**Performance- versus Risk Factor-Based Approaches to Coronary Artery Disease Screening in Waitlisted Kidney Transplant Candidates**

**Supplemental Documents:**

S1: Our center’s algorithm for coronary artery disease (CAD) screening prior to kidney transplantation. 2

S2: How a patient progressed from initial evaluation to inclusion in the study cohort. 3

S3: Baseline characteristics and outcomes of cohorts #2 and #3. 4

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**Supplemental S1.** Our center’s algorithm for coronary artery disease (CAD) screening prior to kidney transplantation.

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|  | Etiology of End-Stage Kidney Disease |
|  | Diabetic | Non-diabetic |
| Initial screening | Coronary angiography if any of:Age ≥45 yearsDiabetes mellitus ≥25 yearsSmoker ≥5 yearsAbnormal electrocardiogramNon-invasive stress test otherwise | Non-invasive stress test if any of:Age ≥50 yearsDialysis ≥5 yearsCorticosteroid useObesitySystemic lupus erythematosusAutosomal dominant polycystic kidney diseaseNo testing otherwise |
| Repeat screening | Non-invasive stress test every year or coronary angiography every 3 years if any of: |
| Age ≥45 yearsKnown CADDiabetes mellitus ≥25 yearsSmoker ≥5 yearsAbnormal electrocardiogram | Age ≥50 years *and* Known CAD |

**Supplemental S2.** How a patient progressed from initial evaluation to inclusion in the study cohort. Triangles represent cardiac ischemic testing: filled triangles represent tests we requested and performed based on our center criteria (see Supplemental S1); solid-rimmed, hollow triangles represent tests that we possibly (and inconsistently) performed earlier in the waitlist process; notch-rimmed, hollow triangles represent tests ordered by outside physicians for non-transplant purposes, which we reviewed and included if it fell within 6 months of TRAC evaluation.



**Supplement S3**. Baseline characteristics and outcomes of cohorts #2 and #3, stratified by 6-minute walk test (6MWT) results.

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| **Cohort 2** |  |  |  |
| **Baseline Characteristics** | **6MWT <400 meters****N=107** | **6MWT ≥400 meters****N=89** | **p-value** |
| *Demographics* |
| Age (years) | 61±6 | 55±12 | <0.0001 |
| Sex (% male) | 57 (53%) | 62 (68%) | 0.04 |
| Race |  |  |  |
| White | 35 (14%) | 12 (13%) | 0.11 |
| Black | 10 (9%) | 8 (9%) |  |
| Hispanic | 56 (51%) | 43 (47%) |  |
| Asian | 18 (17%) | 26 (29%) |  |
| Other | 10 (9%) | 2 (2%) |  |
| Time from listing (years) | 5.9±2.7 | 5.5±2.7 | 0.4 |
| *Cardiac Risk Factors and Comorbidities* |
| CAD testing prior to visit | 83 (76%) | 65 (71%) | 0.4 |
| Coronary artery disease with revascularization | 31 (29%) | 24 (26%) | 0.7 |
| Any atherosclerotic disease (CAD equivalent)1 | 56 (51%) | 34 (38%) | 0.05 |
| Dialysis vintage (years) | 7.1±3.1 | 6.1±3.5 | 0.04 |
| Dialysis modality |  |  | 0.3 |
| Hemodialysis | 94 (87%) | 78 (91%) |  |
| Peritoneal dialysis | 14 (13%) | 8 (9%) |  |
| Diabetes mellitus | 78 (72%) | 35 (39%) | <0.0001 |
| Hypertension | 96 (88%) | 83 (91%) | 0.5 |
| Any history of smoking | 36 (33%) | 45 (49%) | 0.02 |
| Non-cardiac factors affecting the 6MWT result | 48 (44%) | 23 (25%) | 0.006 |
| Lung disease2 | 12 (11%) | 14 (15%) | 0.4 |
| Lower extremity amputation | 14 (13%) | 2 (2%) | 0.005\* |
| Active orthopedic issue3 | 6 (6%) | 1 (1%) | 0.09\* |
| Assistive walking device use4 | 18 (17%) | 2 (2%) | 0.003\* |
| *Cardiac Symptoms, Screening and Testing* |
| Cardiac symptoms5 at rest | 8 (9%) | 5 (5%) | 0.9\* |
| Cardiac symptoms5 during 6MWT | 10 (9%) | 1 (1%) | 0.01\* |
| Meets AHA/ACCF criteria6 for screening | 100 (92%) | 80 (88%) | 0.04 |
| CAD testing within 6 months | 107 (100%) | 89 (100%) | 1.0 |

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| **Cohort 3** |  |  |  |
| **Baseline Characteristics** | **6MWT <400 meters****N=38** | **6MWT ≥400 meters****N=51** | **p-value** |
| *Demographics* |
| Age (years) | 59±6 | 54±14 | 0.04 |
| Sex (% male) | 22 (58%) | 32 (63%) | 0.6 |
| Race |  |  |  |
| White | 7 (18%) | 7 (14%) | 0.7 |
| Black | 5 (13%) | 4 (8%) |  |
| Hispanic | 16 (42%) | 26 (51%) |  |
| Asian | 8 (21%) | 13 (25%) |  |
| Other | 2 (5%) | 1 (2%) |  |
| Time from listing (years) | 5.4±2.8 | 5.5±2.8 | 0.9 |
| *Cardiac Risk Factors and Comorbidities* |
| CAD testing prior to visit | 29 (76%) | 35 (67%) | 0.4 |
| Coronary artery disease with revascularization | 5 (13%) | 10 (20%) | 0.4 |
| Any atherosclerotic disease (CAD equivalent)1 | 12 (43%) | 15 (29%) | 0.8 |
| Dialysis vintage (years) | 6.3±3.1 | 6.1±3.8 | 0.8 |
| Dialysis modality |  |  | 0.9 |
| Hemodialysis | 29 (78%) | 42 (89%) | 0.2 |
| Peritoneal dialysis | 8 (22%) | 5 (11%) |  |
| Diabetes mellitus | 19 (50%) | 14 (27%) | 0.03 |
| Hypertension | 30 (79%) | 45 (88%) | 0.2 |
| Any history of smoking | 18 (47%) | 22 (43%) | 0.69 |
| Non-cardiac factors affecting the 6MWT result | 17 (45%) | 12 (24%) | 0.03 |
| Lung disease2 | 4 (11%) | 8 (16%) | 0.8\* |
| Lower extremity amputation | 2 (5%) | 0 (0%) | 1.0\* |
| Active orthopedic issue3 | 1 (3%) | 0 (0%) | 0.4\* |
| Assistive walking device use4 | 10 (25%) | 0 (0%) | 0.0005\* |
| *Cardiac Symptoms, Screening and Testing* |
| Cardiac symptoms5 at rest | 1 (3%) | 5 (10%) | 0.2\* |
| Cardiac symptoms5 during 6MWT | 2 (5%) | 1 (2%) | 0.7\* |
| Meets AHA/ACCF criteria6 for screening | 33 (87%) | 43 (84%) | 0.7 |
| CAD testing within 6 months | 38 (100%) | 51 (100%) | 1.0 |
| **Outcomes** |  |  |  |
| Follow-up time (days) | 573±281 | 564±228 | 0.9 |
| Received a kidney transplant during follow-up | 18 (47%) | 26 (51%) | 0.7 |
| Primary outcome: CAD-related event |  |  | 0.3 |
| Cardiac death | 0 (0%) | 1 (2%) |  |
| Non-fatal MI | 1 (3%) | 1 (2%) |  |
| Type 1 | 1 | 1 |  |
| Type 2 | 0 | 0 |  |
| Revascularization | 2 (5%) | 1 (2%) |  |
| Urgent | 1 | 0 |  |
| Non-urgent | 1 | 1 |  |
| Removal from waitlist for advanced CAD | 1 (3%) | 1 (2%) |  |
| Removed from waitlist | 6 (16%) | 4 (8%) | 0.2 |
| Non-cardiac death on the waitlist | 3 (8%) | 1 (2%) | 0.1 |

1Any atherosclerotic disease (CAD equivalent): Any history of revascularized CAD, ischemic cerebrovascular accidents, or peripheral artery disease (active claudication, revascularization or amputation).

2Lung disease: Airway disease (chronic obstructive pulmonary disease, reactive airway disease, or adult asthma) or parenchymal lung disease.

3Active orthopedic issue or non-weight-bearing: Issues impairing locomotion, including fracture, casts/prosthesis/boots, or active lower extremity ulcer requiring non-weight-bearing.

4Assistive devise use: Cane or walker use.

5Cardiac symptoms: Chest pain, dyspnea on exertion, unexplained upper gastrointestinal symptoms with exertion, or fatigue requiring stopping during the 6MWT.

6AHA/ACCF criteria: From the 2012 American Heart Association / American College of Cardiology Foundation Scientific Statement endorsed by the American Society of Transplantation3 – High-risk is defined as having CAD or CAD-equivalent, diabetes mellitus, or 2 or more risk factors including hypertension, age (>45 for men or >55 for women), cigarette smoking, or left ventricular hypertrophy. Dyslipidemia and family history were two additional risk factors that we did not have in our database.

6MWT: 6-minute walk test. CAD: coronary artery disease.

\*Calculated by fisher’s exact test due to small cell size.

**Supplemental S4.** Identification of a low-risk cohort: prediction of CAD-related event within 1 year in a cohort of 343 patients with 6MWT>0. Statistically significant results are **bolded**. AUC(t) refers to the area-under-the-curve for 1-year time-dependent receiver operator curve for the CAD-related event.

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| --- | --- | --- | --- | --- |
| Predictor of Low Risk | N (%) meeting low-risk definition | sHR for CAD-related event | sHR for competing event | AUC(t) |
| 6MWT result (continuous, per 50m) | n/a | 1.02 (0.91-1.15) | **0.62 (0.56-0.68)** | 0.56 |
| 6MWT result ≥400m | 161 (47%) | 0.69 (0.38-1.24) | **0.11 (0.05-0.26)** | 0.55 |
| 6MWT result ≥400m + no cardiac symptom during 6MWT | 159 (47%) | 0.70 (0.39-1.27) | **0.09 (0.04-0.23)** | 0.51 |
| No self-reported cardiac symptom | 292 (85%) | 0.80 (0.32-2.00) | 0.70 (0.32-1.52) | 0.50 |
| Does not meet AHA/ACCF criteria | 32 (9%) | **0.12 (0.02-0.87)** | 0.49 (0.20-1.20) | 0.54 |

**Supplemental S5.** Identification of a low-risk cohort: prediction of positive invasive or non-invasive cardiac ischemia test result within 6 months, stratified by type of cardiac testing (non-invasive versus invasive). All p-values for testing by interaction were >0.05, suggesting no detectable effect modification.

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| --- | --- |
| **Predictor** | **Odds Ratio** |
|  | Non-Invasive | Invasive |
| N (% positive) | 94 (11%) | 102 (33%) |
| 6MWT result (continuous, per 50m) | 0.87 (0.62-1.22) | 1.12 (0.90-1.38) |
| 6MWT result ≥400m | 0.58 (0.16-2.04) | 1.22 (0.51-2.92) |
| 6MWT result ≥400m + no cardiac symptom during 6MWT | 0.58 (0.17-2.06) | 1.22 (0.51-2.92) |