

**ExplorinG frailty and mild cognitive impairmEnt in adult kidney tRansplant recipients to enhance risk prediction for biomedicAl, psychosocial, and health costs outcomeS: A multi-center repeated measures study design nested in the Swiss Transplant Cohort Study.**

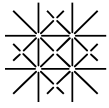
**GERAS** (Greek mythology 'God of old age')

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## Abstract

### Background

There is a lack of evidence to guide clinical decision-making for organ allocation and to optimize clinical management for the rapidly growing cohort of older patients being evaluated for KTx. Frailty is a state of vulnerability and decline in functional ability. Emerging evidence indicates frailty as a risk factor for 'hard' clinical outcomes in adult KTx recipients, independent of chronological age and comorbidities. Frailty is highly prevalent in adult KTx recipients: 25.1 % are frail, and 33.0% are pre-frail). There is hence growing consensus that frailty might be a valuable criterion to guide clinicians' risk prediction when evaluating patients for KTx. Additionally, mild cognitive impairment (MCI) is highly prevalent in this cohort ( $\leq 55.0\%$ ) and predictive of mortality. Links between frailty and MCI, and a modifying impact of psychosocial factors on frailty have been established in older adults, and therefore urgently require exploration in the KTx cohort. Frail and/or cognitively impaired patients also use more healthcare resources, yet the impact of both conditions on resource use in KTx remains unexplored. This project is innovative by being the first study in KTx examining the impact of frailty and MCI from a comprehensive bio-psychosocial and health economic perspective. Our **leading hypothesis** is that frailty and MCI assessed pre-Tx negatively impact patient survival, HR-QOL, graft survival, delayed graft function and acute rejections, health care and societal costs, and QALYs up to 2 years post-Tx. We also postulate that chronic, low-grade systemic inflammation is predictive for changes in frailty and MCI up to 2 years post-Tx.

### Methods

The GERAS project is a prospective, nationwide, multi-center, repeated measures study nested in the Swiss Transplant Cohort Study (STCS). This provides a unique and innovative research framework, with samples representative for the Swiss context and a comprehensive set of biomedical, psychosocial and behavioral data. A consecutive convenience sample of adult deceased- and living-donor KTx recipients ( $n=250$ ) who participate in the STCS will be included at time of KTx. Follow-up will occur at 6 months, 1 and 2 years post-Tx. Primary data will be collected using a modified Fried Frailty Instrument, the Montreal Cognitive Assessment, and STCS Psychosocial Questionnaire. Inflammatory biomarkers will be analyzed from blood samples at time of KTx, 1 and 2 years post-Tx. For the health economic analysis, data from management control units of KTx centers (SwissDRGs), claims data of sickness funds, a structured self-report questionnaire, the Swiss Federal Statistical Office and the European Renal Association – European Dialysis and Transplant Association registry will be used. For all analyses, data available in the STCS will be applied. Statistical analyses will consist of descriptive statistics, graphical representations, competing risks survival analysis and mixed effects models.

### Impact

The GERAS project will provide highly needed evidence to enhance risk prediction for adverse outcomes in KTx for patients of all ages, and especially for the growing older cohort. Nursing's role in clinical decision-making is of utmost importance and requires careful nursing assessment and monitoring. Findings from this study will provide evidence for Advanced Practice Nurses (APNs) in managing the complexity of frail patients dealing with chronic health conditions, in order to intervene early and improve transplant outcomes. Moreover, APNs can be influential in ameliorating frailty by promoting optimal chronic illness and symptom management, and by providing psychosocial support. Project findings will fuel the development of feasible, effective and scalable intervention programs targeting frailty and MCI to improve outcomes in KTx, and nurses will play an essential part in delivering such new programs. We will moreover provide initial evidence on the impact of frailty and MCI on health care resources use in Tx, informing various stakeholders about the optimal use of limited resources to maximize health outcomes in adults with end-stage renal disease.