

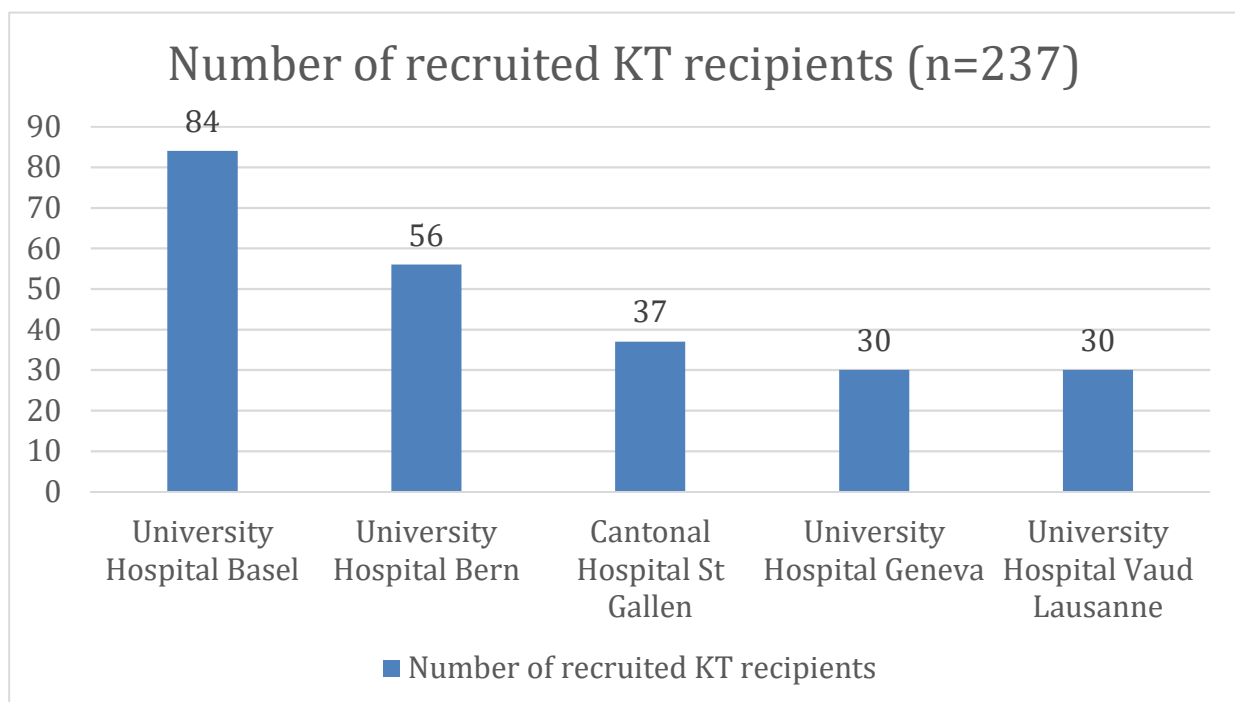


WHAT'S NEW WITH GERAS

July/August 2020

Having achieved the targeted GERAS sample size by July last year, we are very happy to announce that the 1-year follow-up evaluations of our study participants have been completed. We would like to thank all collaborators for their constant commitment and hard work!

The figure below shows the number of study participants who meet all inclusion criteria and were recruited at each center between March 2016 and July 2019



Why are we conducting the GERAS-Study?

As numbers of patients considered for kidney transplantation are increasing worldwide, the count of individuals aged ≥ 65 years of age at the time of transplantation is constantly growing. Age is a known significant factor influencing transplant outcomes. However, individuals with similar age can show diverse physical and cognitive conditions and chronological age alone is an inaccurate representation of patients' functional ability. Frailty, a better predictor of biological age, and mild cognitive impairment were both found to be strong independent predictors for adverse health outcomes and functional decline in kidney transplant recipients.

The GERAS study is exploring frailty and mild cognitive impairment in adult kidney transplant recipients to enhance risk prediction for biomedical, psychosocial and health economic outcomes.

Primary objectives of the GERAS study

1. To evaluate if frailty and mild cognitive impairment assessed immediately prior to KTx are predictive for clinical and psychosocial outcomes up to 2 years post-KTx. Primary outcomes: patient survival, health-related quality of life (HR-QOL), Length of Stay (LOS) Secondary outcomes: graft survival, acute rejections, healthcare utilization.
2. To explore if frailty and MCI assessed pre-KTx are predictive for healthcare and societal costs of KTx up to 2 years post-KTx from a societal perspective; and To assess and compare the QALYs of adult KTx recipients who are non-frail, pre-frail/frail, and pre-frail/frail with MCI.
3. To assess the prevalence, evolution and interrelationships of frailty and mild cognitive impairment from immediately prior to KTx up to 2 years post-KTx.

Secondary objectives of the GERAS study

4. To examine the levels of selected inflammatory biomarkers (IL-6, TNF- α , albumin and CRP) in relation with physical frailty status and MCI
and
To explore whether pre-KTx levels of selected inflammatory biomarkers are predictive for changes in frailty status (non-frail, pre-frail, frail) and MCI from pre-KTx up to 2 years post-KTx.

GERAS Findings and current Manuscripts

Physical Frailty and Mild Cognitive Impairment at the time of kidney transplantation and their implication on length of stay and hospital readmission.

Background

Despite emerging evidence, there is limited information about the prevalence of physical frailty and mild cognitive impairment as well as their implication on length of hospital stay (LOS) and readmission in the kidney transplant population.

The objective of this study was to assess the prevalence of physical frailty and MCI at the time of KTx and their association with LOS and hospital readmission to understand their ability to predict negative health outcomes in KTx patients. This may support clinical decision-making and guide individual pre- or post-intervention programs in kidney transplantation.

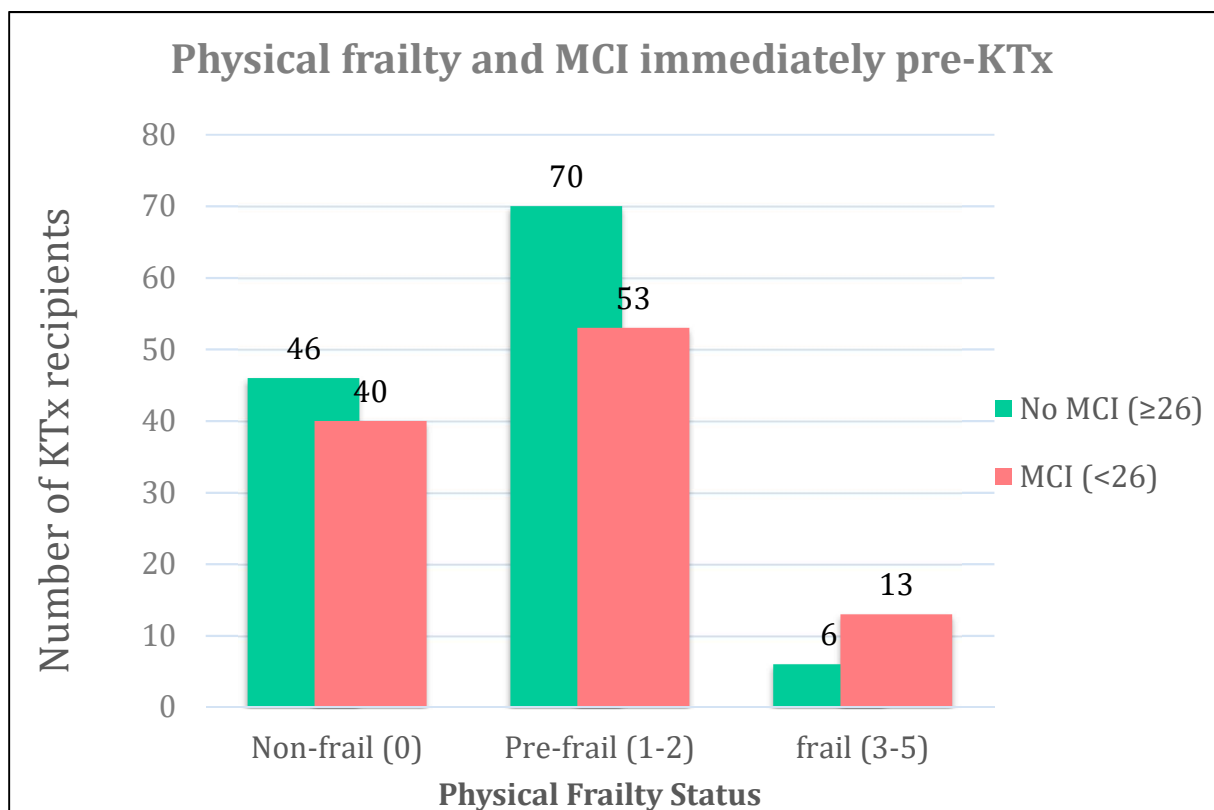
Current status of the manuscript

Analysis and manuscript writing (advanced).

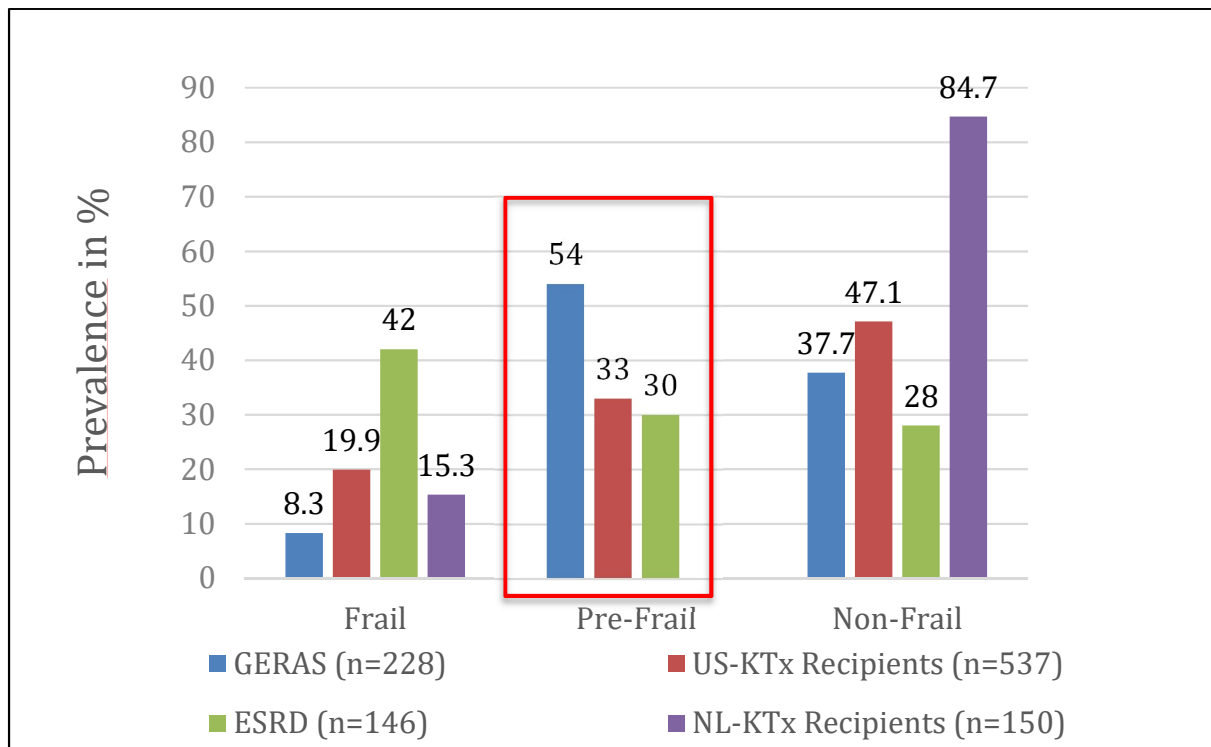
Results

KTx recipient characteristics (n=237)	
Age (years)	53.0 ±14.4 (range 20-75 with 25.2% aged ≥ 65)
Gender	31.7% female, 68.3% male
Physical Frail	8.3% (n=19)
Physical Pre-Frail	54.0% (n=123)
Non-frail	37.7% (n=86)
MCI	46.1% (n=106)
Education <13 years	24.3% (n= 56)
Median LOS (days)	13.3 ±10 (range 5-51)

The figure below displays the distribution of physical frailty and mild cognitive impairment immediately pre KTx in our study population.



GERAS sample: Higher prevalence of pre-frailty than US ESRD and KTx patients:

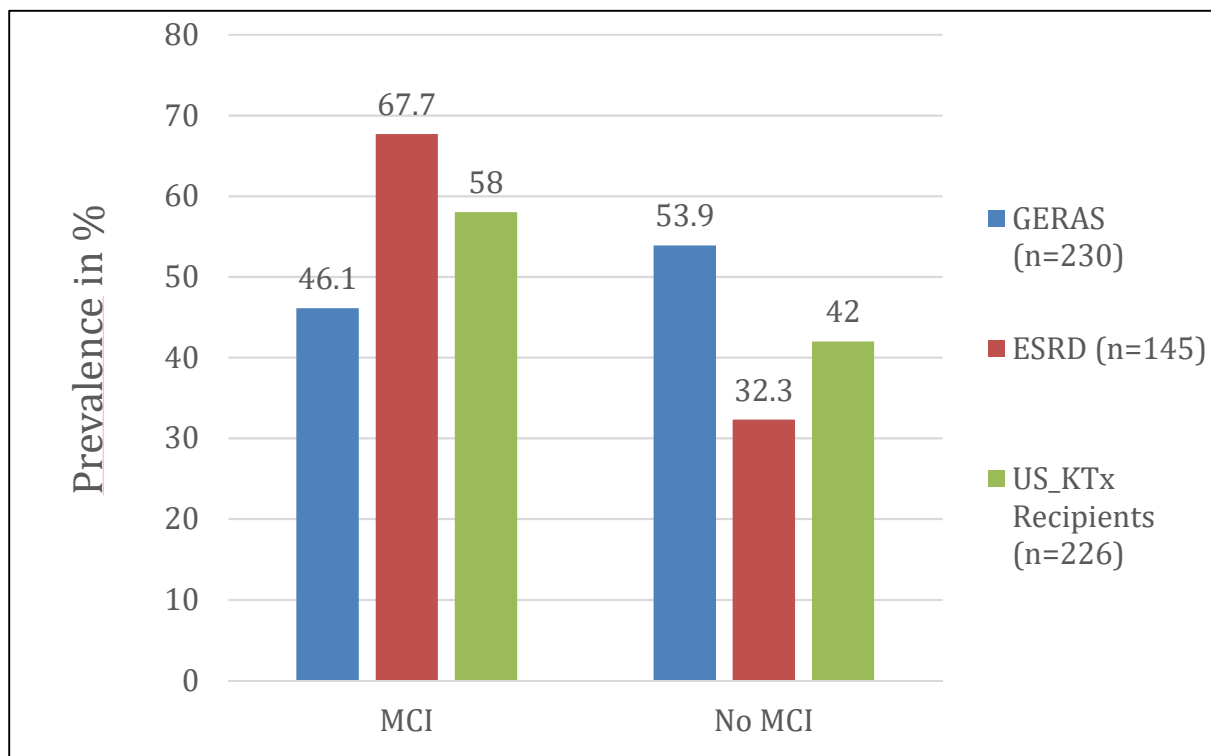


McAdams De Marco, J Am Geriatr Soc., 2013, Frailty as a novel predictor of mortality and hospitalization in individuals of all ages undergoing hemodialysis.

McAdams De Marco, Am J Transplant, 2015, Frailty and Mortality in Kidney Transplant Recipients.

Schopmeyer et al. Transplant International, 2019, Frailty has a significant influence on postoperative complications after kidney transplantation.

GERAS sample: High prevalence of MCI, coherent with other international studies:



Gupta, BMC Nephrology, 2017, Prevalence and correlates of cognitive impairment in kidney transplant recipients.

Griva et al., Am J Kidney Dis, 2010, Cognitive impairment and 7-year mortality in dialysis patients.

Discussion

The GERAS sample shows a lower prevalence of physical frailty but a higher prevalence of pre-frailty compared to other international studies. The high prevalence of mild cognitive impairment is coherent with other studies. The median length of stay after KTx in Switzerland accounts 13.2 days according to Swiss DRG, Medcode 2019, which is concordant with the GERAS sample's median length of stay of 13.3 days. In the US length of stay is lower compared to our sample.

- ✓ Prevalence of pre-frail/frail individuals is high at the time of kidney transplantation.
- ✓ Prevalence of individuals with mild cognitive impairment is high at the time of kidney transplantation.
- ✓ Incorporating frailty screening into clinical practice would systematically identify pre-frail/frail individuals before transplantation – ultimately they are at risk for negative health outcomes.
- ✓ Pre-transplant screening for mild cognitive impairment would systematically identify individuals with mild cognitive impairment before transplantation – ultimately they are at risk for negative health outcomes.
- ✓ Frailty is a dynamic syndrome and patients could potentially benefit from prehabilitation.
- ✓ Longitudinal data is needed.

Are individual components of the Fried frailty assessment equally predictive of physical frailty in kidney transplant recipients? A secondary data analysis of a multicenter, prospective cohort study.

Background

Frailty is a better predictor of transplant outcomes than chronological age alone. However it is neither mandatory nor a daily routine to screen for frailty prior to kidney transplantation. The aim of this study is, therefore, to investigate whether certain individual components or combinations of components of the Fried frailty assessment are equally predictive of physical frailty.

Current status of the manuscript

Data analysis is almost completed.

Results

We performed analyses for single items, item pairs and trios. The results were consistent in terms of correlations between items and total score of the Fried frailty phenotype: the highest correlation was found for exhaustion as a single item, exhaustion and appetite as a pair of items and exhaustion, appetite and walking speed for trios. When examining the receiver operating characteristic curves, Area under the curves, sensitivity, specificity and likelihood ratios, the results differ depending on how groups were divided.

Discussion

A reduction of items seems possible without losing much in accuracy, but it is still under discussion which groups are best to be analysed. One possibility is to distinguish between pre-frail and frail from non frail patients, the other is to divide them into non frail/pre-frail and frail patients.

Next Steps

Manuscripts

- Age at time of kidney transplantation as a predictor for patient and graft survival: a bio-psychosocial competing risks survival analysis of the Swiss Transplant Cohort Study. (Submitted)
- Physical Frailty and Mild Cognitive Impairment at the time of kidney transplantation and their implication on length of stay and hospital readmission. (Data analysis and manuscript writing)
- Are individual components of the Fried frailty assessment equally predictive of physical frailty in kidney transplant recipients? A secondary data analysis of a multicenter, prospective cohort study. (Data analysis and manuscript writing)

Project Steps

- Finalization 1-year follow-up assessments in July 2020
- July/August 2020 GERAS Update Newsletter with progress report
- 2-year follow-up assessments to be performed according to the study protocol
- Analysis of blood samples and longitudinal GERAS data