Characterization of frailty phenotypes, analysis of gene expression and the association with perioperative/interventional complications in elderly cardiac patients

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Background

Transcriptomic analysis on skeletal muscle of frail patients can provide information on the physiological pathways underscoring common phenotypes of frailty, and finally can be used to develop novel treatment options.

Purpose:

Determination of gene expression levels in frailty phenotypes associated with perioperative/interventional complications in older cardiac patients undergoing surgery (e.g. coronary artery bypass graft) or transcatheter aortic valve implantation (TAVI).

Methods

Patients included: n= 63 patients (mean 77.6 ± 4.3 years standard deviation (SD); 74.6% male)

Phenotypes of frailty (assessed once at hospital admission): Physical frailty: Timed Up-and-Go (TUG), 5-meters Walk Test (5-mWT), handgrip strength (dynamometer). Nutritional frailty: Mini Nutritional Assessment-short form (MNA-sf). Cognitive frailty: Mini Mental State Examination (MMSE)

Muscle sample: M. quadriceps femoris (during surgery/intervention)

Outcomes: presence of complications (primary) and number of complications (secondary)

Statistical analysis: associations were determined with Logistic regression and analysis of covariance (adjusted: age, sex, num. of comorbidities, estimated glomerular filtration rate)

Gene expression analysis: DESeq2 (adjusted: age, sex, num. of comorbidities, estimated glomerular filtration rate)

Results

a) In total n= 37 patients (59%) experienced ≥ 1 complication; one patient died [Surgery n= 28 (82.4%); TAVI n= 9 (31.0%)].

Number of complications (e.g. transfusion, atrial fibrillation, delirium) was significantly higher in surgery patients (mean 1.50 ± 1.15 SD) than TAVI (mean 0.66 ± 1.25 SD).

Tab. 1 Characteristic of frailty phenotypes.

Frailty phenotypes and assessments	Surgery n= 34 (54%)		TAVI n= 29 (46%)		*p*
Physical frailty	Mean	SD	Mean	SD	
TUG (sec) n=61	10.82	3.37	14.89	5.19	0.001
Moderate-severe impaired mobility [≥ 10 sec; n (%)]	18 (54.5)		25 (89.3)		0.003
5-mWT (sec) n=62	5.32	1.65	6.40	2.85	0.204
Low gait speed [≥ 6 sec; n (%)]	8 (24.2)		11 (37.9)		0.243
Handgrip (kg) n=63	30.45	9.40	26.73	8.17	0.102
Low handgrip [≤ 27 kg ♂; ≤ 16 kg ♀; n (%)]	7 (20.6)		12 (41.4)		0.730
Nutritional frailty					
MNA-sf (score 0-14) n= 63	12.9	1.7	12.3	2.8	0.643
Risk of malnutrition [≤ 12 pts; n (%)]	8 (23.5)		9 (31.0)		0.504
Cognitive frailty					
MMSE (score 0-30) n= 62	26.5	2.9	26.5	2.5	
Moderate-severe dementia [≤ 27 pts; n (%)]	17 (51.5)		16 (55.2)		0.773

TAVI: transchateter aortic valve implantation; 5-mWT: 5 meter Walk Test; TUG: Timed Up-and-Go test; MNA-sf: Mini Nutritional Assessment-short form; MMSE: Mini Mental State Examination; SD: standard deviation

b) Physical frailty was associated with the presence of complications (odds ratio (OR): 4.64, 95% confidence interval (CI) 1.18-18.28), particularly in TAVI patients. Nutritional (OR: 0.91, 95% CI 0.63-1.31) or cognitive frailty (OR: 0.95, 95% CI 0.63-1.44) were not associated.

Physical frailty (Tab. 1) was mainly characterized by limited mobility (TUG).

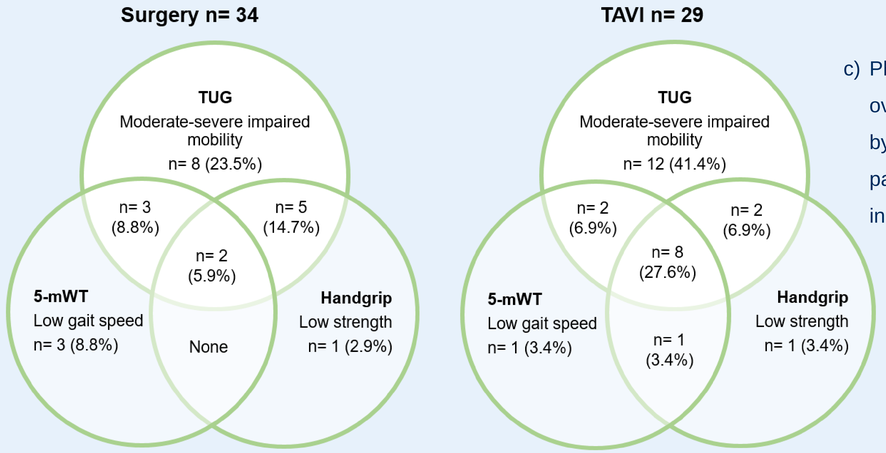

Fig. 1 Intersections show the number of patients with ≥ 2 overlapping parameters of physical frailty.

c) Physically frail patients are characterized by overlapping parameters of frailty (Fig. 1), underscored by a partial overlap of altered gene expression patterns (Fig. 2), with 10 genes simultaneously altered in all parameters.

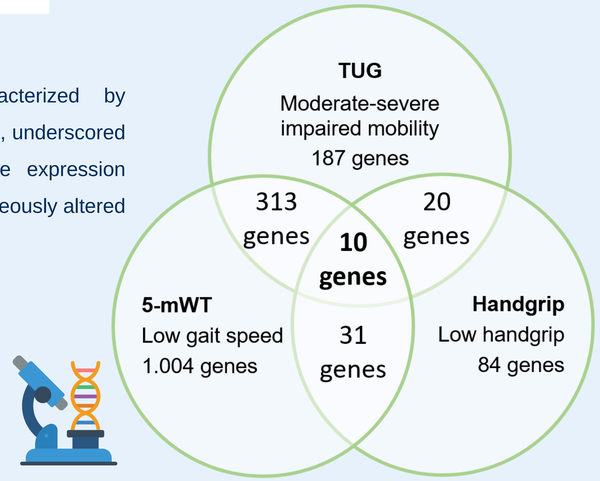

Fig. 2 Number of altered genes (up & down regulated) in the parameters of physical frailty.

Conclusions

Dysregulation of genetic determinants underscores physical frailty, while moderate to severe limited mobility in particular is associated with perioperative/interventional complications in elderly TAVI patients.

Implications for future research

The detection of corresponding biomarkers (e.g. in plasma) could improve the accuracy of detection of physical frailty phenotypes associated with complications in elderly patients.

Declaration of interest: NO conflict to declare / Contact: omar.baritello@fgw-brandenburg.de