Association of Cachexia and Gut Microbiome in Dialysis: Investigation of the Interactions with Uremic Toxins and Inflammation.

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Background

Cachexia is common in patients with chronic kidney disease (CKD) and is associated with increased morbidity and mortality. It is estimated that approximately half of all patients with CKD will develop cachexia with an estimated annual mortality rate of 20%. Cachexia is a complex syndrome, in which inflammation and retention of uremic toxins are two main contributing factors. In this context, the role of the gut microbiome in CKD cachexia and the potential benefit of increasing the dialysis dose have been poorly explored.

Aims of the study

The goal of the DYNAMICA study is to investigate the links between cachexia and the gut microbiome, in association with inflammation and uremic toxins, in dialysis patients. The specific objectives are: (1) To set up a prospective cohort of deeply characterized kidney failure patients treated with peritoneal dialysis or hemodialysis (in-center, self-care dialysis in a satellite unit and at home), including evaluation of cachexia, body composition by bioelectrical impedance analysis and CT scan (L3), collection of faeces and blood to characterize the gut microbiota, measure serum levels of uremic toxins and inflammatory markers, with a longitudinal follow-up of one year; (2) To evaluate the incidence of cachexia in this cohort, and compare cachectic versus non-cachectic dialysis patients in terms of gut microbiota, inflammatory markers, level of uremic toxins, dialysis dose and modality; (3) To investigate the mechanisms of muscle cell damage by uremic toxins *in vitro*, and the contribution of the gut microbiota to the production of these toxins; (4) To confirm the pathophysiological mechanisms *in vivo* using human muscle biopsies from dialysis patients.

Figure 1 – Aims of the DYNAMICA study

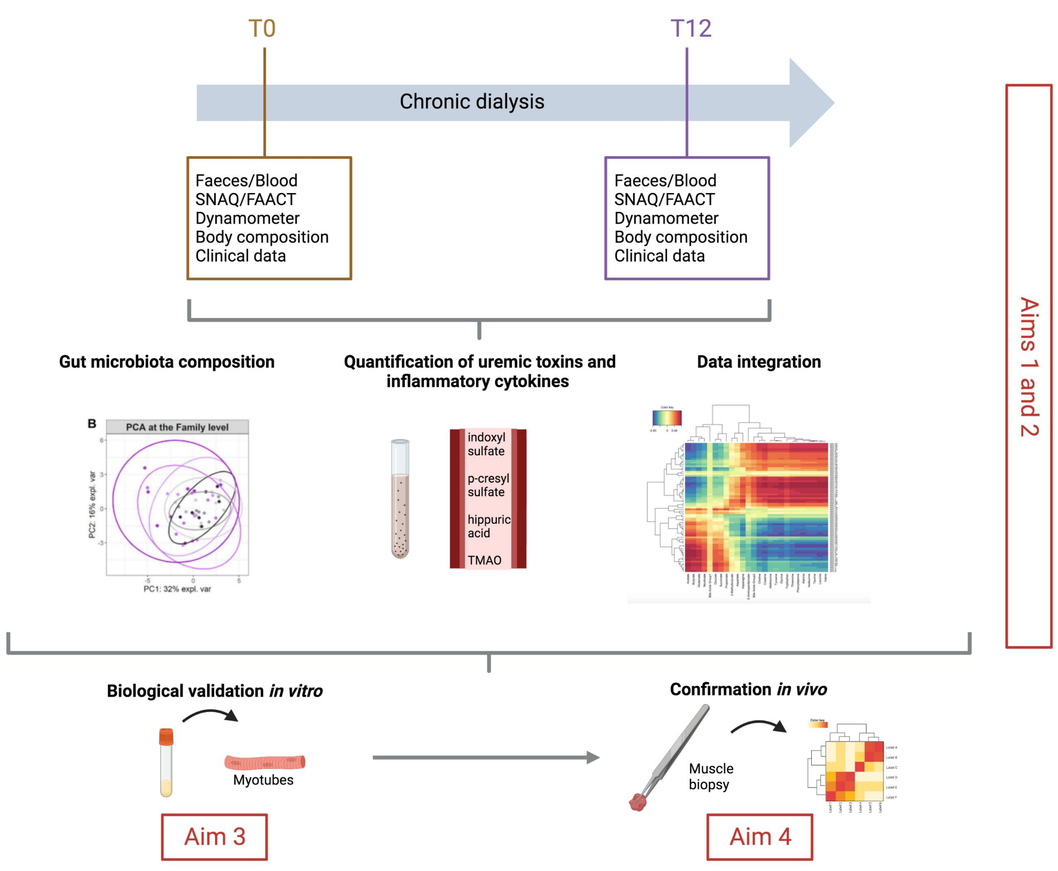
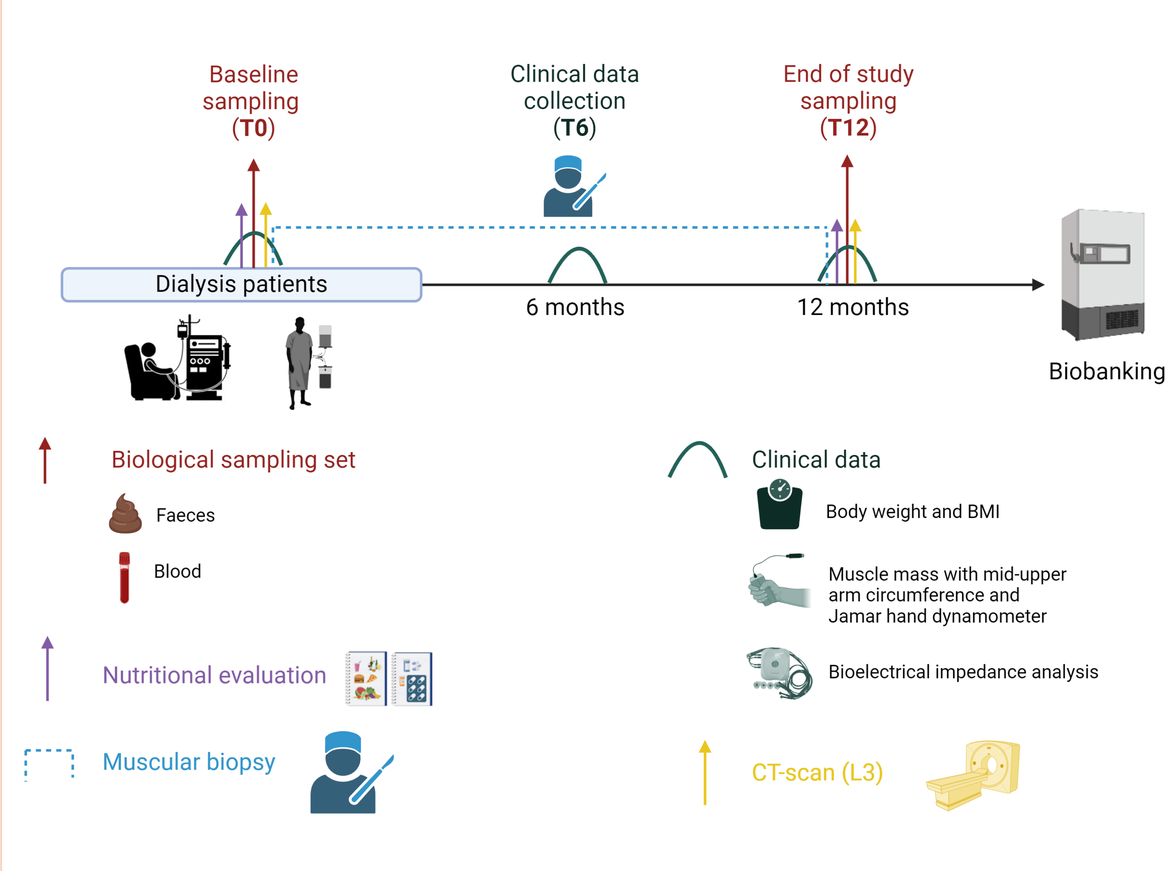


Figure 2 – Timeline of the study



Conclusion

These studies will provide the first longitudinal evaluation focusing on cachexia, inflammatory markers, uremic toxins and gut microbiota in a large cohort of dialysis patients, paving the way to the development of new strategies targeting the gut microbiota to improve nutrition, cachexia and clinical outcomes in dialysis patients.

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