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ESPEN Congress Madrid 2018

Nutrition In Solid Organ Transplant Patients

Perioperative Nutritional Care In Transplant Patients

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ESPEN CONGRESS

on Clinical Nutrition & Metabolism

Madrid, Spain | 1st - 4th September 2018

Nutrition Without Borders



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Nutrition in solid organ transplant patients - Perioperative nutritional care in transplant patients -

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Disclosure

None





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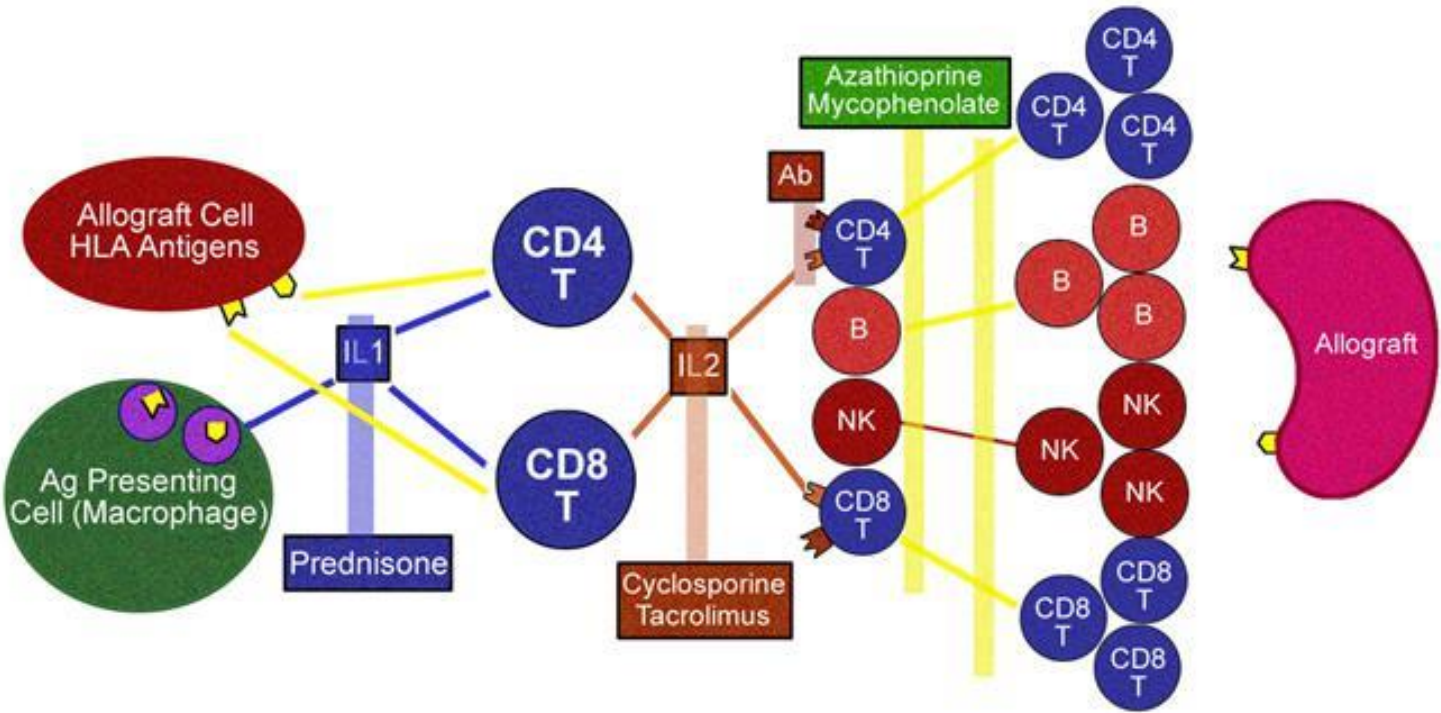
Learning Objectives

- Know about the food safety and hygiene in transplant patients
- Know about the interactions of food and drugs
- Know about the indications and effects of perioperative medical nutrition





No transplantation without Maintenance Immunosuppression:



inhibition of T-cell activation

- HLA Class I
- HLA Class II
- CD-3
- IL-2



Transplant Nutrition Therapy

Immunosuppression: steroids, calcineurin inhibitors, TOR inhibitors

- ↑ susceptibility for cancer
- ↑ susceptibility for opportunistic infection
- ↑ metabolic problems:
 - hypercholesterolemia & hypertriglyceridemia
 - hyperglycemia
 - hypertension
 - excessive weight gain
 - osteoporosis
 -

→ Aim = to reduce problems associated with this maintenance immunosuppression



Transplant Nutrition Therapy

→ towards a strategy for a “**safe & healthy living**” with an organ transplant

1. food safety and hygiene
 - + water safety/exposure
 - + preventions of infections by direct contact
 - + measures about animal contact and pet safety
 - + travel safety ...
2. healthy “transplant” diet
3. awareness of some food-drug and herb-drug interactions



1. Food safety and hygiene in solid organ transplantation



Infections remain a long-life risk to recipients of solid organ transplants:

- the recipient's net state of immunosuppression
- epidemiologic exposures
- consequences of invasive procedures to the recipient

- Guidelines? No hard data/controlled studies regarding safe living practices
- Guidelines "extrapolated" from hematopoietic stem cell (HSC) transplantation (CDC, Infectious Disease Society of America, American Blood and Marrow Transplantation)

Risk stratification according to

- Timing after transplantation : periop *versus* 3-6 months *versus* long term
- Immunogenicity:
BM/HSC >>> heart/lung > kidney/pancreas >> small bowel > liver



1. Food safety and hygiene in solid organ transplantation



Recommendations: **AVOID**

- **Drinking unpasteurized milk, fruit or vegetable juice/cider** in order to decrease their risk of infection with *E. coli*, *Salmonella*, *Brucella*, *Listeria*, *Yersinia* and *Cryptosporidium*
- **Eating cheeses made with unpasteurized milk** (such as the soft cheeses such as brie, camembert, feta) to decrease the risk of *Listeria*.
- **Eating raw or undercooked eggs** including foods containing raw eggs (e.g. preparations of Caesar salad dressing, mayonnaise, or hollandaise sauce) particularly a risk for *Salmonella* infection
- **Eating raw or undercooked meat, poultry or fish** with particular risk not only for bacterial contamination but also for parasitic infections such as *T. gondii*, and Tapeworms.
- **All raw or undercooked seafood** (oysters, clams, mussels) to prevent exposure to *Vibrio* species, viruses that cause gastroenteritis or hepatitis, and parasitic infections including *Cryptosporidium*.
- **Ingesting raw seed sprouts** (alfalfa sprouts, mung beans).
- **Uncooked pate**, meat spreads, cold cuts and smoked seafood.

Beware of cross-contamination when preparing food (e.g. keep cooked and raw foods separate; use cleaned or separate cutting boards).

Carefully wash lettuce and vegetable products even when labeled as "prewashed."

Updates to review current outbreaks as well as general food safety recommendations:

<http://www.foodsafety.gov/~dms/lmrisk5.html>.





2. Transplant Nutrition Therapy



"Heart Healthy" diet (no added salt, low fat)

- **Sodium restriction:** usual recommended intake \pm 2g/d
→ look for salt-free and sodium-free seasonings
- Use **low-fat dairy products** instead of full-fat milk, yogurt and cheeses
- **Limit egg yolks** to 3-4/week, including processed and baked goods. Egg substitutes may be used to replace eggs, which are low in cholesterol
- **Go lean with protein:** skinless chicken or turkey, fish, extra-lean fresh beef or pork, dry beans, unsalted nuts, tofu or egg whites
- **Increase dietary fiber to lower blood fat levels:** whole grain breads, cereals, fruits, vegetables, and dried beans; whole grain breads, rice, pasta, whole grain wild rice and whole grain unsweetened cereals
- **Diet low in saturated fats:** less than 300 mg/day of cholesterol
→ Choose healthy fats like olive oil, canola oil, soy, safflower, sunflower, corn, sesame and walnut.



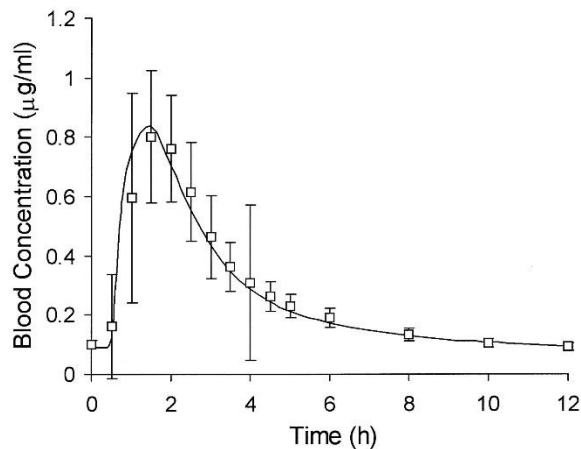


3. Food & Drug Interaction in transplantation



Drug-drug and herb-drug pharmacokinetic interactions can compromise the safety of immunosuppression in organ transplant patients by its effect on cytochrome P450 enzymes

Calcineurin inhibitor-based immunosuppression is at risk because of its narrow therapeutic range.

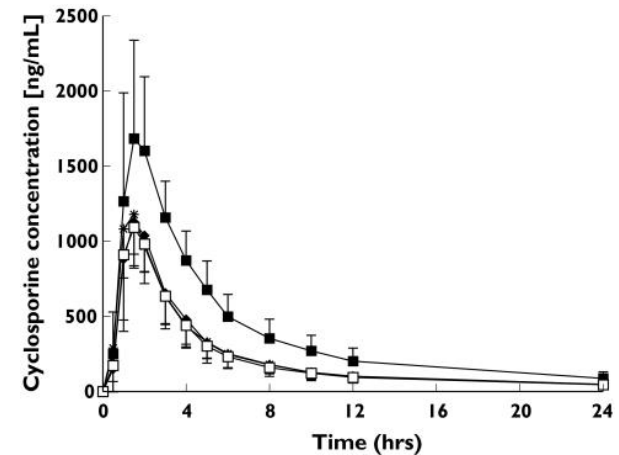
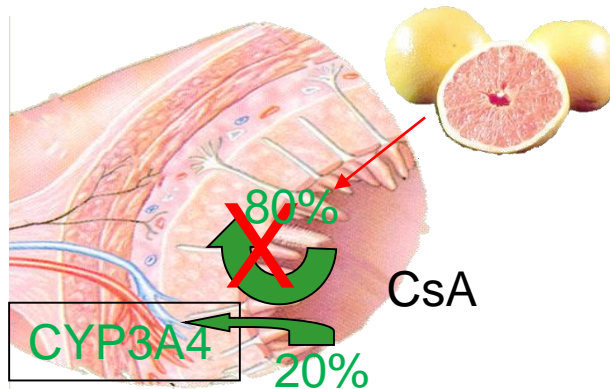
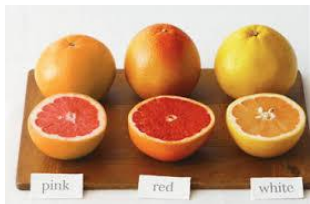




3. Food & Drug Interaction in transplantation

Grapefruit (juice)/ Citrus Maxima

- GFJ reduces the first-pass effect of CsA/Tac by inhibition of its metabolism by the intestinal enzyme CYP3A4, so reducing first-pass effect
- calcineurin toxicity and increased side effects



→ but sweet oranges or orange juice SAFE !



3. Food & Drug Interaction in transplantation

St-John's Wort (anti-depression herbal medicine): effect on cytochrome P450 enzymes



- SJW increases activity of the cytochrome P450 enzyme 3A4 (CYP3A4) and the drug transport protein p-gp
- accelerates the clearance of calcineurin inhibitors
- eventually leads to ineffective drug treatment and elicits rejection

Also documented effects for (some) red wine, camomile tea, peppermint, pepper, cranberry juice, ...

→ Important in case of unexplained undertreatment or toxicity of drugs





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Clinical Nutrition in perioperative transplant surgery

- different from other surgeries? -



Perioperative Transplant Nutrition Therapy

From a metabolic and nutritional point of view, the key aspects of perioperative care include (37 recommendations):

- integration of nutrition into the overall management of the patient
- avoidance of long periods of preoperative fasting
- re-establishment of oral feeding as early as possible after surgery
- start of nutritional therapy early, as soon as a nutritional risk becomes apparent
- metabolic control e.g. of blood glucose
- reduction of factors which exacerbate stress-related catabolism or impair gastrointestinal function
- minimized time on paralytic agents for ventilator management in the postoperative period
- early mobilisation to facilitate protein synthesis and muscle function

→ also applicable in Transplant Surgery



Perioperative Transplant Nutrition Therapy

Pretransplant period (waiting list)

Due to chronic (multi) organ failure, every patient on organ transplant waiting list is **malnourished** (liver, bowel, lung) and/or has an **inadequate body composition** (kidney)

- timely and regular assessment of nutritional status mandatory
- qualified dietary counselling required when monitoring patients on the waiting list
 - *prolonged waiting times worsen outcomes when patients are already malnourished*
- additional ONS or even tube feeding is strongly advised
- obesity remains a significant metabolic risk for outcome



Perioperative Transplant Nutrition Therapy

Pretransplant period (waiting list)

Intervention study in end-stage COPD lung waiting list patients:

- effects on energy intake and body weight of an intensified nutritional support compared to the regular support during hospitalization.
- underweight patients were randomized to receive either an energy-rich diet planned for 10 MJ/day and 45-50 energy percentage fat (+ offered supplements) (group 1), or the normal hospital diet planned for 8.5-9 MJ/day and 30-35 energy percentage fat (group 2, control group); normal-weight control patients (group 3) received the normal diet

	Group 1	Group 2	Group 3
Weight change, (median) kg	1.2 (p < 0.01) ^a	0	-0.3 (p < 0.001) ^b
BMI (mean ± SD), kg/m ²	18.3 ± 1.7	17.0 ± 2.2 (p < 0.001) ^c	22.2 ± 1.6 (p < 0.001) ^b
Total intake (median), kJ/kg	215	169 (p < 0.01) ^c	111 (p < 0.001) ^b
Total intake/REE predicted (median), %	217 (p < 0.02) ^a	151 (p < 0.03) ^c	126 (p < 0.001) ^b

Statistical analysis by Wilcoxon's rank sum test.

- ^a Group 1 compared with group 2.
- ^b Group 1 compared with group 3.
- ^c Group 2 compared with group 3.

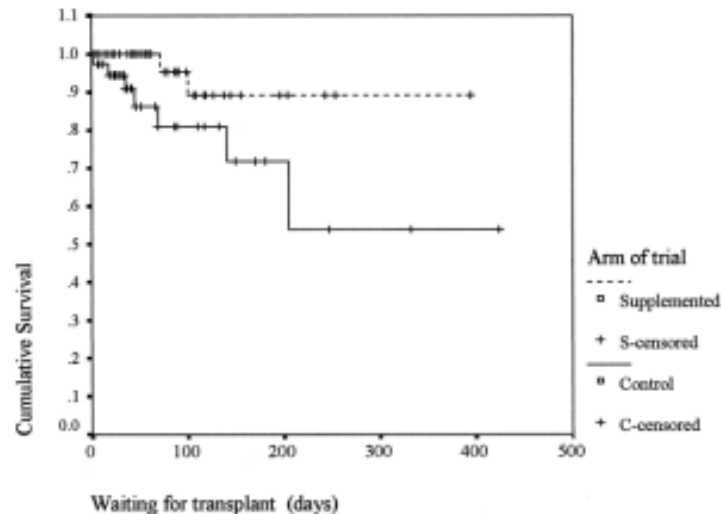
Pedersen, Respiration 2001



Perioperative Transplant Nutrition Therapy

Pretransplant period (waiting list)

- Prospective randomized controlled trial in liver waiting patients
- effect of pretransplant nutritional supplementation of calorie-dense enteral feed taken daily (in addition to diet)
 - improved some parameters of nutritional status
 - no effect on overall survival



Le Cornu, Transplantaion 2000



Perioperative Transplant Nutrition Therapy

Pretransplant period (waiting list)

- Protocol based nutrition planning compared with matched control groups in liver waiting patients
- Customized nutrition intervention and personalized counseling helps achieve nutrition targets
- No significant differences in outcome



Daphnee, Clinical Nutrition 2017



Perioperative Transplant Nutrition Therapy

Acute posttransplant phase

- Early intake of normal food or enteral nutrition is recommended within 24
→ exception: caloric intake < 18 kcal/kg/d in early graft dysfunction after liver transplantation (I/R damage)
- Even after small bowel transplantation, enteral nutrition can be initiated early, but very carefully increased within the first week
- Absorption and blood levels of tacrolimus are not affected by EN
- Organ transplantation complications including rejection, infection, wound healing, renal insufficiency, hyperglycemia, and surgical complications require specific nutritional requirements and therapies.



Perioperative Transplant Nutrition Therapy

Acute posttransplant phase

Particularities in liver transplantation:

- Use of high soluble fibre formula with probiotic bacteria reduce the rate of bacterial infections (Rayes 2002, Rayes 2005)
- More favourable regeneration of the function of RES with MCT/LCT emulsions (Kuse 2002, Delafosse 1997)
- Enteral immunonutrition : meta-analysis showed reduced risk of infections an shorter hospital stay, however no effect on liver function recovery, mortality of rejection rates (Lei 2015)
- Additional PN with 20% MCT/LCT + omega-3 fish oil lipids (Zhu 2013):
 - benefit I/R damage of the liver
 - less infectious complications
 - shorter hospital stay



Take home message

- Strategies for a **safe living** after solid organ transplantation taking life-long immunosuppressive agents, include:
 - Occupational counseling and detailed patient education regarding food safety
 - A "heart healthy" diet
 - Awareness that natural products like grapefruit juice and St John's Wort can act as modifiers of the bioavailability of key immunosuppressive drugs
- Due to chronic (multi) organ failure, every patient on organ transplant waiting list is **malnourished** and/or has an **inadequate body composition**
→ requires qualified dietary counselling and intervention
- Clinical nutrition in the acute posttransplant phase should be immediate and adequate to the situation
- Long-term dietary counseling recommended



Further reading

- “Espen guideline: Clinical Nutrition in Surgery”
A. Weiman et al, Clinical Nutrition (2017)36: 623-650
- “Strategies for safe living after solid organ transplantation”
R. Avery et al., American Journal Transplantation (2013) 13:304-313
- “Review: cytochrome P450 enzyme and transport protein mediated herb-drug interactions in renal transplant patients”
Novack R. Nephrology 2008 13(4):337-47
- “National Kidney Foundation”
<https://www.nkfs.org/prevention/healthy-eating/nutrition-in-kidney-transplant/>

