Does body composition predict insulin sensitivity during major abdominal surgery?

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Background:

- Major surgery ➔ metabolic and systemic inflammatory responses ➔ insulin resistance ➔ poor nutrient utilization, muscle wasting, increased risk of adverse outcomes
- In previous studies, it was shown that the degree of intraoperative insulin resistance was a significant predictor of morbidity after open heart surgery: for each 20% decrease in insulin sensitivity during surgery the risk of a serious adverse event doubled. *(PMID 29537981, 21346060)*

Rationale and objective:

Given the association between muscle and fat mass, particularly fat stored in muscle cells, and insulin sensitivity, we intend to retrospectively quantify muscle mass, fatty muscle infiltration (myosteatosis) and fat mass (visceral and subcutaneous) using CT scans to determine whether there is a relationship between pre-surgery body composition and insulin sensitivity as assessed by a hyperinsulinemic-normoglycemic clamp (HNC) during major abdominal surgery.

Scope of the project, methods:

Population: patients participating in a large clinical trial on the effect of HNC on surgical site infection *(ClinicalTrials.gov NCT0152818)*

Outcome: intraoperative insulin sensitivity, as quantified by the glucose infusion rate (mg/Kg/min) during steady state of a HNC (insulin infused at 2 mU/Kg/min, blood glucose clamped at 4.0 to 6.0 mmol/L)

Variable: body composition evaluated on abdominal CT scans, using a 3-dimensional and fully automated body composition imaging analysis software (Data Analysis Facilitation Suite (DAFS) by Voronoi Health Analytics Inc, CA). After verification of the segmentation, total area of skeletal muscle and adipose tissues, as well as the radiodensity of muscle tissue, at the L3 are normalized for height, and sex- and age-specific values of these features are calculated. The following body composition parameters will be defined as reduced muscle mass (z-score <-0.5), myosteatosis (z-score <0), and visceral obesity (z-score >0.5)

Other collected data: demographics, comorbidities, adverse outcomes

Achievements in the next 12 months:

- Analysis of 300 CT scans (convenient sample, based on the ancillary study sample)
- Statistical analysis using a multivariable regression model with an interaction term to test whether intraoperative insulin resistance changes across levels of body composition profiles
- Publication of the results (at the ESPEN annual meeting and in a peer-reviewed journal)

Factors that will make it successful:

- Three experts with large experience in studying metabolic and nutritional aspects of perioperative and critical care



- Recruitment completed
- High quality data, generated by reference standards: HNC for Insulin resistance (rarely performed), CT scan, which is the reference standard for evaluating skeletal tissue at the tissue-organ level. An innovative but already validated tool (DAFS software) will be used, enabling an automated segmentation of CT scans images

Resources needed to run the project:

Category		Budget
Personnel (confirmed)	0.3 FTE clinical investigator	25000€
Equipment (confirmed)	DAFS software annual license	3000€
	Processing scan cost (25€ / scan – 300 scans)	7500€
Statistical analysis (planned)		2000€
Publication fees (planned)		2500€
Total		40000€

No other funding is needed. No other funding has been sought.

Impact:

Body composition is a preoperative characteristic that is potentially modifiable. Understanding how preoperative body composition influences surgical stress response will allow to figure out the variability in response to per-operative interventions and outcomes. Subsequently, it will help identifying patients at high risk of postoperative complications and allow us to personalize therapeutic strategies, such as nutritional prehabilitation. The results of this study will further enhance our understanding of the metabolic response to acute illness and will inform future precision nutrition investigations aimed at optimizing outcomes in acutely ill patients.

X **Please tick to confirm the PEN letter of endorsement is attached. Incomplete submissions will not be considered.**