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Impact of Frailty in HF

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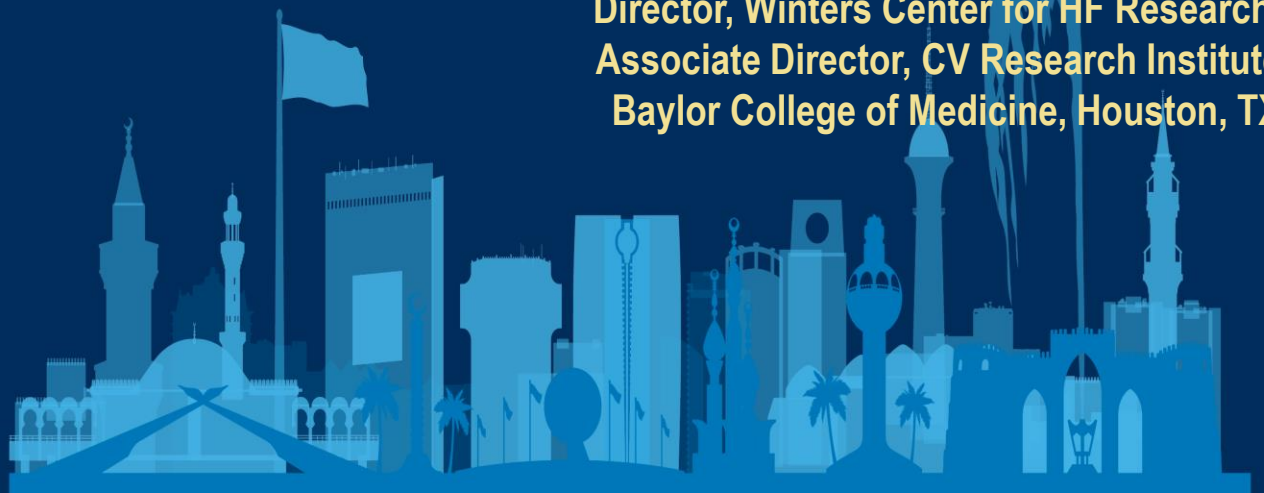


Frailty

- Frailty: syndrome characterized by weakness, fatigue, and increased vulnerability to physiologic stressors.
- Often associated with aging, a recognized component of HF
- Five Domains:
  - Slowness
  - Weakness
  - Low physical activity
  - Exhaustion
  - Decreased muscle mass
- Objective assessments of domains:
  - 4 meter gait speed test (slowness)
  - Handgrip/knee extensor strength test (weakness)

Phenotypes of frailty –Measurement Tools

(Fried's Index) (3 of 5)

- Unintentional weight loss
- Self-reported exhaustion
- Low energy expenditure
- Slow gait speed
- Weak grip strength

Disadvantages – Ambulation may not be possible, does not incorporate cognition/depression

Cumulative deficit model (using deficit index)

Cumulative deficit index	Cut-points
1. Need help preparing meals	Yes = 1, No = 0
2. Need help feeding yourself	Yes = 1, No = 0
3. Need help dressing yourself	Yes = 1, No = 0
4. Need help using the toilet	Yes = 1, No = 0
5. Need help with housekeeping	Yes = 1, No = 0
6. Need help climbing stairs	Yes = 1, No = 0
7. Need help bathing	Yes = 1, No = 0
8. Need help walking	Yes = 1, No = 0
9. Need help using transportation	Yes = 1, No = 0
10. Need help getting in and out of bed	Yes = 1, No = 0
11. Need help managing medications	Yes = 1, No = 0
12. Depend on assistive devices (walker, cane, etc.) or other people to perform activities of daily life	Yes = 1, No = 0
13. Dependent on a device for normal breathing	Yes = 1, No = 0
14. Climb 2 flights of stairs without rest	No, cannot do at all = 1; Yes, with difficulty = 0.5; Yes with no difficulty = 0
15. Myocardial infarction	Yes = 1, No = 0
16. Diabetes	Yes = 1, No = 0
17. Peripheral vascular disease	Yes = 1, No = 0
18. Cerebrovascular disease	Yes = 1, No = 0
19. Chronic obstructive pulmonary disease	Yes = 1, No = 0
20. Ulcer	Yes = 1, No = 0
21. Hemiplegia	Yes = 1, No = 0
22. Moderate/severe renal insufficiency	Yes = 1, No = 0
23. History of liver disease	Yes = 1, No = 0
24. Rheumatologic disease	Yes = 1, No = 0
25. History of malignancy	Yes = 1, No = 0
26. History of dementia	Yes = 1, No = 0
27. Hypertension	Yes = 1, No = 0
28. Hyperlipidemia	Yes = 1, No = 0
29. Body mass index	Underweight or obese = 1; overweight = 0.5; normal = 0
30. Depression	Yes = 1, No = 0
31. Anemia	Yes = 1, No = 0

cumbersome and difficult

Dunlay et al JHLT 2014; Dobbels et al JHLT 2014

Canadian study of health and ageing score

Clinical Frailty Scale

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

3 Managing Well – People whose medical problems are well controlled, but are not regularly active beyond routine walking.

4 Vulnerable – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 Terminally Ill – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia,** recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia,** they cannot do personal care without help.

Symptoms Overlap

HF

- Breathlessness
- Edema
- Orthopnea, PND
- Fatigue, weakness
- Cognitive decline
- Reduced Exercise Tolerance
- Cachexia, Satiety
- Depression

Frailty

- Fatigue, weakness
- Reduced Exercise Tolerance
- Cachexia
- Depression
- Cognitive Decline
- Diminished reserve
- Weak grip strength

Pathophysiology of HF and Frailty

Shared mechanisms of inflammation, metabolic dysfunction, and neurohormonal dysregulation

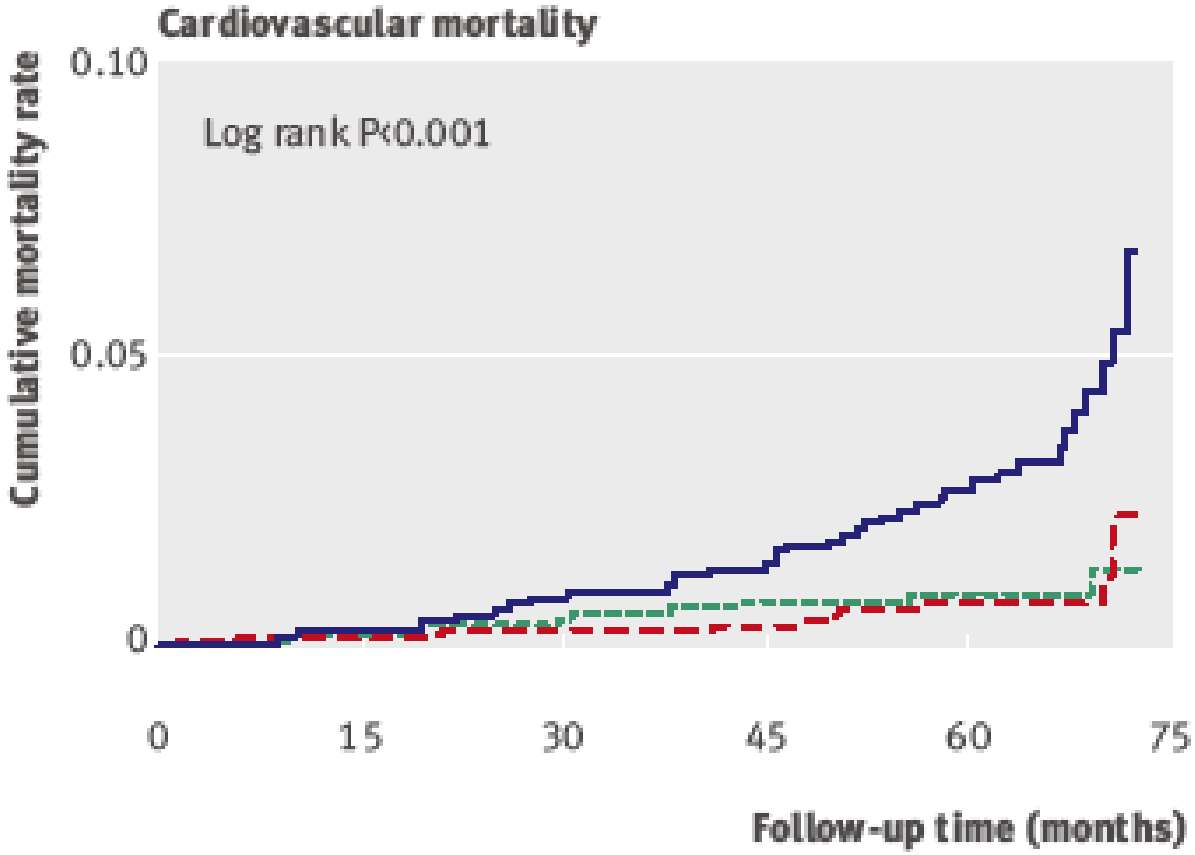
Oxidative stress, DNA damage, metabolic changes

C-reactive protein, interleukin-6, and TNF-α correlate both with incident HF as well as frailty components

both associated with insulin resistance, abnormal cortisol patterns, and steroid hormone deficiencies

Frailty and CV disease

- **French 3 City study – slow gait associated with 3 x increase in *CV mortality* over 5 years**
- **more important than sex, age or vascular profile (DM, PAD)**



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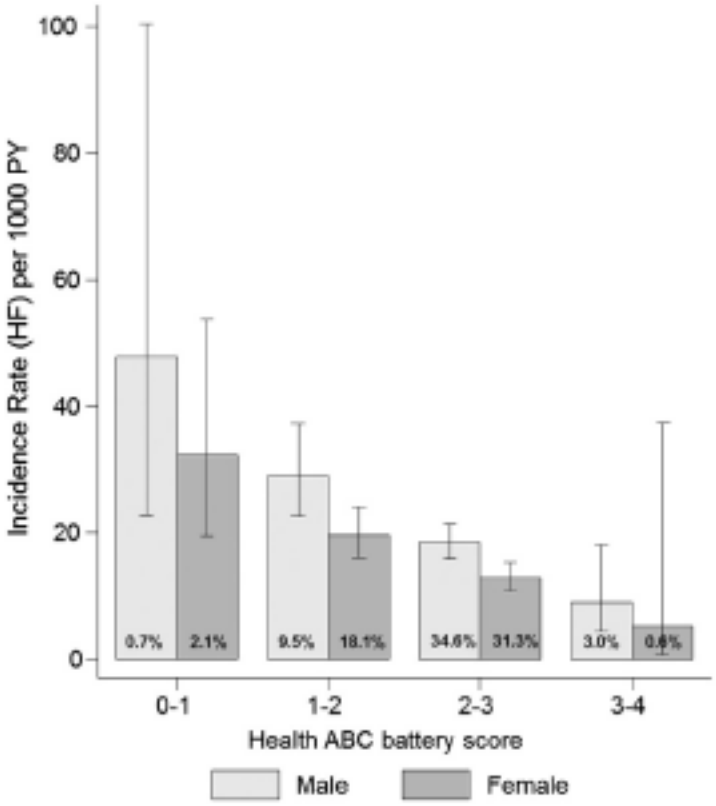
Dumurgier et al. BMJ 2009

Frailty Associated with Development of HF

- 70-79 year old pts in Memphis and Pittsburgh assessed with Gill criteria (chair stand and walk speed) and HABC battery
- Lower is more frail
- Lower score higher rates of HF (30 % increased risk)
  - No mention of EF
  - HFpEF may be higher %



HABC Battery score and incident heart failure. Lower baseline HABC Battery score was associated with a higher risk for heart failure. Rates are shown per 1000 person-years.

Khan et al. AHJ 2013

Frailty Prevalence and Outcomes in HF

- 25-50% of CV patients , 30-35 % of HF patients (regardless of EF)
- 3-7% of general population age 65-75 yo , 20-26% of 80yo
- Aging Interplay : Almost 80% of HF patients are over age 65, 20% HF patients > 80 yrs

Author, y	N	Patient Population	Frailty Tool	Prevalence of Frailty	Outcome(s) for Frail vs Nonfrail
Dominguez-Rodriguez et al,[8] 2015	102	NYHA III-IV LVEF <30% Age ≥70 y Nonischemic Undergoing CRT-D	Fried scale ≥3	28% (n = 29)	1-y risk of acute decompensated HF: 56% vs 16%; HR 4.55, 95% CI 1.7–12.0
Jha et al,[37] 2016	120	NYHA III–IV Mean LVEF 27% ± 14% Age 53 ± 12 y Referred for and/or listed for heart transplantation	Fried scale ≥3	33% (n = 39)	1-y actuarial survival: 54% ± 9% vs 79% ± 5%, *P*<.005 1-y BTT-LVAD and transplant-free survival: 58% ± 12% vs 78% ± 6%, *P*<.05
Chung et al,[10] 2014	72	NYHA III–IV Mean LVEF 17.9% ± 0.6% Age 59 ± 2 y Undergoing LVAD	Grip strength Weak if <25% total body weight	22% (n = 16)	6-mo survival: 75% vs 93%, log rank 0.02 Postoperative bleeding: 54% vs 17%, *P* = .002 Postoperative infection: 85 vs 54, *P* = .01
Dunlay et al,[9] 2014	99	INTERMACS profile 4 (IQR 3,5) Mean LVEF 18.5% ± 6.8% Age 65 ± 9 y Undergoing LVAD	Deficit index Frail if >32% deficits (lower tertile)	34% (n = 33) 62% by standard definition[45]	1-y all-cause mortality: adjusted[a] HR 3.08, 95% CI 1.2–5.0 Rehospitalizations (1.9 ± 1.6 y mean follow-up): adjusted[a] HR 1.42, 95% CI 0.98–2.1 Days alive outside of hospital at 1 y: 250 vs 293
Khawaja et al,[26] 2014	15	Age 62 ± 7 y Undergoing LVAD vs 10 controls (no cardiac disease, nonsmokers)	Grip strength	Mean grip strength 35.8 ± 7.8 vs 55.6 ± 12.7 kg (*P* = .001)	Change in grip strength at 6 mo on LVAD: +25.5% ± 27.5%

Frailty and HF

- 1314 pts followed in HF clinics, mean age 66.7 years
- 75% with EF < 40%, mean EF 32.8%
- 4 scales to measure frailty – (any positive score qualified)
- 44.2% were fragile

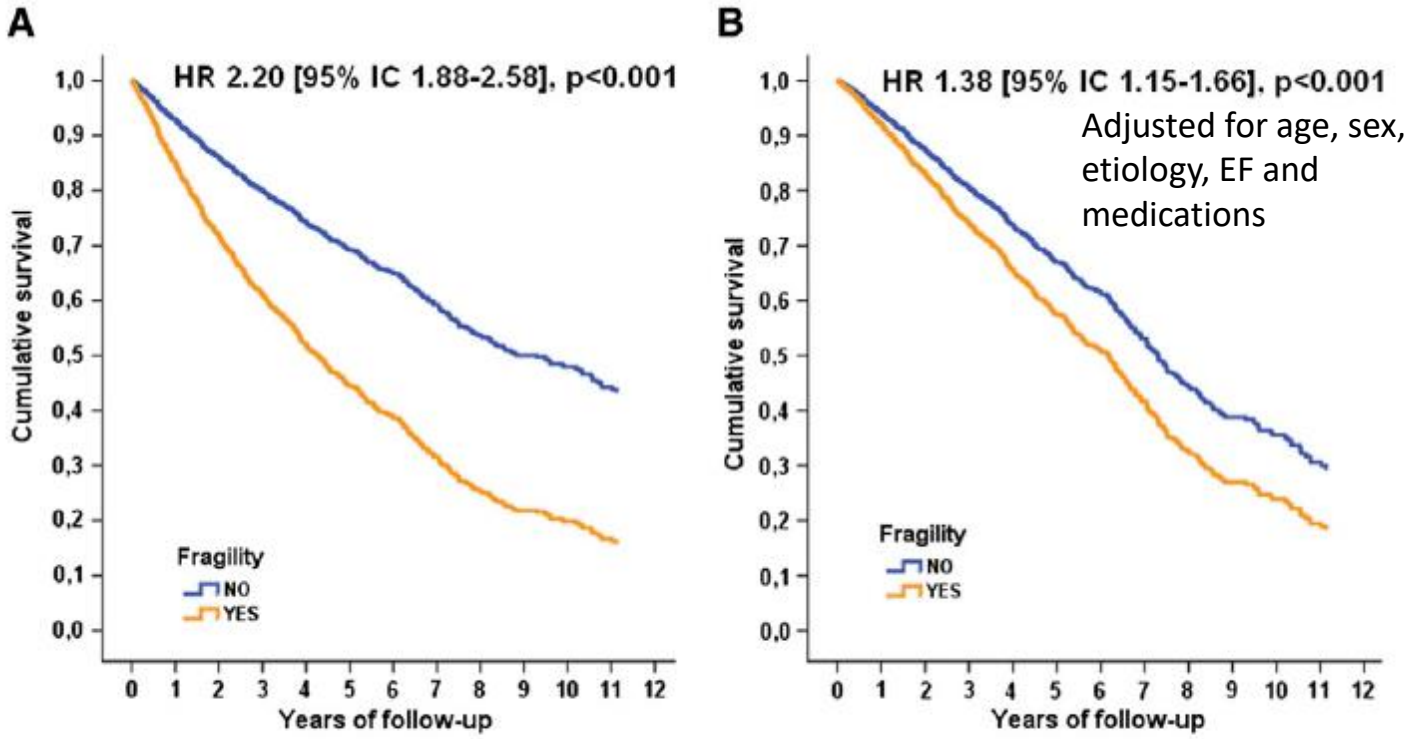
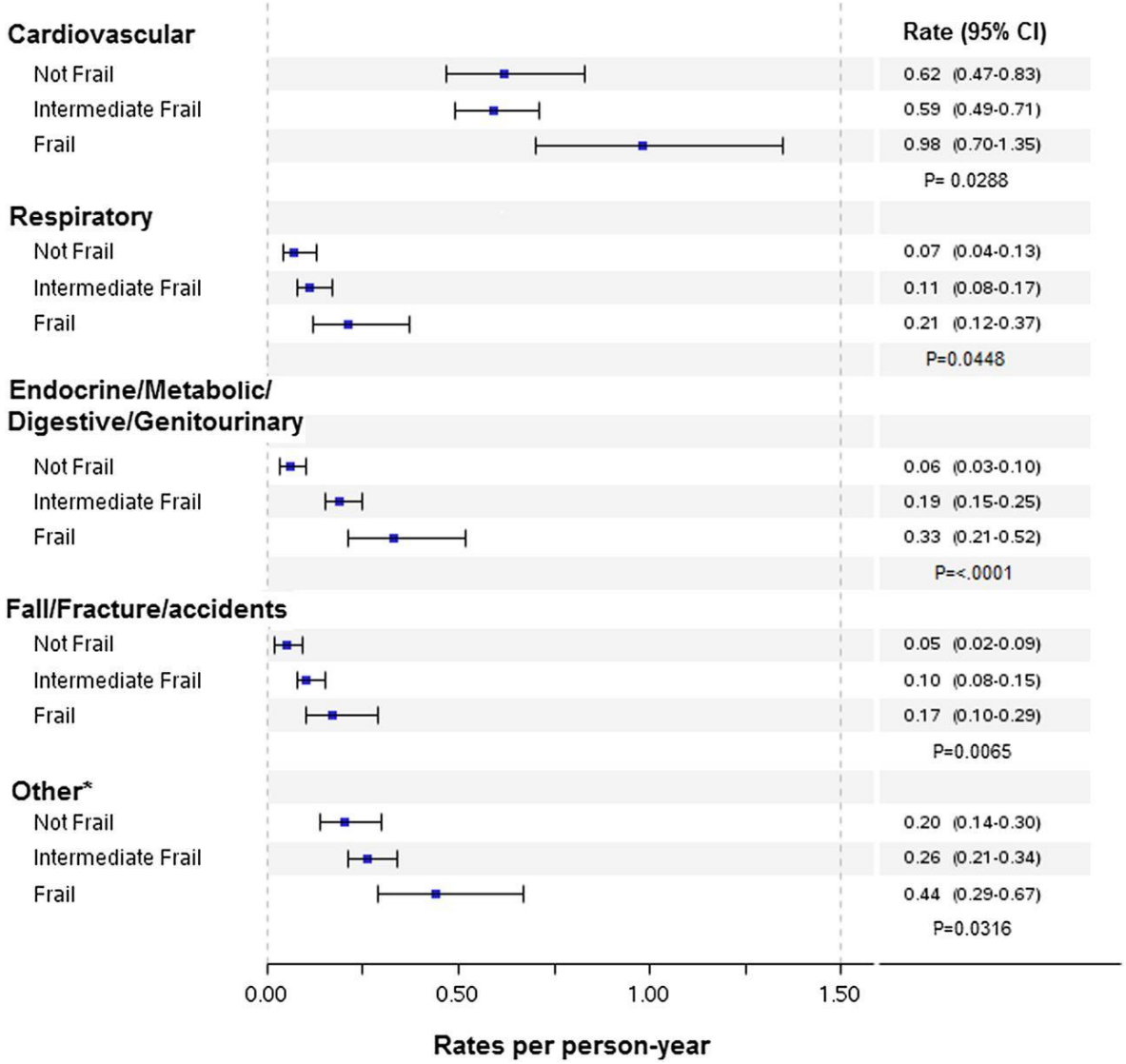


Fig. 1. Non-adjusted (A) and adjusted (by classic prognostic factors) (B) Cox survival curves for heart failure patients grouped according to the presence of fragility.

Gastelurrutia et al Int Jrl Card 2014

Rates of Hospitalizations by Frailty Status and Reason for Admission



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Sheila M. McNallan et al. JCHF 2013;1:135-141

Frailty not associated with EF

- 33 % pts referred for heart transplant had frailty
- Frailty associated with NYHA Class IV, lower BMI, higher PCWP, lower CI, cognitive impairment and depression
- Not associated with sex, age, LVEF or HF duration
- Independent predictor of increased all-cause mortality

Wilson ME, et al . Pretransplant frailty is associated with decreased survival after lung transplantation. *J Heart Lung Transplant* 2016;35:173-8

Management

- Formal assessment of frailty
- Patient-centered goal-oriented care
- Prioritize symptom management, functional status, and QOL over survival
- Interdisciplinary care team approach
- Optimize GDMT of HF as tolerated, watch out for side effects
- Treat comorbidities (Anemia, OSA, DM, HTN, Depression , Afib)
- Encourage exercise training, physical activity, respiratory muscle training

Pilotto A, Addante F, Franceschi M, et al. *Circ Heart Fail* 2010;3:14-20.

Reversibility ?

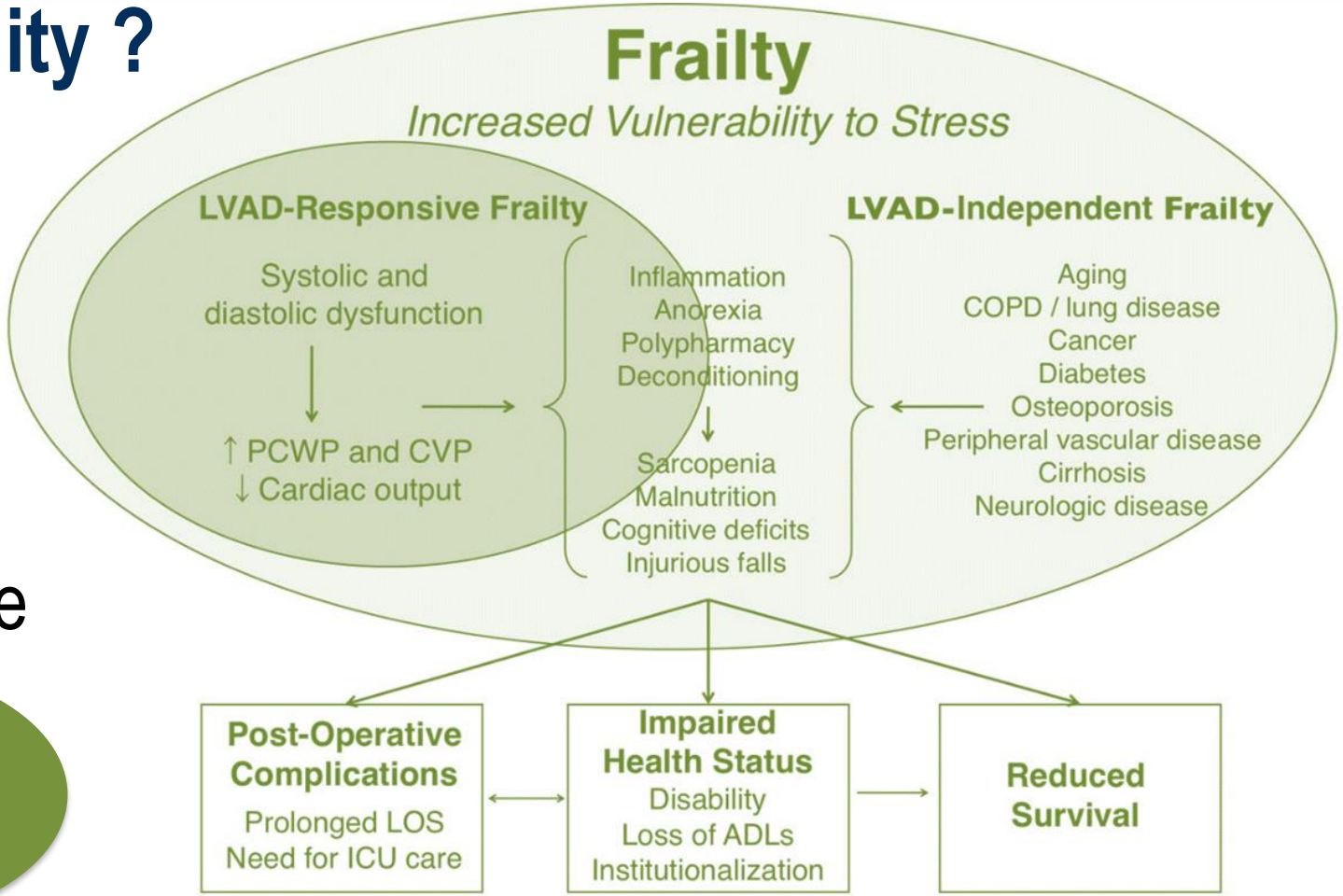
Frailty

Sarcopenia

Aging

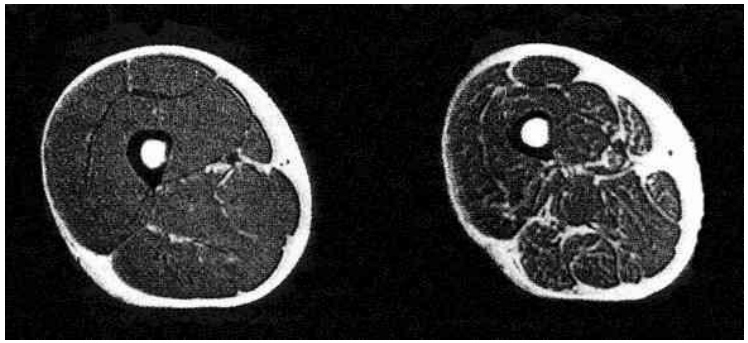
Heart Failure

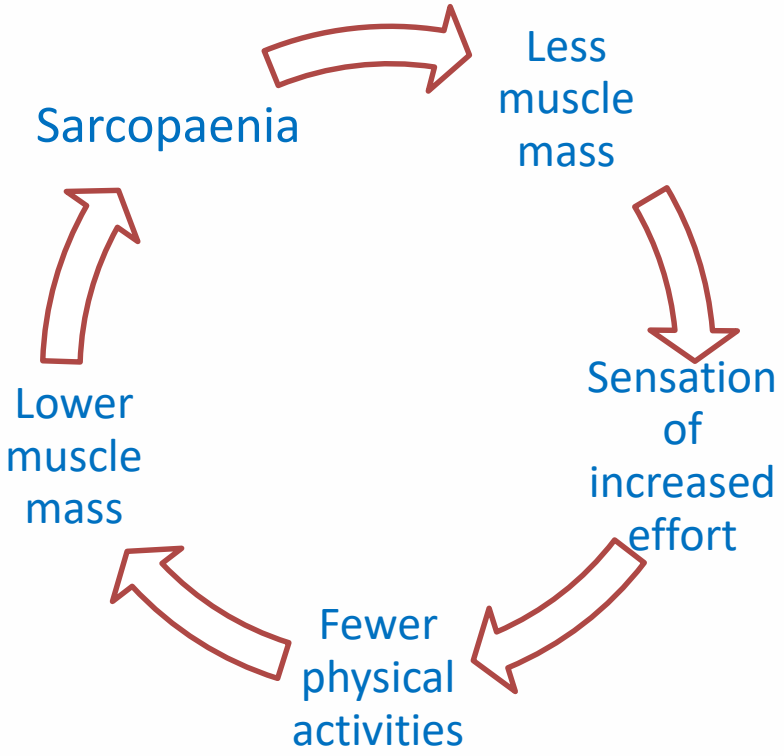
Inflammation
Deconditioning
Anorexia



Flint et al. Circ Heart Fail. 2012

Cycle of functional decline





Frailty is (partially) reversible

- Structured physical activity over 12 weeks –
- Nutritional shakes and memory workshops
- Benefits seen at 3 months, durable to 18 months

Romera-Lievana J Gerontol A Biol Sci Med 2018
Tze Pin Ng Am Jrl Medicine 2015

- Additional studies in the elderly population with improvement in frail phenotypes
- Exercise is recommended : improves physical strength and cognitive function

Exercise R_x for LVAD

With exercise/respiratory muscle strengthening – increase in VO2, 6MWD, QoL and decrease in VE/VCO2

Table 2 Exercise Capacity Data

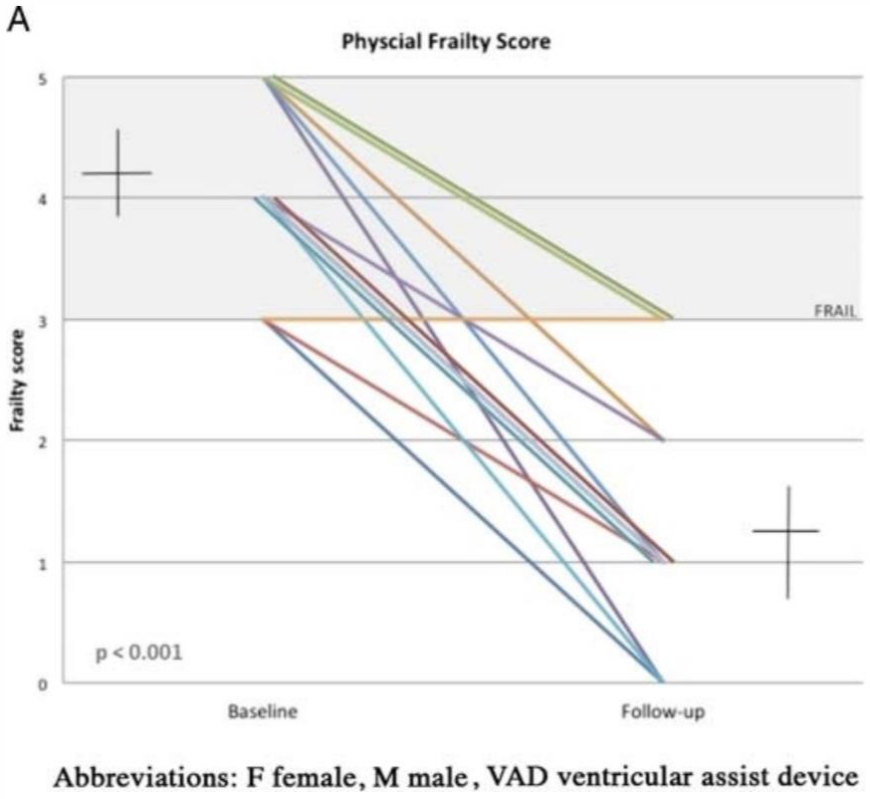
	Exercise (n = 7)		Control (n = 7)		
Variable[a]	Pre	Post	Pre	Post	p-value[b]
Peak Vo_2					
ml/kg/min	10.5 ± 2.3	14.8 ± 4.9	12.4 ± 1.7	15.3 ± 4.4	0.43
liters/min	0.75 ± 0.2	1.14 ± 0.6	0.94 ± 0.3	1.26 ± 0.6	0.48
Peak workload, W	42.0 ± 15.4	74.5 ± 31.3	50.4 ± 21.6	79.4 ± 45.0	0.53
6MWD, meters	351 ± 77	531 ± 131	367 ± 129	489 ± 95	0.25

6MWD, 6-minute walk test distance; Vo_2, oxygen consumption.
[a]Values are presented as mean ± standard deviation.
[b]p-value for comparison between groups (analysis of covariance).

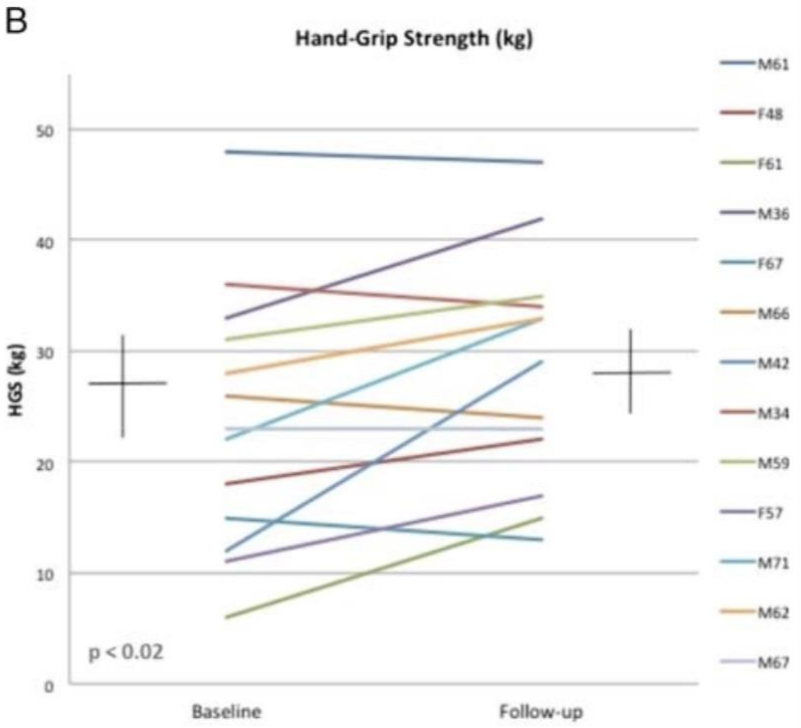
decreases IL-6 and TNF α

Laoutaris et al Eur J Cardiovasc Prev Rehabil. 2011
Hayes et al. JHLT 2012

LVAD - Changing Frailty



Abbreviations: F female, M male, VAD ventricular assist device



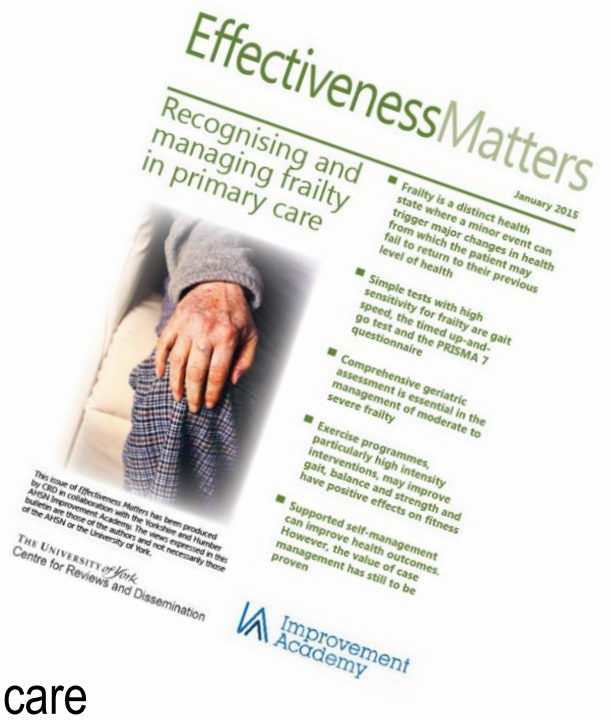
Hand grip strength improved in pts
Only 1 frail LVAD remained unchanged

Jha et al Transplantation Direct 2017

Once identified

Categorize

- Mildly frail – Supported Self Management
- Moderately frail – Care and Support Planning
- Severely frail – anticipatory care planning
  - Case management, palliative care and end of life care



Supported self management plan

Preventable components for 'Frailty'

- Affect (Mood problems)
- Avoid toxins, alcohol
- Cognitive impairment
- Falls
- Functional impairment
- Hearing problems
- Nutritional compromise
- Physical inactivity
- Polypharmacy
- Smoking
- Social isolation and loneliness
- Vision problems

Additional topics:

- Make your home safe
- Vaccinations
- Wound care
- Mobility
- End of Life

……others……??

Stuck et al. Soc Sci Med. 1999 (Systematic review of 78 studies)

Medication and Falls Risk

Group	Common Drug Names	Contributing Factors	Possible Actions for Prescribers
Sedatives and hypnotics	Temazepam, diazepam, lorazepam, nitrazepam Zopiclone, Zolpidem, chlordiazepoxide, chloral betaine (Welldorm), clomethiazole	Orthostatic hypotension, sedation which can last into the next day, lightheadedness, slow reactions, impaired balance, confusion	• Stop if possible • Long term use will need slow, supervised withdrawal • No new initiation
Antipsychotics	Chlorpromazine, haloperidol, lithium, promazine, trifluoperazine, quetiapine, olanzapine, risperidone	orthostatic hypotension, confusion, drowsiness, slow reflexes, loss balance. Long term use - Parkinsonian symptoms.	• Review indication and stop if possible (may need specialist opinion/support) • Reduce dose/frequency if unable to stop
Antidepressants	**Tricyclics** - amitriptyline, dosulepin (Dothiepin), imipramine, lofepramine Other sedating – trazadone, mirtazepine **SnRI** – venlafaxine and **MAOI** **SSRI** – citalopram, fluoxetine	Double risk of falls Drowsiness, blurred vision, dizziness, orthostatic hypotension, constipation, urinary retention Orthostatic hypotension (OH)	• Review indication (do not use amitriptyline as night sedation) • Stop if possible, may need slow supervised withdrawal • Populations studies show increased falls risk with SSRI but mechanism unclear, probably safest class to use
Drugs with anticholinergic side effects	Procyclidine, trihexyphenidyl (Benzhexol), prochlorperazine, oxybutynin, tolterodine	Dizziness, blurred vision, retention of urine, confusion, drowsiness, hallucinations.	• Review indication • Reduce dose or stop
Drugs for Parkinson's disease	Co-beneldopa, co-careldopa, rotigotine, amantadine, entacapone, selegiline, rivastigmine.	Sudden daytime sleepiness, dizziness, insomnia, confusion, low blood pressure, orthostatic hypotension, blurred vision.	• Check L&S BP, drugs and PD itself can cause OH • Poorly controlled PD can cause falls • It may not be possible to change the medication • Do not change treatment without specialist advice
Vestibular Sedatives	**Phenothiazines** – prochlorperazine **Antihistamines**- cinnarazine, betahistine	Movement disorder with long term use Sedating, orthostatic hypotension	• Do not use long term – no evidence of benefit
Cardiovascular drugs	**ACE inhibitors/Angiotensin-II antagonists** Ramipril, lisinopril, captopril, irbesartan, candesartan **Vasodilators** - Hydralazine **Diuretics -** bendroflumethiazide, bumetanide, indapamide, furosemide, amiloride, spironolactone, metolazone. **Beta-blockers -** Atenolol, bisoprolol, carvedilol, propranolol, sotalol **Alpha-blockers - d**oxazosin, alfuzosin, terazosin, tamsulosin	Low blood pressure, orthostatic hypotension, dizziness, tiredness, sleepiness, confusion, hyponatraemia, hypokalaemia Bradycardia, hypotension, orthostatic hypotension, syncope	• Check L&S BP • Review indication, use alternative if possible, especially for alpha blocker • Reduce dose if possible Symptomatic OH + LVF – if *systolic* LVF then try to maintain ACEi and β Blocker as survival benefit clear. Stop nitrates, CCB, other vasodilators and if no fluid overload reduce or stop diuretics. • Seek specialist advice if needed
Analgesics	Codeine, tramadol. Opiates – morphine, oxycodone.	Drowsiness, confusion, hallucinations, orthostatic hypotension, slow reactions	• Start low, go slow, review dose and indication regularly
Anti-epileptics	Carbamazepine*, phenytoin*, phenobarbitone*, primidone* sodium valproate*, gabapentin lamotrigine, topiramate, levatiracetam, pregabalin	Unsteadiness & ataxia if levels high Phenytoin – permanent cerebellar damage and unsteadiness in long term use Newer agents – insufficient data regarding falls risk	• Consider indication (many used for pain or mood) • May need specialist review • *Consider Vitamin D supplements for at risk patients on long term treatment with these drugs

Never stop or withhold medication without agreement from the medical team

Medication and Falls Risk

All patients who present with a fall must have a medication review with modification/withdrawal (NICE CG 161)

Whilst any medication changes will be finally decided by the doctor (GP or consultant) anyone working in falls can help to make this review as useful as possible:

Take a comprehensive list of all medications currently taken (NB this should be what they actually take, not what has been prescribed!). Anyone on FOUR or more medications are at increased risk of falls.

Check the patient's understanding of their medication and how they take them. Consider concordance and compliance aids.

Check lying and standing BP (5 mins lying down, check BP, stand, check BP then every minute for 3 minutes). A drop of 20 systolic or 10 diastolic is abnormal. Record any symptoms experienced and send this in to the doctor who is doing the medication review.

Look for high or moderate risk drugs – see chart and highlight these for the doctor.

Medication review:

- Is it still the right drug? (eg methyl dopa should no longer be used for hypertension)
- Is it still necessary? (eg analgesia given for acute flare OA, now resolved)
- Is it a moderate or high risk drug (see chart)? If so what is the risk/balance ratio?
- Is there a safer alternative?
- Could the dose be reduced? (eg 5mg bendroflumethiazide no significant increase in antihypertensive effects, but significant increase in side effects compared with 2.5mg)
- Should they be on calcium and vitamin D? – Ca and Vit D (800iu daily) reduce falls by up to 20% by improving muscle function and reducing body sway. Consider vitamin D level in patients with falls over age 65 (see pathway for management of deficiency). Consider supplements in all people who fall and are housebound or in residential or nursing homes. Don't forget osteoporosis risk assessment / treatment.

Stopping or reducing medication isn't always easy and requires commitment and understanding by the prescriber and patient. Advice on complex cases is always available from the consultant geriatricians at Ipswich Hospital, in the community sessions or via the Rapid Assessment Falls Clinic.

The attached table is provided as a guide to medication review in falls only. Each patient must be assessed as an individual and the risk/benefit for each drug considered and discussed and a decision made by the prescriber in consultation with the patient.

Higher risk drugs Moderate risk drugs

Never stop or withhold medication without agreement from the medical team

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Shared Goals of Care

- Clinicians, patient and family
- Collaborative approach to identify
  - What is important to that individual
  - Goals
  - Support needs
  - Action plans
- Progress is monitored
- Continuous process