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| TABLE 1 Baseline Characteristics of HF Cohort Vs. Control Patients | | | | |
| Control Patients (n ¼ 87) | | HF  (n ¼ 467) | p Value | Missing |
| Demographics |  |  |  |  |
| Age, yrs | 73 (69–77) | 76 (69–82) | 0.11 | 0 |
| Male | 69 (79) | 313 (67) | 0.02 | 0 |
| HR, beats/min | 61 (55–70) | 70 (60–80) | <0.001 | 0 |
| BP systolic, mm Hg | 144 (130–152) | 139 (126–162) | 0.98 | 0 |
| BP diastolic, mm Hg | 76 (70–82) | 75 (66–83) | 0.40 | 0 |
| NYHA functional class III/IV | NA | 103 (22) | NA | 0 |
| HeFREF | NA | 291 (62) | NA | 0 |
| Moderate LV impairment |  | 174 (59) |  |  |
| Moderate-severe LV impairment |  | 63 (22) |  |  |
| Severe LV impairment |  | 54 (19) |  |  |
| HeFNEF |  | 176 (38) |  |  |
| Height, m | 1.71 (1.63–1.75) | 1.68 (1.61–1.75) | 0.20 | 0 |
| Weight, kg | 81 (73–92) | 83 (69–99) | 0.22 | 0 |
| BMI, kg/m2 | 27.8 (25.2–30.8) | 29.0 (25.0–33.2) | 0.08 | 0 |
| Comorbidities |  |  |  |  |
| Charlson score | 6 (4–7) | 8 (6–10) | <0.001 | 0 |
| MI | 27 (31) | 198 (42) | 0.05 | 0 |
| PVD | 16 (18) | 72 (15) | 0.49 | 0 |
| HTN | 61 (70) | 313 (67) | 0.57 | 0 |
| CVA/TIA | 5 (6) | 71 (15) | 0.02 | 0 |
| Diabetes | 35 (40) | 163 (35) | 0.24 | 0 |
| Dementia | 1 (1) | 48 (10) | 0.006 | 0 |
| COPD | 16 (18) | 140 (30) | 0.03 | 0 |
| Depression | 9 (10) | 93 (20) | 0.03 | 0 |
| Anemia | 22 (25) | 218 (47) | <0.001 | 0 |
| Recurrent falls | 5 (6) | 173 (37) | <0.001 | 0 |
| Incontinence | 1 (1) | 33 (7) | 0.04 | 0 |
| Medications |  |  |  |  |
| BB | 57 (66) | 392 (84) | <0.001 | 0 |
| ACEi/ARB | 51 (59) | 389 (83) | <0.001 | 0 |
| MRA | 1 (1) | 214 (46) | <0.001 | 0 |
| Digoxin | 0 | 100 (21) | <0.001 | 0 |
| Loop diuretic | 3 (3) | 347 (74) | <0.001 | 0 |
| Thiazide | 8 (9) | 17 (4) | 0.02 | 0 |
| $5 medications | 58 (67) | 404 (87) | <0.001 | 0 |
| Blood tests |  |  |  |  |
| NT-proBNP, ng/l | 170 (99–278) | 1,156 (496–2,463) | <0.001 | 2 |
| Hb, g/l | 139 (127–147) | 131 (118–142) | 0.007 | 0 |
| Na, mmol/l | 137 (136–139) | 137 (135–138) | 0.10 | 0 |
| K, mmol/l | 4.4 (4.2–4.6) | 4.4 (4.2–4.7) | 0.11 | 0 |
| eGFR, ml/min/1.73 m2 | 77 (64–87) | 55 (40–73) | <0.001 | 0 |
| Values are median (interquartile range: 25th to 75th percentiles) or n (%).  ACEi ¼ angiotensin converting enzyme inhibitor; ARB ¼ angiotensin receptor blocker; BB ¼ beta-blocker; BMI ¼ body mass index; BP ¼ blood pressure; COPD ¼ chronic obstructive pulmonary disease; CVA/TIA ¼ ce- rebrovascular accident/transient ischemic attack; eGFR ¼ estimated glomerular ﬁltration rate; Hb ¼ hemoglobin; HeFNEF ¼ heart failure with normal ejection fraction; HeFREF ¼ heart failure with reduced ejection fraction; HF ¼ heart failure; HR ¼ heart rate; HTN ¼ hypertension; K ¼ potassium; LV ¼ left ventricular; MI ¼ myocardial infarction; MRA ¼ mineralocorticoid receptor antagonist; Na ¼ sodium; NA ¼ not available; NT-proBNP ¼ N- terminal pro-B-type natriuretic peptide; NYHA ¼ New York Heart Association; PVD ¼ peripheral vascular disease. | | | | |

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| TABLE 2 Prevalence of Pre-Frailty and Frailty in HF Vs. Control Patients According to Different Frailty Tools | | | | | | | | | | | |
|  | Fried 1-2  (n ¼ 184) | Pre-Frailty  DI Middle Tertile (n ¼ 177) | | EFS 6-7  (n ¼ 93) | Fried $3 (n ¼ 250) | Assessment Tools  DI Upper Tertile (n ¼ 193) | | Frailty  EFS $8 (n ¼ 142) | CFS >4  (n ¼ 209) | Screening Tools  AFN Frail DFI Frail (n ¼ 230) (n ¼ 230) | |
| HF (n ¼ 467) | 32 (148) | DI <0.15  0 | DI <0.25  22 (32) | 19 (90) | 52 (244) | DI ¼ 0.40-0.49 35 (57) | DI $0.5  29 (48) | 30 (140) | 44 (206) | 47 (217) | 48 (224) |
| Control patients (n ¼ 87) | 41 (36) | 70 (21) | 100 (30) | 3 (3) | 7 (6) | 7 (2) | 4 (1) | 2 (2) | 3 (3) | 15 (13) | 7 (6) |
| p value (HF vs. control patients) | 0.08 | NA | | <0.001 | <0.001 | NA | | <0.001 | <0.001 | <0.001 | <0.001 |
| AFN ¼ acute frailty network frailty criteria; CFS ¼ clinical frailty scale; DFI ¼ Derby frailty index; DI ¼ deﬁcit index; EFS ¼ Edmonton frailty scale; Fried ¼ Fried criteria; other abbreviations as in [Table 1](#_bookmark4). | | | | | | | | | | | |

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| TABLE 3 Prevalence of Frailty in Different Subgroups of Patients With CHF | | | | | | | |
|  | Fried (n ¼ 250) | Assessment Tools DI EFS  (n ¼ 165) (n ¼ 142) | | Frailty | CFS  (n ¼ 209) | Screening Tools AFN DFI  (n ¼ 230) (n ¼ 230) | |
| Heart rhythm |  |  | |  |  |  | |
| SR (n ¼ 252) | 46 (116) | 32 (80) | 25 (64) |  | 39 (98) | 40 (100) | 43 (108) |
| AF (n ¼ 215) | 60 (128) | 40 (85) | 35 (76) |  | 50 (108) | 54 (117) | 54 (116) |
| p value (SR vs. AF) | 0.004 | 0.02 | 0.02 |  | 0.02 | 0.001 | 0.02 |
| BMI categories, kg/m2 |  |  | |  |  |  | |
| <24.9 (n ¼ 111) | 60 (67) | 41 (46) | 41 (46) |  | 53 (59) | 62 (69) | 64 (71) |
| 25.0-29.9 (n ¼ 158) | 50 (79) | 30 (48) | 25 (39) |  | 42 (66) | 45 (71) | 54 (86) |
| $30 (n ¼ 198) | 50 (98) | 36 (71) | 28 (55) |  | 41 (81) | 39 (77) | 34 (67) |
| p value (BMI categories) | 0.15 | 0.17 | 0.009 |  | 0.09 | <0.001 | <0.001 |
| HF phenotype |  |  | |  |  |  | |
| HeFREF (n ¼ 291) | 47 (138) | 31 (90) | 27 (79) |  | 40 (117) | 39 (114) | 42 (122) |
| HeFNEF (n ¼ 176) | 60 (106) | 43 (75) | 35 (61) |  | 51 (89) | 59 (103) | 58 (102) |
| p value (HeFREF vs. HeFNEF) | 0.007 | 0.01 | 0.09 |  | 0.03 | <0.001 | 0.001 |
| NYHA functional class |  |  | |  |  |  | |
| I/II (n ¼ 364) | 44 (159) | 28 (102) | 22 (81) |  | 35 (128) | 40 (145) | 42 (154) |
| III/IV (n ¼ 103) | 83 (85) | 61 (63) | 57 (59) |  | 76 (78) | 70 (72) | 68 (70) |
| p value (I/II vs. III/IV) |  |  | | <0.001 |  |  | |
| NT-proBNP, ng/l |  |  | |  |  |  | |
| <1,000 (n ¼ 215) | 41 (88) | 26 (56) | 22 (47) |  | 33 (70) | 32 (68) | 35 (76) |
| 1,000-2,000 (n ¼ 108) | 55 (59) | 35 (38) | 30 (32) |  | 45 (49) | 52 (56) | 54 (58) |
| >2,000 (n ¼ 144) | 67 (97) | 49 (71) | 42 (61) |  | 60 (87) | 65 (93) | 63 (90) |
| p value (NT-proBNP categories) |  |  | | <0.001 |  |  | |
| Age, yrs |  |  | |  |  |  | |
| <65 (n ¼ 82) | 28 (23) | 20 (16) | 12 (10) |  | 22 (18) | NA | NA |
| 65-75 (n ¼ 139) | 35 (49) | 23 (32) | 18 (25) |  | 27 (38) | 32 (44) | 9 (13) |
| >75 (n ¼ 246) | 70 (172) | 48 (117) | 43 (105) |  | 61 (150) | 70 (173) | 86 (211) |
| p value (age categories) |  |  | | <0.001 |  |  | |
| Values are % (n).  AF ¼ atrial ﬁbrillation; SR ¼ sinus rhythm; other abbreviations as in [Tables 1](#_bookmark4) and [2](#_bookmark5). | | | | | | | |

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| TABLE 4 Baseline Characteristics of Frail Vs. Non-frail HF Patients Categorized According to Different Frailty Assessment Tools | | | | | | | | | |
|  | Frailty Assessment  Fried  Non-Frail Frail Non-Frail (n ¼ 223) (n ¼ 244) p Value (n ¼ 302) | | | in Patients With HF DI  Frail  (n ¼ 165) | (n ¼ 467)  p Value | Non-Frail (n ¼ 327) | EFS  Frail (n ¼ 140) | p Value | Missing |
| Demographics |  | | |  |  |  |  |  |  |
| Age, yrs | 72 (64–78) 80 (74–84) | <0.001 | 74 (66–80) | 80 (74–85) | <0.001 | 74 (66–80) | 80 (75–85) | <0.001 | 0 |
| Male | 165 (74) 148 (61) | 0.002 | 214 (71) | 99 (60) | 0.02 | 224 (69) | 89 (64) | 0.30 | 0 |
| HR, beats/min | 70 (61–77) 71 (60–82) | 0.14 | 70 (60–80) | 70 (62–82) | 0.80 | 70 (60–79) | 70 (61–83) | 0.21 | 0 |
| BP systolic, mm Hg | 140 (125–157) 138 (126–166) | 0.17 | 140 (125–158) | 137 (128–167) | 0.15 | 141 (126–162) | 137 (125–162) | 0.79 | 0 |
| BP diastolic, mm Hg | 74 (67–83) 75 (65–83) | 0.35 | 75 (67–83) | 74 (65–83) | 0.43 | 75 (67–83) | 73 (64–82) | 0.02 | 0 |
| NYHA functional | 18 (8) 85 (35) | <0.001 | 40 (13) | 63 (38) | <0.001 | 44 (14) | 59 (42) | <0.001 | 0 |
| class III/IV |  | | |  |  |  |  |  |  |
| HeFREF | 153 (69) 138 (57) | 0.007 | 201 (67) | 90 (54) | 0.10 | 212 (65) | 79 (56) | 0.09 | 0 |
| HeFNEF | 70 (31) 106 (43) |  | 101 (33) | 75 (46) |  | 115 (35) | 61 (44) |  |  |
| Height, m | 1.70 (1.64–1.76) 1.66 (1.59–1.74) | <0.001 | 1.70 (1.63–1.75) | 1.65 (1.59–1.74) | 0.001 | 1.69 (1.62–1.75) | 1.65 (1.59–1.74) | 0.003 | 0 |
| Weight, kg | 86 (74–102) 79 (66–96) | 0.006 | 84 (72–99) | 78 (66–97) | 0.05 | 84 (72–99) | 78 (64–97) | 0.003 | 0 |
| BMI, kg/m2 | 29.4 (26.0–33.3) 28.7 (24.4–32.8) | 0.15 | 29.1 (25.6–33.2) | 28.8 (24.3–33.1) | 0.52 | 29.1 (25.8–33.3) | 28.6 (23.6–32.7) | 0.07 | 0 |
| Comorbidities |  | | |  |  |  |  |  |  |
| Charlson score | 7 (5–9) 9 (8–11) | <0.001 | 7 (5–9) | 10 (9–12) | <0.001 | 8 (6–9) | 10 (8–12) | <0.001 | 0 |
| MI | 98 (44) 100 (41) | 0.52 | 121 (40) | 77 (47) | 0.17 | 142 (43) | 56 (40) | 0.49 | 0 |
| PVD | 28 (13) 44 (18) | 0.10 | 34 (11) | 38 (23) | 0.001 | 42 (13) | 30 (21) | 0.02 | 0 |
| HTN | 139 (62) 174 (71) | 0.04 | 192 (64) | 121 (73) | 0.03 | 221 (68) | 92 (66) | 0.69 | 0 |
| CVA/TIA | 22 (10) 49 (20) | 0.002 | 26 (9) | 45 (27) | <0.001 | 37 (11) | 34 (24) | <0.001 | 0 |
| Diabetes | 69 (31) 94 (39) | 0.05 | 90 (30) | 73 (44) | 0.002 | 106 (33) | 57 (41) | 0.21 | 0 |
| Dementia | 4 (2) 44 (18) | <0.001 | 8 (3) | 40 (24) | <0.001 | 5 (2) | 43 (31) | <0.001 | 0 |
| COPD | 47 (21) 93 (38) | <0.001 | 73 (24) | 67 (41) | <0.001 | 78 (24) | 62 (44) | <0.001 | 0 |
| Depression | 28 (13) 65 (27) | <0.001 | 42 (14) | 51 (31) | <0.001 | 48 (15) | 45 (32) | <0.001 | 0 |
| Anemia | 77 (35) 141 (58) | <0.001 | 110 (36) | 108 (66) | <0.001 | 126 (39) | 92 (66) | <0.001 | 0 |
| Recurrent falls | 32 (14) 141 (58) | <0.001 | 63 (21) | 110 (67) | <0.001 | 83 (25) | 90 (64) | <0.001 | 0 |
| Incontinence | 8 (4) 25 (10) | 0.005 | 11 (4) | 22 (13) | 0.001 | 13 (4) | 20 (14) | <0.001 | 0 |
| Medications |  | | |  |  |  |  |  |  |
| BB | 201 (90) 191 (78) | <0.001 | 263 (87) | 129 (78) | 0.01 | 280 (86) | 112 (80) | 0.13 | 0 |
| ACEi/ARB | 202 (91) 187 (77) | <0.001 | 274 (91) | 115 (70) | <0.001 | 291 (89) | 98 (70) | <0.001 | 0 |
| MRA | 109 (49) 105 (43) | 0.21 | 153 (51) | 61 (37) | 0.005 | 162 (50) | 52 (37) | 0.01 | 0 |
| Digoxin | 42 (19) 58 (24) | 0.19 | 69 (23) | 31 (19) | 0.31 | 69 (21) | 31 (22) | 0.80 | 0 |
| Loop diuretic | 146 (66) 201 (82) | <0.001 | 213 (71) | 134 (81) | 0.01 | 230 (70) | 117 (84) | 0.003 | 0 |
| Thiazide | 4 (2) 13 (5) | 0.04 | 5 (2) | 12 (7) | 0.002 | 9 (3) | 8 (6) | 0.12 | 0 |
| $5 medications | 176 (79) 228 (93) | <0.001 | 247 (82) | 157 (95) | <0.001 | 269 (82) | 135 (96) | <0.001 | 0 |
| Blood tests |  | | |  |  |  |  |  |  |
| NT-proBNP, ng/l | 1,020 (436–2,124) 2,465 (1,372–4,143) | <0.001 | 919 (402–1,899) | 1,669 (812–3,426) | <0.001 | 963 (426–1,919) | 2,613 (1,013–4,712) | <0.001 | 2 |
| Hb, g/l | 132 (120–143) 121 (110–131) | <0.001 | 135 (123–144) | 121 (112–134) | <0.001 | 134 (121–144) | 120 (109–131) | <0.001 | 0 |
| Na, mmol/l | 137 (135–138) 136 (133–138) | 0.05 | 137 (135–138) | 136 (134–138) | 0.09 | 137 (135–138) | 136 (134–138) | 0.22 | 0 |
| K, mmol/l | 4.4 (4.2–4.7) 4.3 (4.1–4.8) | 0.32 | 4.5 (4.2–4.7) | 4.4 (4.1–4.7) | 0.11 | 4.5 (4.2–4.7) | 4.3 (4.1–4.6) | 0.007 | 0 |
| eGFR, ml/min/ | 59 (37–76) 55 (40–73) | 0.99 | 61 (45–76) | 48 (32–63) | 0.004 | 56 (41–74) | 52 (33–70) | 0.02 | 0 |
| 1.73 m2 |  | | |  |  |  |  |  |  |
| Values are median (interquartile range: 25th to 75th percentiles) or n (%). Abbreviations as in [Table 1](#_bookmark4). | | | | | | | | | |

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| TABLE 5 Correlation Coefﬁcients for Frailty Tools | | | | | | |
| Indices | DFI | Screening  AFN | Tools | CFS | Assessment  Fried | Tools  EFS |
| AFN | 0.60 |  |  | |  |  |
| CFS | 0.54 | 0.59 |  | |  |  |
| Fried | 0.54 | 0.57 | 0.86 | |  |  |
| EFS | 0.50 | 0.56 | 0.89 | | 0.81 |  |
| DI | 0.48 | 0.53 | 0.87 | | 0.77 | 0.86 |
| All p < 0.001.  Abbreviations as in [Table 2](#_bookmark5). | | | | | | |

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| TABLE 6 Agreement Between Frailty Screening Vs. Assessment Tools | | | | | | | | | |
| Assessment Tools | Non-Frail (n ¼ 261) | CFS | Frail  (n ¼ 206) | Screening Tools  Non-Frail (n ¼ 250) | AFN | Frail (n ¼ 217) | Non-Frail (n ¼ 243) | DFI | Frail (n ¼ 224) |
| Fried |  | | |  | | |  | | |
| Non-frail (n ¼ 223) | 45 (209) |  | 3 (14) | 38 (178) |  | 10 (45) | 37 (172) |  | 11 (51) |
| Frail (n ¼ 244) | 11 (52) |  | 41 (192) | 15 (72) |  | 37 (172) | 15 (71) |  | 37 (173) |
|  | K ¼ 0.72; p < 0.001 | | | K ¼ 0.50; p < 0.001 | | | K ¼ 0.48; p < 0.001 | | |
| DI |  | | |  | | |  | | |
| Non-frail (n ¼ 302) | 54 (250) |  | 11 (52) | 46 (214) |  | 19 (88) | 42 (197) |  | 22 (105) |
| Frail (n ¼ 165) | 2% (11) |  | 33 (154) | 8 (36) |  | 27 (129) | 10 (46) |  | 26 (119) |
|  | K ¼ 0.72; p < 0.001 | | | K ¼ 0.46; p < 0.001 | | | K ¼ 0.35; p < 0.001 | | |
| EFS |  | | |  | | |  | | |
| Non-frail (n ¼ 327) | 55 (255) |  | 15 (72) | 48 (225) |  | 22 (102) | 45 (209) |  | 25 (118) |
| Frail (n ¼ 140) | 1 (6) |  | 29 (134) | 5 (25) |  | 25 (115) | 7 (34) |  | 23 (106) |
|  | K ¼ 0.65; p < 0.001 | | | K ¼ 0.44; p < 0.001 | | | K ¼ 0.34; p < 0.001 | | |
| Values are % (n).  K ¼ kappa coefﬁcient; other abbreviations as in [Table 2](#_bookmark5). | | | | | | | | | |

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| TABLE 7 Sensitivity, Speciﬁcity, and Misclassiﬁcation Rates of Different Frailty Tools (Screening Vs. Assessment Vs. Single Physical Tests) in Identifying Frailty According to the Combined Index (the Presumed Gold Standard for Identifying Frailty) | | | | | | | | | |
| Frailty Tools  Screening Assessment Single Physical Tests DI  CFS AFN DFI Fried EFS (Upper Grip 5-m TUGT  >4 (Frail) (Frail) $3 $8 Tercile) Strength[\*](#_bookmark13) Walk Test[\*](#_bookmark13) >10 s | | | | | | | | | |
| Sensitivity | 87 | 79 | 76 | 93 | 62 | 75 | 93 | 95 | 97 |
| Speciﬁcity | 89 | 78 | 73 | 76 | 98 | 92 | 58 | 59 | 55 |
| PPV | 86 | 72 | 67 | 73 | 96 | 88 | 61 | 62 | 66 |
| NPV | 90 | 83 | 81 | 94 | 74 | 81 | 92 | 94 | 96 |
| False positive | 6 | 13 | 16 | 14 | 1 | 5 | 25 | 24 | 24 |
| False negative | 6 | 9 | 10 | 3 | 18 | 12 | 3 | 2 | 1 |
| Misclassiﬁcation rate | 12 | 22 | 26 | 17 | 19 | 17 | 28 | 26 | 25 |
| Values are %. \*Frail according to Fried criteria.  NPV ¼ negative predictive value; PPV¼ positive predictive value; TUGT ¼ timed get up and go test. | | | | | | | | | |

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| FIGURE 1 Bar Graph Showing Prevalence of Frailty and Pre-Frailty by Different Frailty Tools in the Heart Failure Cohort |
| Image of Figure 1 |
| AFN ¼ acute frailty network; CFS ¼ clinical frailty scale; DI ¼ Deﬁcit Index; DFI ¼ Derby frailty index; EFS ¼ Edmonton frailty score. |

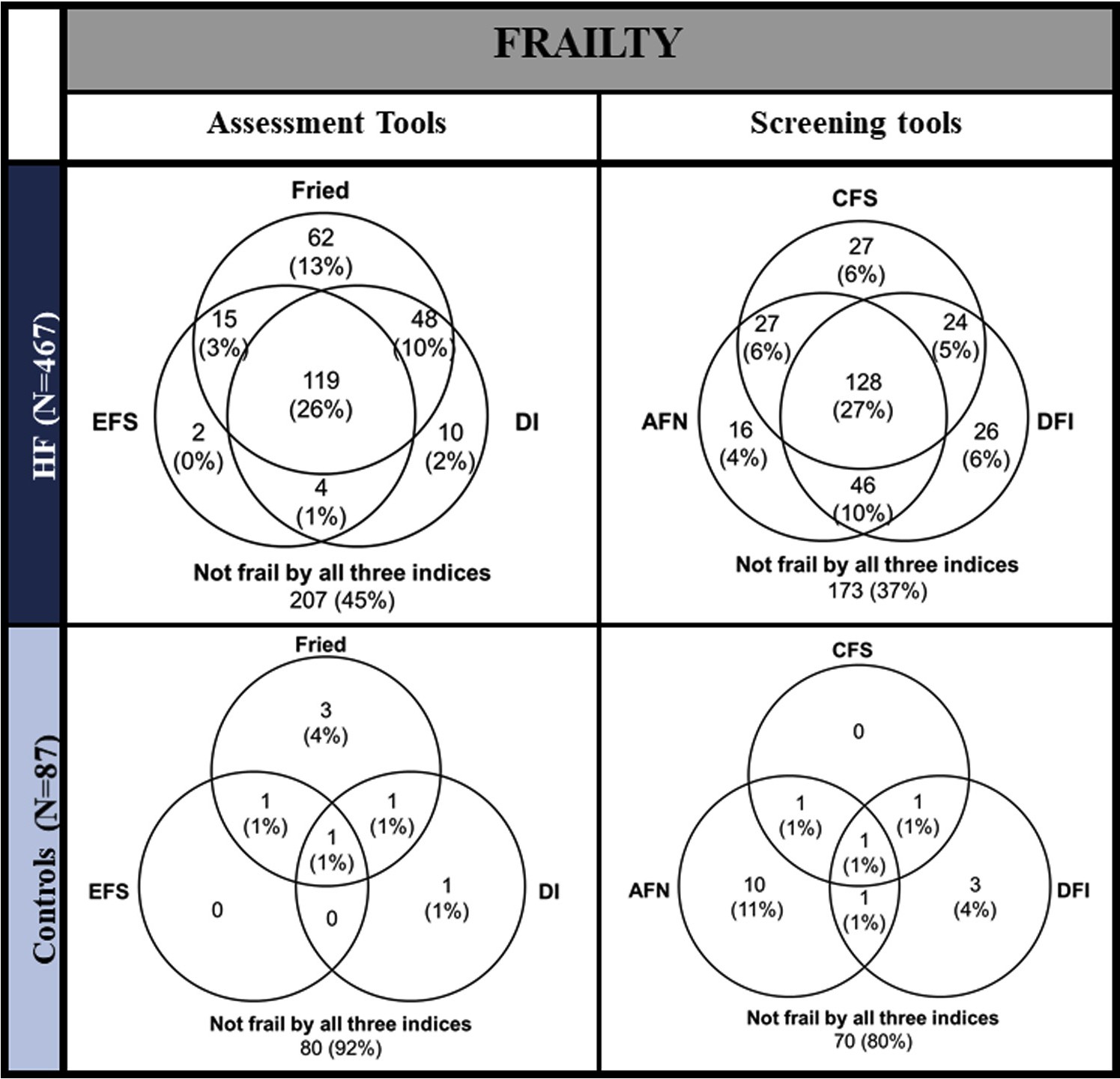


Figure 2: CENTRAL ILLUSTRATION Venn Diagrams Showing the Relationship Between Different Assessment and Screening Tools in Detecting Frailty in Patients With HF and in Control Patients