant interference with daily living	☐ Symptoms associated with significant weight loss* >15%, requires nutritional supplement for most calorie needs **OR** esophageal dilation **OR** severe diarrhea with significant interference with daily living

43% of pts with cGvHD are malnourished:

- 29% moderate malnourished
- 14% severe malnourished

Pts with active cGvHD have significantly lower BMIs compared to pts with inactive cGvHD

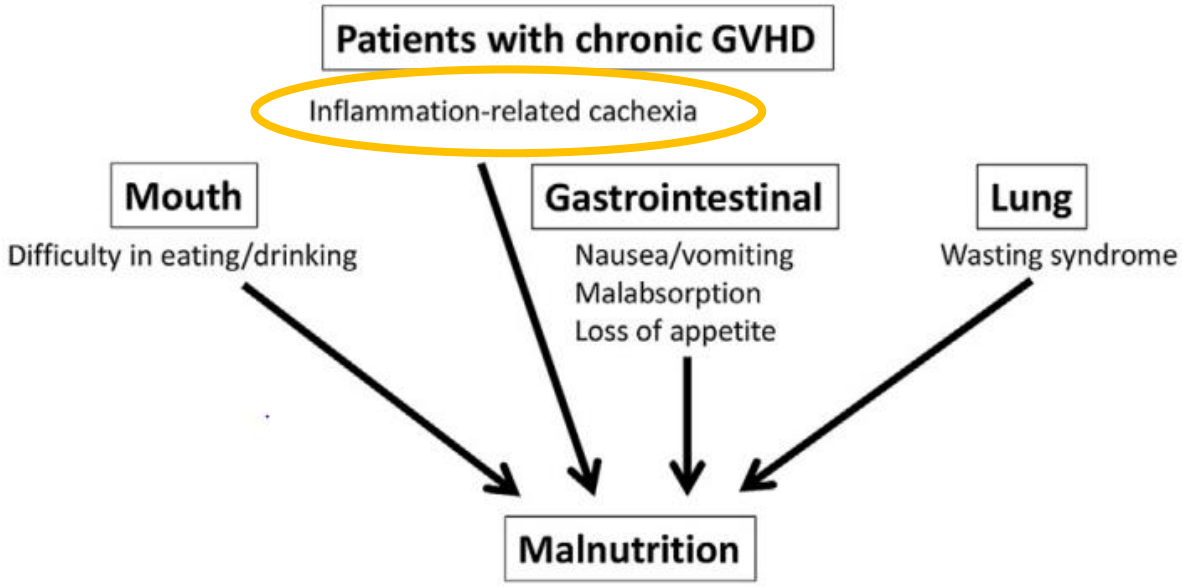
Important tool to treat malnutrition is to treat cGvHD

Jagasia et al. BBMT 2015; Jacobsohn et al. BMT 2002

Malnutrition in cGvHD is linked to certain cGvHD-associated symptoms and also to elevated resting energy expenditure

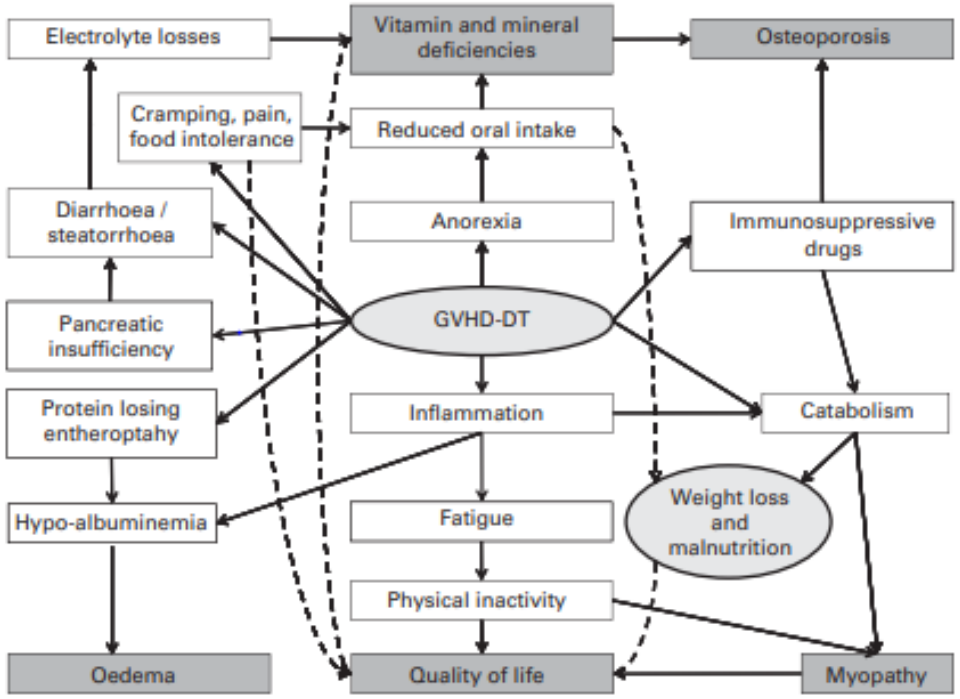
	Odds ratio 5–10% weight loss	*Odds ratio >10% weight loss*
Active *vs* inactive cGVHD	1.80 (0.31–10.38)	2.88 (0.86–9.48)
Odynophagia	0.77 (0.08–7.69)	0.86 (0.21–3.60)
Dysphagia	4.95 (0.97–25.8)	2.43 (0.83–7.24)
Nausea	1.28 (0.27–6.05)	0.79 (0.28–2.18)
Anorexia	1.80 (0.35–9.28)	0.95 (0.30–3.07)
Oral sensitivity[a]	0.95 (0.47–1.93)	1.23 (0.79–1.93)
Abdominal pain	3.22 (0.44–23.6)	2.53 (0.57–11.1)
Skin cGVHD	0.47 (0.09–2.46)	0.63 (0.20–1.97)
Age[b]	1.02 (0.95–1.10)	0.98 (0.93–1.03)
Time since BMT[b]	1.02 (0.70–1.48)	1.21 (0.96–1.52)
Time of therapy for CGVHD[b]	1.08 (0.76–1.55)	1.20 (0.96–1.51)

[a]Expressed as odds ratio for each increasing grade in severity of oral sensitivity.
[b]Expressed as odds ratio for each additional year.



Fuji et al. TCT 2015; Jacobsohn et al. BMT 2002; Zauner et al., Transplantation 2001

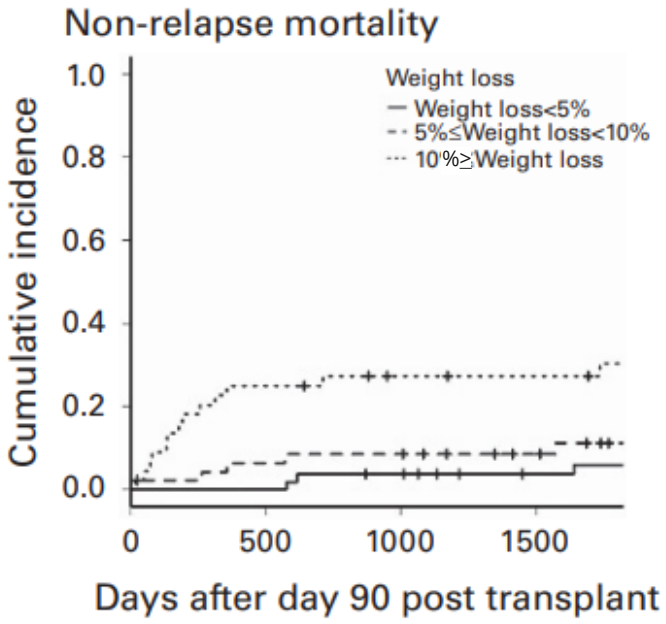
Not only cGvHD itself, but also side effects associated with medication for cGvHD contribute to malnutrition

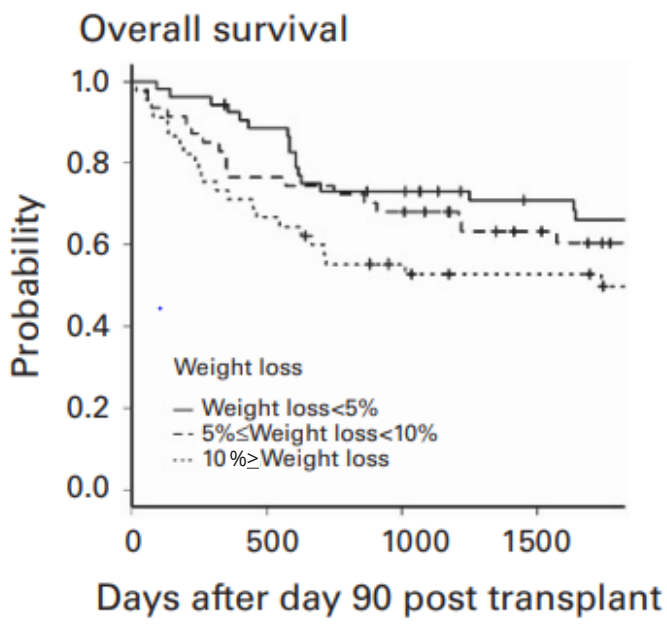


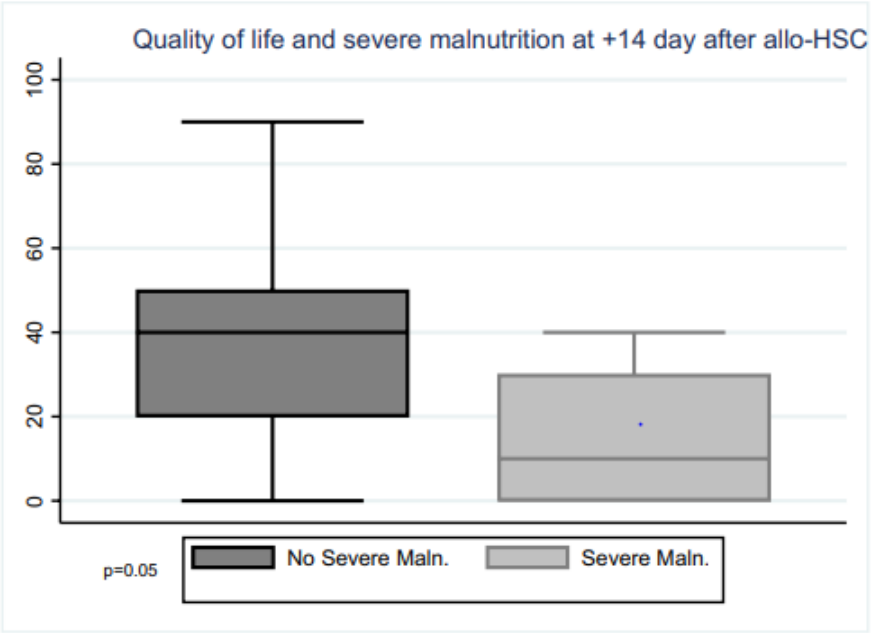
Drugs	Side Effects
Corticosteroids & CNIs	Hyperglycemia & DM, Osteopenie/Osteoporosis
CNIs & Sirolimus	Renal Dysfunction
Corticosteroids, CNIs, MTX, Ibrutinib, Ruxolitinib	Liver Dysfunction
MMF, CNIs, Ibrutinib	**GI-Side Effects**
Corticosteroids, CNIs, Sirolimus, Ruxolitinib	Hyperkalemia, Hypo-magnesemia, Hyperlipidemia

Arai et al., BBMT 2015; adapted by Pereira et al. BBMT 2020

Malnutrition is associated with worse outcome and reduced QoL after allo-SCT

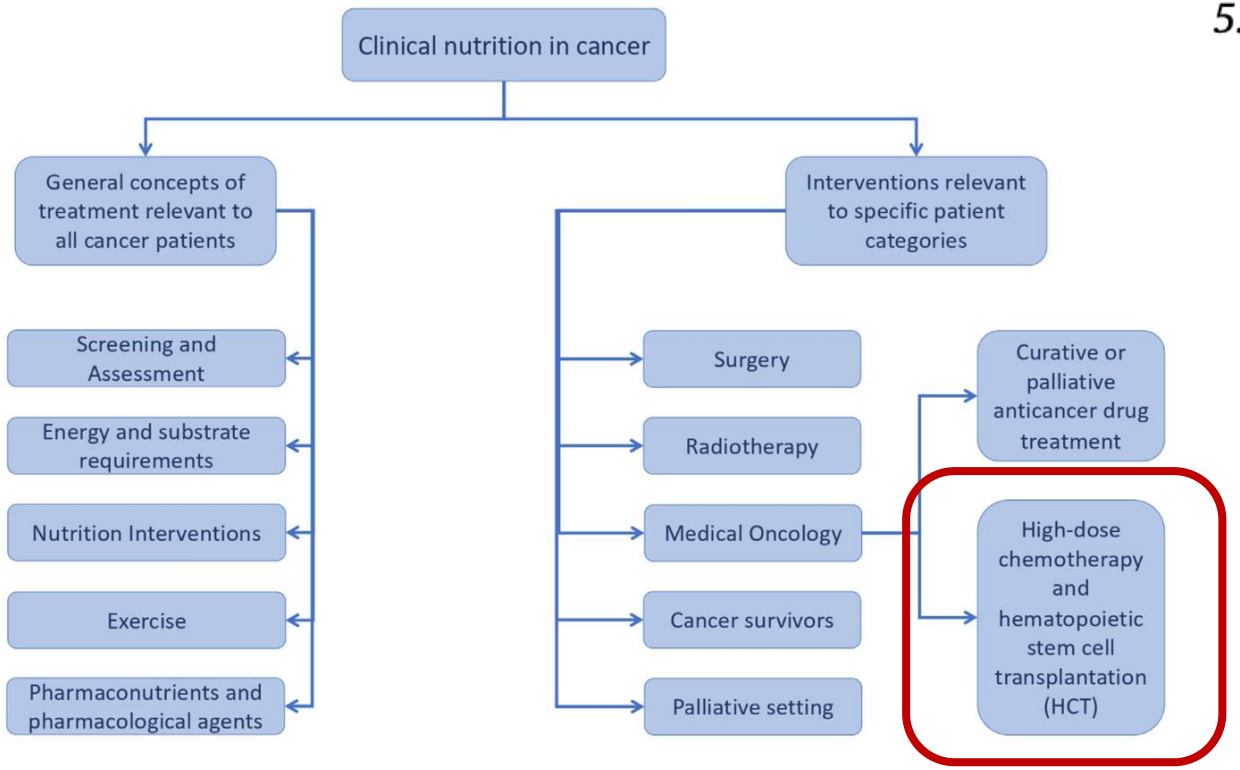






Fuji et al. BMT 2015; Cioce et al. IJH 2022

Practical Guideline for Clinical Nutrition in Cancer by the European Society for Clinical Nutrition & Metabolism (ESPEN)



5.4. Medical oncology: high-dose chemotherapy and HSCT

35) During intensive chemotherapy and after stem cell transplantation we recommend maintaining physical activity and to ensure an adequate nutritional intake. This may require EN and/or PN. (Recommendation C4-1; strength of recommendation strong – Level of evidence very low – strong consensus)

- **early screening**
- **early nutritional support**
- **regularly re-screening**

  → avoid or minimize loss of body weight

Screening, Assessment & Grading of Malnutrition according to the Global Leadership Initiative on Malnutrition (GLIM)

Risk screening

At risk for malnutrition

- Use validated screening tools

Table 1. Survey of existing approaches used in screening and assessment of malnutrition and cachexia.

	NRS-2002[12a]	MNA-SF[21a,b]	MUST[22a]	ESPEN 2015[8a]	ASPEN/AND[7a]	SGA[4a]	Evans 2008[5c]	PEW 2008[23d]	Fearon 2011[6c]
Etiologies									
Reduced food intake	X	X	X	X	X	X		X	X
Disease burden/ inflammation	X	X	X	X	X	X	X	X	X
Symptoms									
Anorexia		X				X	X		X
Weakness		X				X	X		
Signs/Phenotype									
Weight loss	X	X	X	X	X	X	X	X	X
Body mass index	X	X	X	X			X	X	X
Lean/fat free/ muscle mass		X		X	X	X	X	X	X
Fat mass					X	X		X	
Fluid retention/ascites					X	X			
Muscle function; e.g. grip strength					X	X	X		
Biochemistry							X	X	

NRS-2002: Nutritional Risk Screening-2002, MNA-SF = Mini Nutritional Assessment-Short Form, MUST = Malnutrition Universal Screening Tool, ESPEN = European Society for Clinical Nutrition and Metabolism, ASPEN = American Society of Parenteral and Enteral Nutrition, AND = Academy of Nutritiona and Dietetics, SGA = Subjective Global Assessment, PEW=Protein Energy Wasting
[a]Malnutrition approach
[b]Adapted for older adults
[c]Cachexia approach
[d]Adapted for chronic kidney disease

Cederholm et al. Journal of Cachexia, Sarcopenia and Muscle 2019

Nutritional Risk Scale 2002 (NRS 2002)

Screening auf Mangelernährung

Nutritional Risk Screening (NRS 2002)

nach Kondrup J et al., Clinical Nutrition 2003; 22: 415-421

Empfohlen von der Europäischen Gesellschaft für Klinische Ernährung und Stoffwechsel (ESPEN)

Vorscreening:

• Ist der Body Mass Index < 20,5 kg/m² ?	ja	nein
• Hat der Patient in den vergangenen 3 Monaten an Gewicht verloren?	ja	nein
• War die Nahrungszufuhr in der vergangenen Woche vermindert?	ja	nein
• Ist der Patient schwer erkrankt? (z.B. Intensivtherapie)	ja	nein

⇒ Wird eine dieser Fragen mit „**Ja**" beantwortet, wird mit dem Hauptscreening fortgefahren

⇒ Werden alle Fragen mit „**Nein**" beantwortet, wird der Patient wöchentlich neu gescreent.

⇒ Wenn für den Patienten z.B. eine große Operation geplant ist, sollte ein präventiver Ernährungsplan verfolgt werden, um dem assoziierte Risiko vorzubeugen.

Hauptscreening:

Störung des Ernährungszustands	Punkte
Keine	**0**
Mild Gewichtsverlust > 5%/ 3 Mo. oder Nahrungszufuhr < 50-75% des Bedarfes in der vergangenen Woche	**1**
Mäßig Gewichtsverlust > 5%/ 2 Mo. oder BMI 18,5-20,5 kg/m² und reduzierter Allgemeinzustand (AZ) oder Nahrungszufuhr 25-50% des Bedarfes in der vergangenen Woche	**2**
Schwer Gewichtsverlust> 5% /1 Mo. (>15% / 3 Mo.) oder BMI <18,5 kg/m² und reduzierter Allgemeinzustand oder Nahrungszufuhr 0-25% des Bedarfes in der vergangenen Woche	**3**

+

Krankheitsschwere	Punkte
Keine	**0**
Mild z.B. Schenkelhalsfraktur, chronische Erkrankungen besonders mit Komplikationen: Leberzirrhose, chronisch obstruktive Lungenerkrankung, chronische Hämodialyse, Diabetes, Krebsleiden	**1**
Mäßig z.B. große Bauchchirurgie, Schlaganfall, schwere Pneumonie, hämatologische Krebserkrankung	**2**
Schwer z.B. Kopfverletzung, Knochenmarktransplantation, intensivpflichtige Patienten (APACHE-II >10)	**3**

+ **1 Punkt, wenn Alter ≥ 70 Jahre**

Intervention, wenn:
- **NRS ≥4**
- **NRS <4, aber BMI ≤ 18kg/qm**
- **NRS <4, aber orale Nahrungsaufnahme ≤60% des individuellen Bedarfs**

Kondrup et al. Clinical Nutrition 2003; adapted by Schütz et al. Akt Ernaehr Med 2005; adapted by EBMT Handbook 2019

Screening, Assessment & Grading of Malnutrition according to the Global Leadership Initiative on Malnutrition (GLIM)

Risk screening

At risk for malnutrition

- Use validated screening tools

Cederholm et al. Journal of Cachexia, Sarcopenia and Muscle 2019

Screening, Assessment & Grading of Malnutrition according to the Global Leadership Initiative on Malnutrition (GLIM)

Risk screening

Diagnostic Assessment

At risk for malnutrition

- Use validated screening tools

Assessment criteria

- **Phenotypic**
  - Weight loss
  - Low body mass index
  - Reduced muscle mass
- **Etiologic**
  - Reduced food intake or assimilation
    Disease burden/inflammatory condition

Table 3. Phenotypic and etiologic criteria for the diagnosis of malnutrition.

Phenotypic Criteria*			Etiologic Criteria*	
Weight loss (%)	Low body mass index (kg/m^2)	Reduced muscle mass[a]	Reduced food intake or assimilation[b, c]	Inflammation[d,e,f]
>5% within past 6 months, or>10% beyond 6 months	<20 if <70 years, or <22 if >70 years Asia: <18.5 if <70 years, or <20 if >70 years	Reduced by validated body composition measuring techniques[a]	≤50% of ER >1 week, or any reduction for >2 weeks, or any chronic GI condition that adversely impacts food assimilation or absorption[b,c]	Acute disease/injury[d,f] or chronic disease-related[e,f]

Cederholm et al. Journal of Cachexia, Sarcopenia and Muscle 2019

Screening, Assessment & Grading of Malnutrition according to the Global Leadership Initiative on Malnutrition (GLIM)

Risk screening

At risk for malnutrition
- Use validated screening tools

Diagnostic Assessment

Assessment criteria
- **Phenotypic**
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Diagnosis

Meets criteria for malnutrition diagnosis
- Requires at least 1 Phenotypic criterion and 1 Etiologic criterion

Table 3. Phenotypic and etiologic criteria for the diagnosis of malnutrition.

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Cederholm et al. Journal of Cachexia, Sarcopenia and Muscle 2019

Screening, Assessment & Grading of Malnutrition according to the Global Leadership Initiative on Malnutrition (GLIM)

Risk screening

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Diagnostic Assessment

Assessment criteria
- **Phenotypic**
  - Weight loss
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- **Etiologic**
  - Reduced food intake or assimilation
  - Disease burden/inflammatory condition

Diagnosis

Meets criteria for malnutrition diagnosis
- Requires at least 1 Phenotypic criterion and 1 Etiologic criterion

Severity Grading

Determine severity of malnutrition
- Severity determined based on Phenotypic criterion

CAVE: Screening tools are (in part) recommended by the ESPEN/ASPEN in cancer, but have not yet been validated in the context of cGVHD

Table 4. Thresholds for severity grading of malnutrition into stage 1 (moderate) and stage 2 (severe) malnutrition

	Phenotypic Criteria[a]		
	Weight loss (%)	Low body mass index (kg/m^2)[b]	Reduced muscle mass[c]
Stage 1/Moderate Malnutrition (Requires 1 phenotypic criterion that meets this grade)	5–10% within the past 6 mo, or 10–20% beyond 6 mo	<20 if <70 yr, <22 if ≥70 yr	Mild to moderate deficit (per validated assessment methods – see below)
Stage 2/Severe Malnutrition (Requires 1 phenotypic criterion that meets this grade)	>10% within the past 6 mo, or >20% beyond 6 mo	<18.5 if <70 yr, <20 if ≥70 yr	Severe deficit (per validated assessment methods – see below)

Cederholm et al. Journal of Cachexia, Sarcopenia and Muscle 2019; Gupta et al. Ann Nutr Metab. 2011

Baseline Recommendations: Nutritional Strategies

Nutritional Intervention if:
- **NRS ≥4**
- **NRS <4, but underweight (BMI ≤ 18kg/qm)**
- **NRS <4, but oral food intake ≤60% of individual daily needs**

STEP 1: Oral Nutritional Support (ONS)

in/out-patient

Adaption of main courses to personal food preferences

Additional snacks

Protein/Caloric enrichment of food (powder)

Energy/protein dense drinks

Regularly Re-Assessment

in case of intestinal a/cGvHD lactose-free, fat-free/-reduced, gluten-free diet

Adapted by EBMT Handbook 2019; Toenges et al. Clinical Nutrition 2021

Baseline Recommendations: Nutritional Strategies

Nutritional Intervention if:
- **NRS ≥4**
- **NRS <4, but underweight (BMI ≤ 18kg/qm)**
- **NRS <4, but oral food intake ≤60% of individual daily needs**

STEP 1: Oral Nutritional Support (ONS)	**in/out-patient**

Baseline Recommendations: Nutritional Strategies

Nutritional Intervention if:
- **NRS ≥4**
- **NRS <4, but underweight (BMI ≤ 18kg/qm)**
- **NRS <4, but oral food intake ≤60% of individual daily needs**

STEP 1: Oral Nutritional Support (ONS)	**in/out-patient**
STEP 2: Enteral Nutritional Support (EN) + Vit K once weekly	**in/out-patient**
if no severe malabsorption OR intolerance for NGT	**Regularly Re-Assessment**

NGT is used by 19%[1] - 50%[2] of Transplant Centers

Adapted by EBMT Handbook 2019; [1]Peric et al. BMT 2018; [2]Toenges et al. Clinical Nutrition 2021

Baseline Recommendations: Nutritional Strategies

Nutritional Intervention if:
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Baseline Recommendations: Nutritional Strategies

Nutritional Intervention if:
- **NRS ≥4**
- **NRS <4, but underweight (BMI ≤ 18kg/qm)**
- **NRS <4, but oral food intake ≤60% of individual daily needs**

STEP 1: Oral Nutritional Support (ONS)	**out-patient**
STEP 2: Enteral Nutritional Support (EN) + Vit K once weekly	**in/out-patient**
STEP 3: Parenteral Nutritional Support (PN) + lipid- and water-soluble vitamins and trace elements	**in/out-patient**

Enteral vs. Parenteral Nutritional Support

Enteral Nutrition

+ maintains gut barrier

+ microbiota diversity

+ increases IgA level

- difficult access

- intolerance

Parenteral Nutrition

+ fully balanced diet

+ easy administration

- microbiota dysbiosis

- mucosal atrophy

- vascular access

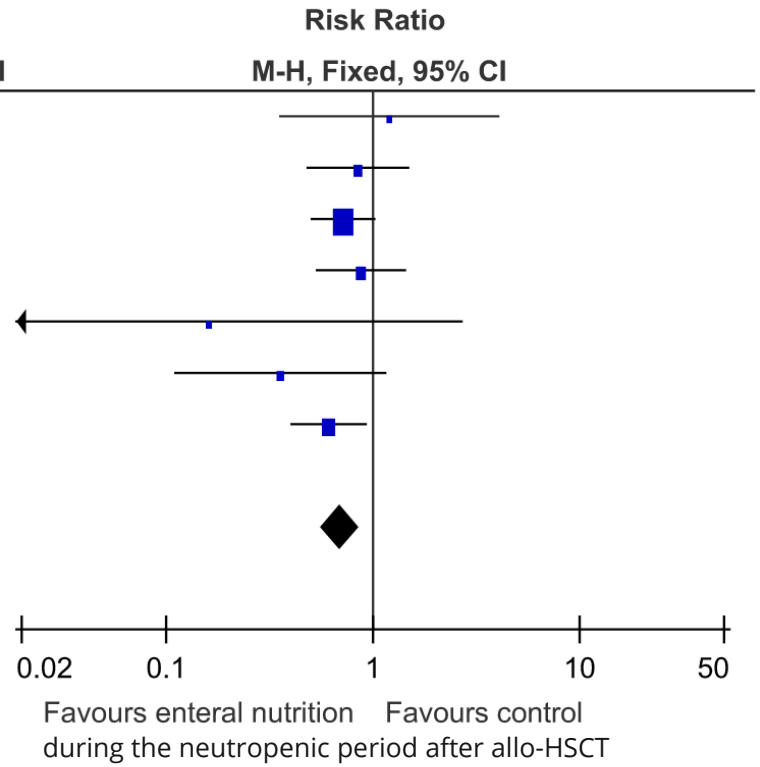
- increased infections

Enteral vs. Parenteral Nutritional Support

	Enteral Nutrition		Control			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Andersen 2015	3	5	2	4	2.0%	1.20 [0.36, 4.04]
Andersen 2020	10	20	13	22	10.9%	0.85 [0.48, 1.48]
Gonzales 2018	33	97	46	97	40.5%	0.72 [0.51, 1.02]
Guieze 2015	14	28	16	28	14.1%	0.88 [0.54, 1.43]
Hopman 2003	0	12	5	22	3.5%	0.16 [0.01, 2.68]
Papadopoulou 1998	3	20	8	19	7.2%	0.36 [0.11, 1.15]
Seguy 2012	34	94	16	27	21.9%	0.61 [0.40, 0.92]
Total (95% CI)		**276**		**219**	**100.0%**	**0.69 [0.56, 0.86]**
Total events	97		106			

Heterogeneity: Chi² = 4.82, df = 6 (P = 0.57); I² = 0%

Test for overall effect: Z = 3.37 (P = 0.0007)



less aGvHD (P=0.0007), less III/IV aGvHD (P<0.0001), less gut aGvHD (P<0.0001), no impact on incidence of mucositis, no impact on OS

Baseline Recommendations: Estimation of Calorie and Protein Intake

BMI, kg/m^2	Calorie Intake, kcal/kg Body Weight	Protein Intake, kcal/kg Body Weight *
≤18.5	30-45	1.5-2.0
18.5< x ≥29.9	25-30	1.5-2.0
≥30	<14 kcal/kg actual weight or 22-25 kcal/kg ideal weight	1.2-1.5 g/kg actual weight or 2-2.5 g/kg ideal weight

BMI indicates body mass index.

* less protein intake for pts with renal insufficiency: 0.8g/kg BW

More exact estimation using:

- **BASAROT Table (BMI-Age-Sex-Adapted Rule Of Thumb)**
- **Harris Benedict Formula**

} **including aspects of body weight (BMI), gender, age**

Pereira et al. BBMT 2020; Valentini et al. Nutrition 2012; Harris et al. Proc Natl Acad Sci 1918

Energiebedarf = Grundumsatz nach BASAROT x (PAL + Stressfaktor)

Tabelle: Erhebung des Ruheenergieumsatzes für Frauen anhand der BMR-Faktoren (kcal/kg KG)

BMI / Alter	< 14	14-16,4	16,5-18,4	18,5-19,9	20-24,9	25-29,9	30-34,9	> 35
18 - 29	31,4	28,3	26,2	23,7	22,6	20,2	16,4	14,3
30 - 39	30,1	27,2	25,2	23,6	21,8	19,2	16,0	14,3
40 - 49	28,9	26,1	24,3	22,9	21,2	18,7	16,0	14,1
50 - 59	27,7	25,1	23,3	21,8	19,8	18,4	15,5	13,3
60 - 69	26,4	24,1	22,4	21,5	19,2	17,8	14,8	13,2
70 - 79	25,2	23,1	21,6	20,8	18,8	17,2	14,5	13,3
80 - 100	24	22,6	20,5	20,1	18,2	16,8	14,5	12,4

Tabelle: Erhebung des Ruheenergieumsatzes für Männer anhand der BMR-Faktoren (kcal/kg KG)

BMI / Alter	< 14	14-16,4	16,5-18,4	18,5-19,9	20-24,9	25-29,9	30-34,9	> 35
18 - 29	30,6	30,3	28,4	27,1	25,4	22,8	19,6	17,7
30 - 39	29,0	28,4	27,0	25,5	23,6	22,5	18,9	17,1
40 - 49	28,7	27,0	25,7	24,6	23,1	21,3	17,8	16,6
50 - 59	26,9	25,6	24,4	23,2	21,9	20,5	17,7	15,9
60 - 69	25,6	24,4	23,2	22,8	21,1	19,8	16,6	14,6
70 - 79	24,6	23,4	22,2	21,2	19,9	18,9	16,1	14,9
80 - 100	22,6	21,6	20,2	19,6	19,0	18,3	15,2	14,0

PAL-Werte bei unterschiedlichen Berufs- und Freizeittätigkeiten

Arbeitsschwere und Freizeitverhalten	PAL
Ausschließlich sitzende oder liegende Lebensweise, Personen in stationärer Behandlung mit Bettlägerigkeit	1,2
Ausschließlich sitzende Tätigkeit mit wenig oder keiner Freizeitaktivität, Patienten im Krankenhaus, die mobil sind	1,4 - 1,5
Sitzende, zeitweilig stehende und gehende Tätigkeiten, normale Freizeitaktivität	1,6 - 1,7
Überwiegend gehende und stehende Tätigkeiten, regelmäßige Freizeitaktivität (30 - 60 Min pro Einheit, 4 - 5 x pro Woche)	1,8 - 1,9
Körperlich anstrengende berufliche Arbeit	2,0 - 2,4

Stress-Faktoren

(Korrektur des Ruheenergieumsatzes aufgrund von zusätzlichen, besonderen Belastungen)

Fraktur	1,15 - 1,30
Tumorerkrankungen	1,10 - 1,30
Peritonitis/ Sepsis	1,10 - 1,30
Schwere Infektion	1,10 - 1,30
Verbrennungen	1,20 - 2,00
Lebererkrankungen:	
Akutes Leberversagen	1,20 - 1,30
Alkoholische Fettleber	1,30
Nichtalkoholische Fettleber	1,00
Leberzirrhose	1,30

Valentini et al. Nutrition 2012

Recommendations for Micronutritiens

Daily Recommendation, Diagnosis, and Treatment of Nutritional Deficiency

Nutrient	Daily Recommendation Age Male Female			Deficiency Diagnosis	Treatment
Vitamin A	14-≥51 yr	900 μg RAE		<.70 μmol/L	Vitamin A palmitate in oil 60,000 UI orally once daily for 2 d, followed by 4500 UI orally once daily
Vitamin D	14-≥ 71 yr	600 UI 800 UI		<20 ng/mL	50,000 UI D2 or D3 once per week or 5000 UI daily for 2-3 mo
Zinc	14-70 yr	12 mg/d	15 mg/d	<70 ug/dL in females; <74 ug/dL in males	≥3 doses of 45 mg $ZnSO_4$/d
Magnesium	14-18 yr 19-30 yr ≥31 yr	410 mg 400 mg 420 mg	360 mg 310 mg 320 mg	<1.4 mEq/L	First day: Mg sulfate 1.0-2.0 g/h i.v. for 3-6 h Second day: Mg sulfate .5-1.0 g/h i.v. for 3-4 d >fifth day: Mg oxide 2 tablets/d
Potassium	14-≥ 51 yr	4.7 mg		Mild (3.0-3.4 mEq/L) Moderate (2.5-2.9 mEq/L) Severe (<2.5 mEq/L)	Tablets (72 mmol/d) or i.v. infusion 25 mL (75 mmol/d) Tablets (96 mmol/d) or i.v infusion 25 mL (100 mmol/d) i.v replacement 40 mmol KCL in 11.9% (glucose 5% may be used)

1 μg RAE = 1 μg retinol, 2 μg beta-carotene from supplements, 12 μg beta-carotene from foods, 24 μg alpha-carotene, or 24 μg beta-cryptoxanthin.

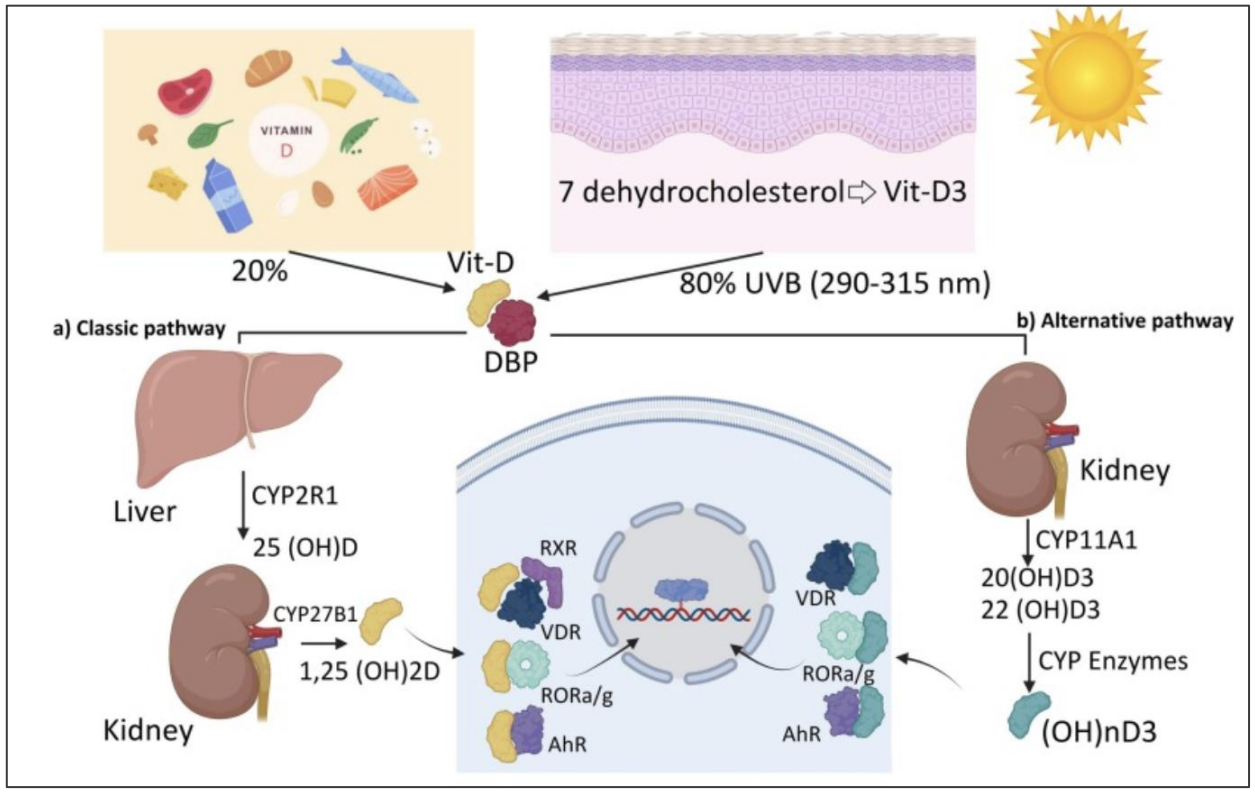
No routine use of immunonutritients:

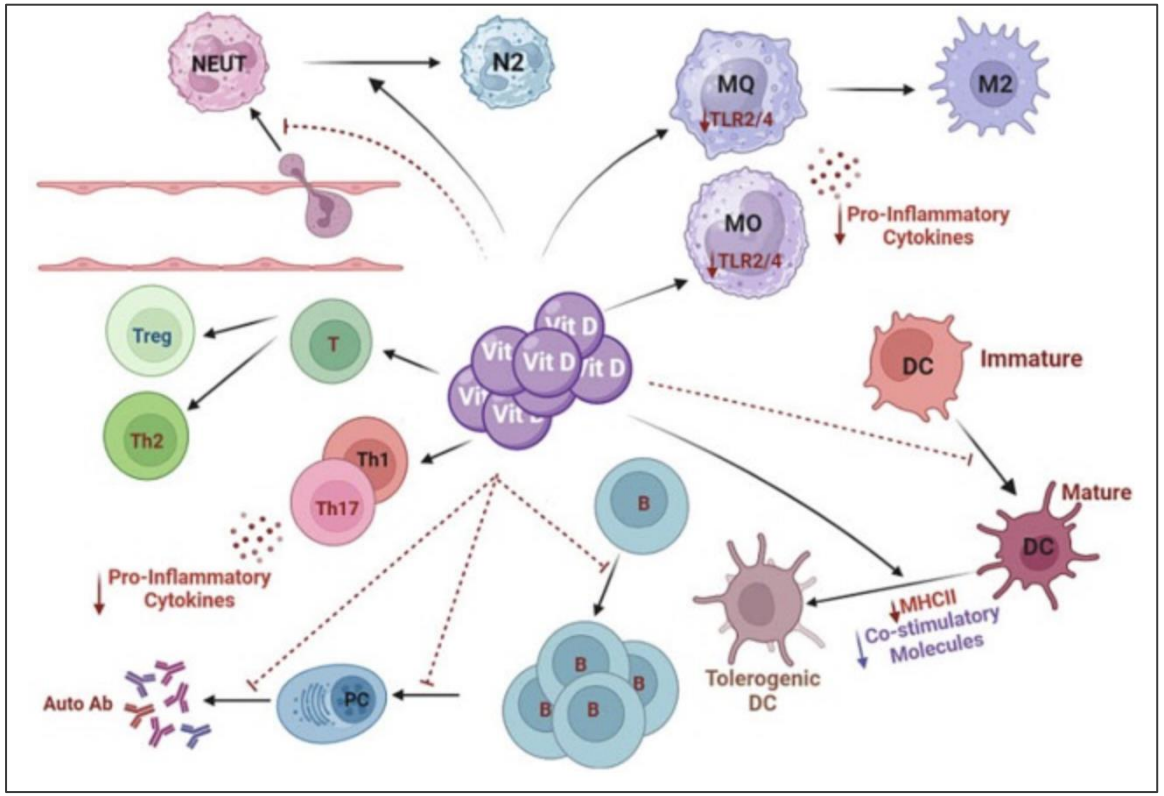
- **Glutamin**
- **Prebiotics/probiotics**
- **Omega-3-fatty acids etc…**

…besides Vit D

Pereira et al. BBMT 2020; EBMT Handbook 2019

Besides calcium homeostasis Vitamin D also exerts immunmodulatory effects





Besides calcium homeostasis Vitamin D also exerts immunmodulatory effects

- **prospective multicenter phase I/II trial**
- **N=150 patients, with 50 pts each group:**
  - **control group, CG** (no VitD)
  - **low-dose group, LdD**
    (1,000 IU VitD daily d-5 until d+100)
  - **high-dose group, HdD**
    (5,000 IU VitD daily d-5 until d+100)

Primary Outcome Measures:

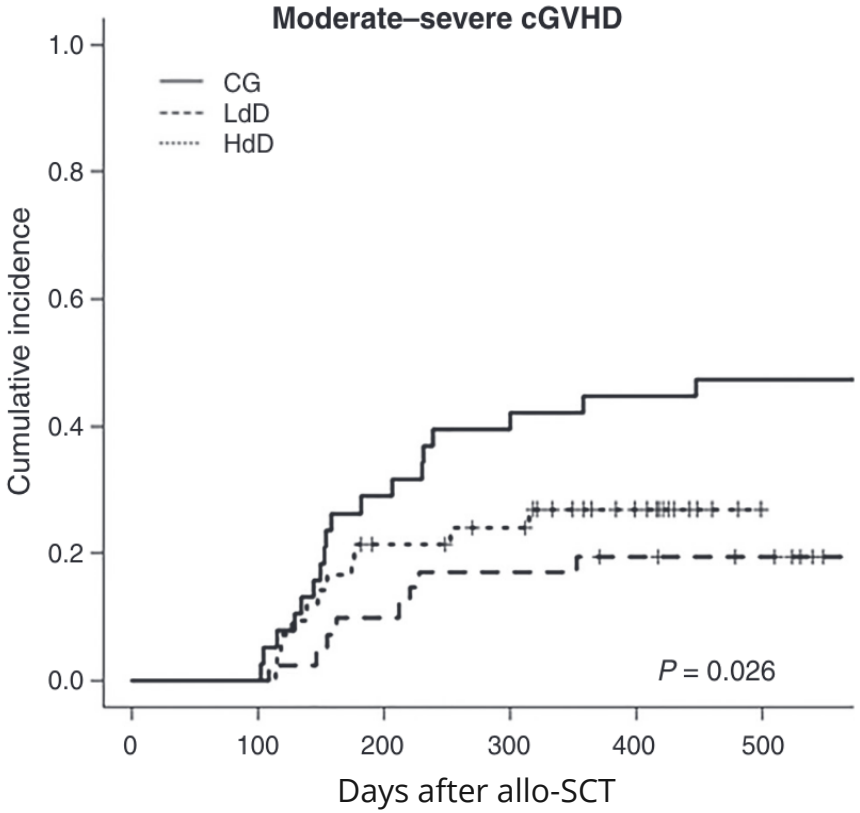
- **Incidence/severity of GvHD d+150**

Secondary Outcome Measures:

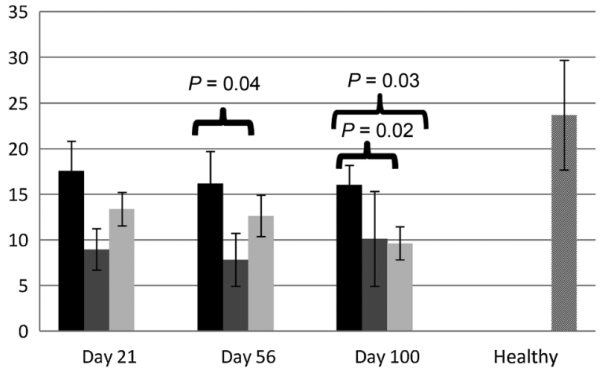
- **Cytokines**
- **Immune subpopulations**

Caballero-Velazquez et al. Clinical Cancer Research 2016

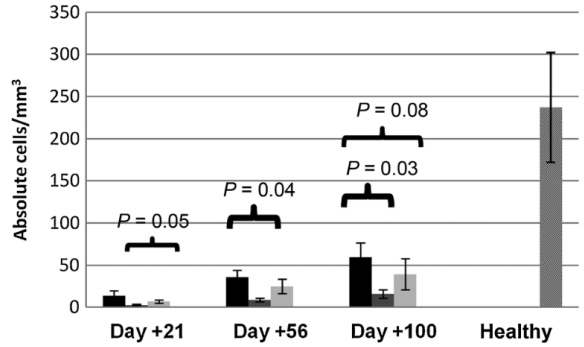
Pts receiving VitD showed lower incidence of cGVHD and a modified immune response after alloSCT



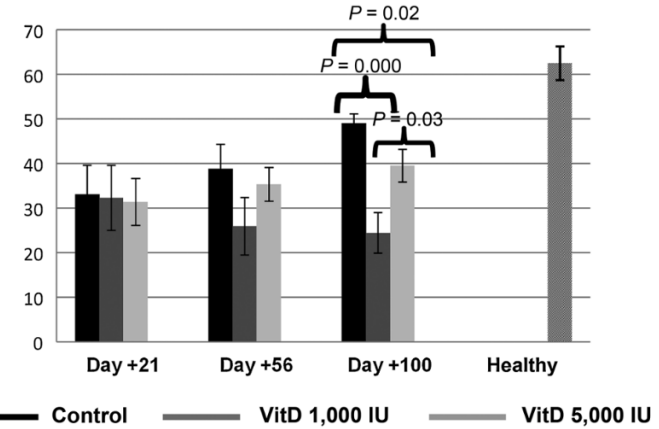
less naive CD8+ T-cells



less B-cells



lower expression of CD40L



- immunomodulatory effect of VitD depends on the VDR SNPs
- patients carrying the FokI CT genotype have the highest benefit from receiving vit D after allo-HSCT

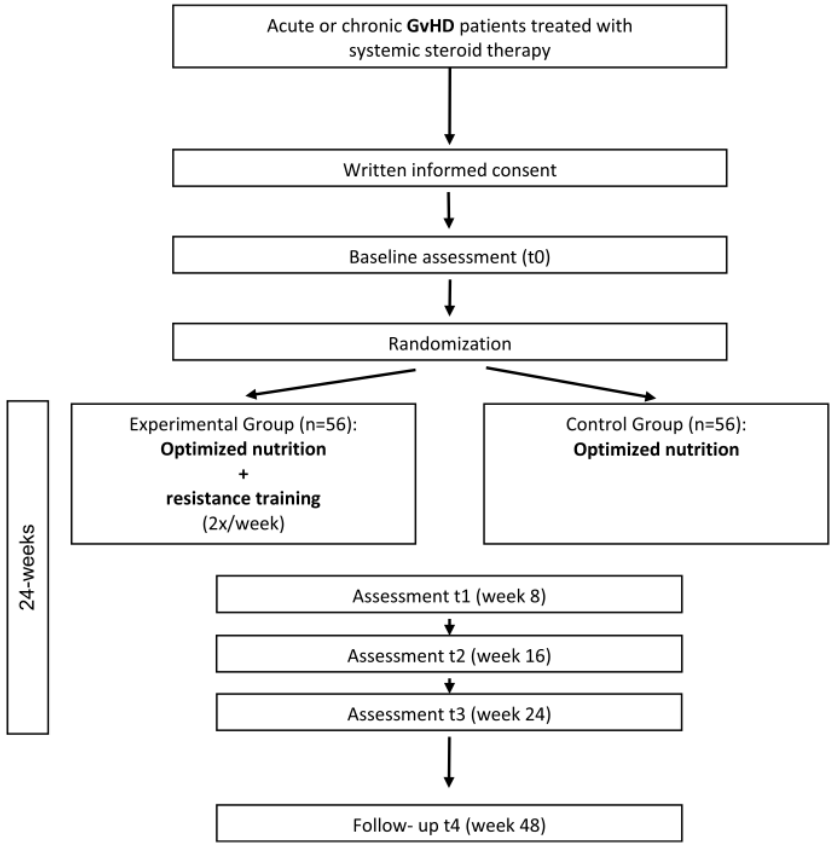
Caballero-Velazquez et al. Clin Cancer Res. 2016; Carrillo-Cruz et al. Clin Cancer Res. 2019

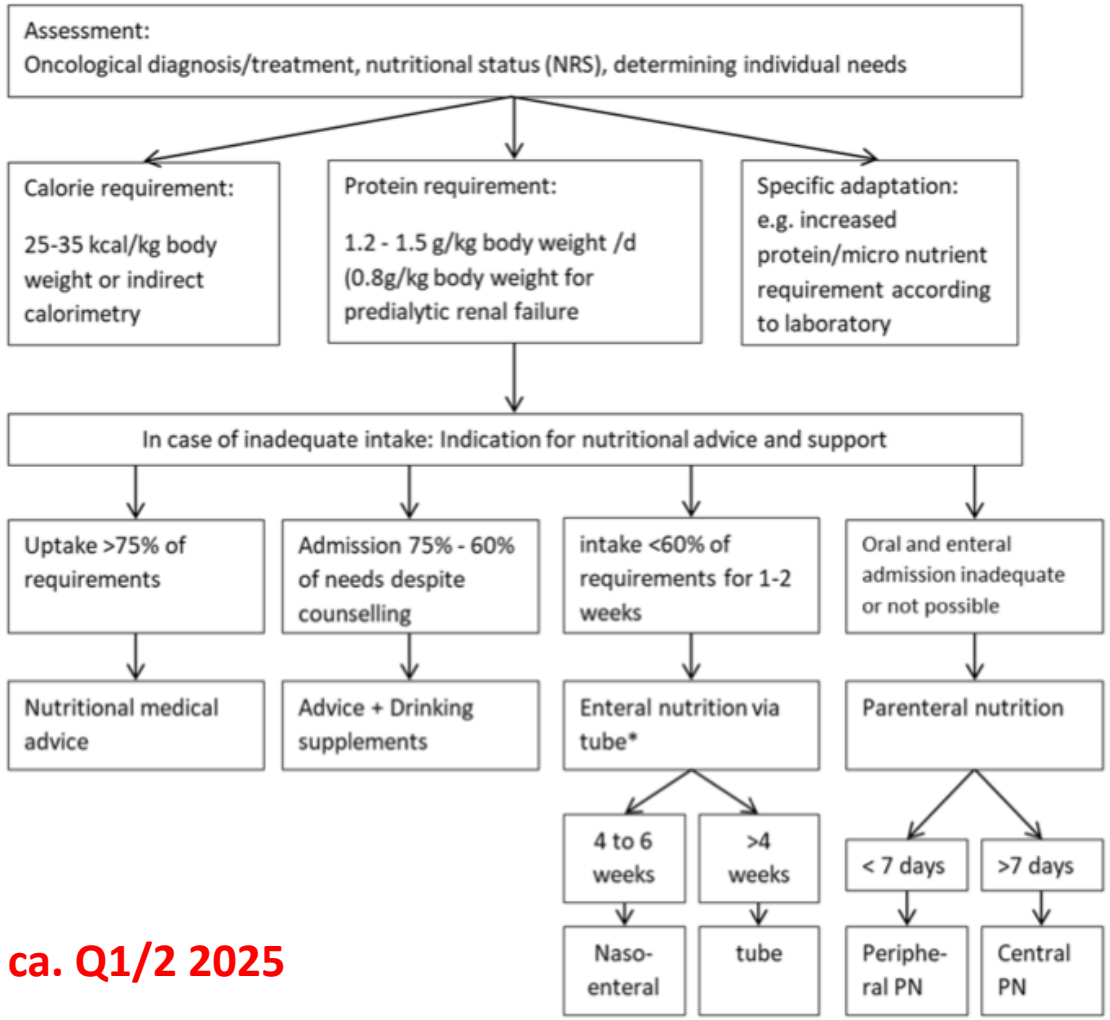
Nutritional Support, Activity & GvHD

STUDY PROTOCOL Open Access

Impact of Resistance Exercise and Nutritional Endorsement on physical performance in patients with GvHD (IRENE-G study) – design and rational of a randomized controlled trial

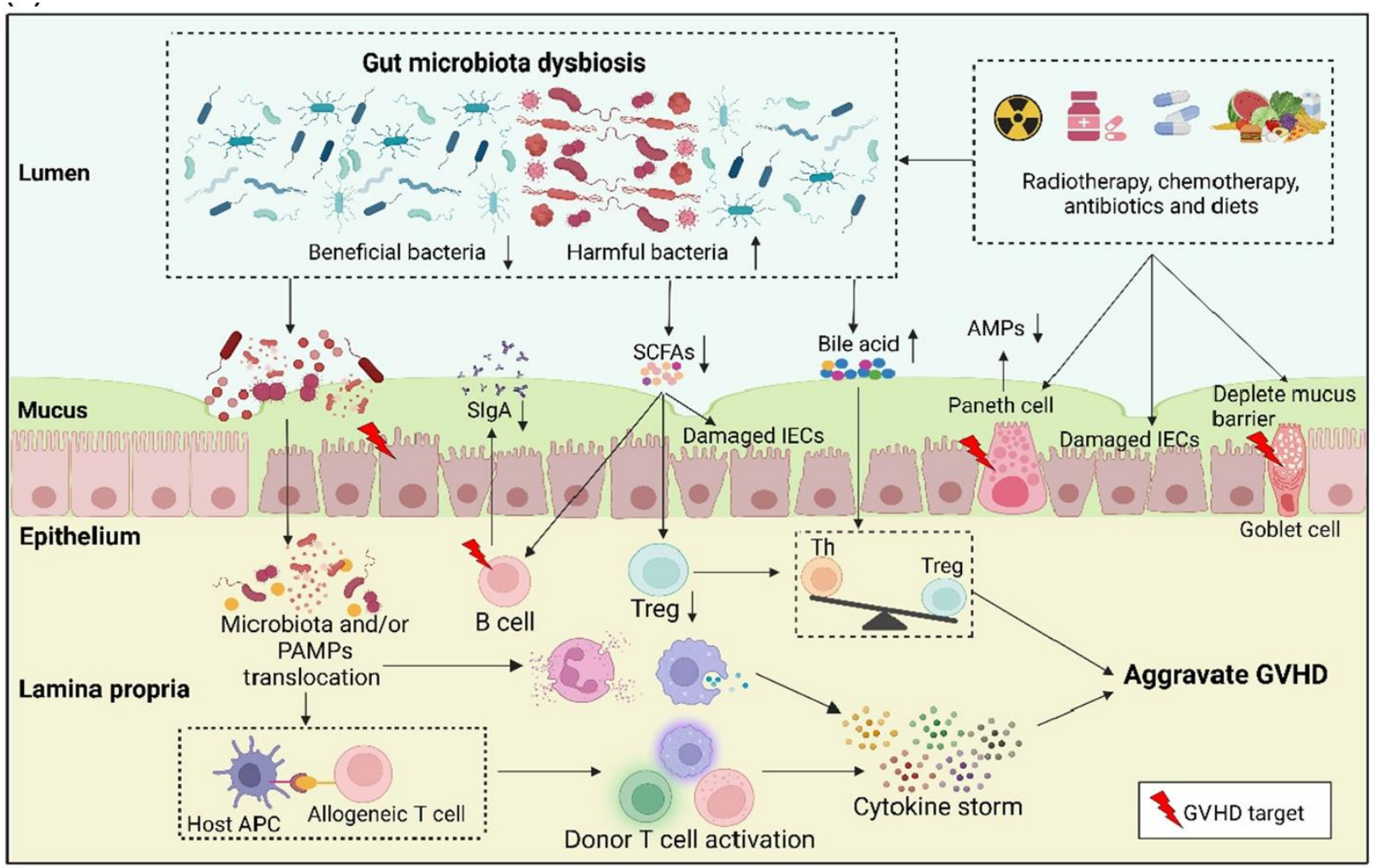
Janina Bujan Rivera[1†], Rea Kühl[1†], Ulrike Zech[2], Anne Hendricks[2], Thomas Luft[3], Peter Dreger[3], Birgit Friedmann-Bette[4], Theresa-Maria Betz[5] and Joachim Wiskemann[1*]





Results ca. Q1/2 2025

From Support to Therapy: Microbiome & Nutrition in GvHD



Patient-Specific Dietary and Nutritional Interventions

Yue et al. Cancer Medicine 2024

From Support to Therapy: Microbiome & Nutrition in GvHD

Trial title	Disease state(s)	Intervention	Phase	Clinicaltrials.gov identifier
Nutritional intervention				
Study on intelligent nutrition support therapy for hematopoietic stem cell transplantation recipients	Allo-HSCT	Parenteral nutrition Enteral nutrition	NA	NCT05590091
Randomized prospective multicenter study to compare enteral nutrition with parenteral nutrition as feeding support in patients presenting with malignant hemopathy who underwent an allogeneic HSC transplantation (NEPHA)	Allo-HSCT	Enteral nutrition alanyl-glutamin, Dipeptiven; Parenteral nutrition	3	NCT01955772
Probiotics				
Lactobacillus plantarum in preventing acute graft-versus-host disease in children undergoing donor stem cell transplant	HSCT recipient	Lactobacillus plantarum strain 299 or 299v	3	NCT03057054
CBM588 in improving clinical outcomes in patients who have undergone donor hematopoietic stem cell transplant	HSCT recipient	Clostridium butyricum CBM 588 probiotic strain	1	NCT03922035
Prebiotics				
Prebiotic galacto-oligosaccharide and acute GVHD	aGVHD	Galacto-oligosaccharide	1/2	NCT04373057
Gluten-free diet in preventing graft-versus-host disease in patients undergoing donor stem cell transplant	HSCT recipient	Gluten-free diet (GFD)	NA	NCT03102060
Dietary manipulation of the microbiome-metabolomic axis for mitigating GVHD in allo HCT patients	HSCT recipient	Potato starch	2	NCT02763033
Effects of prebiotics on gut microbiome in patients undergoing HSCT	HSCT recipient	Prebiotic foods/drinks	NA	NCT04629430
The use of a prebiotic to promote a healthy gut microbiome in pediatric stem cell transplant recipients	HSCT recipient	Prebiotics: inulin	NA	NCT04111471
Oral supplementation of 2′-fucosyllactose in allogeneic bone marrow transplant recipients	HSCT recipient	2′-fucosyllactose	1/2	NCT04263597
High-dose vitamin A in preventing gastrointestinal GVHD in participants undergoing donor stem cell transplant	HSCT recipient	Vitamin A compound	NA	NCT03719092
Fructooligosaccharides in treating patients with blood cancer undergoing donor stem cell transplant	HSCT recipient	Fructooligosaccharides orally	1	NCT02805075

Yue et al. Cancer Medicine 2024

Conclusions

- **Malnutrition can occur during the whole treatment course of allo-SCT, especially in pts with cGvHD and has prognostic impact on outcome & QoL**
- **Recommendations facing malnutrition in allografted pts are important, but are especially focused on peri- and early posttransplant period not on cGvHD itself**
- **This underscores the need for prospective, nutritionally specific studies regarding nutritional assessment, counseling and intervention in pts with cGVHD performed in a multidisciplinary team**

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Danke für Ihre Aufmerksamkeit!