**Supplementary Material**

**Figure S1**. Combined Biomarker Model performance

A graph of a number of different colored lines

Description automatically generated with medium confidence

**Table S1. Combined Biomarker Model Patient Cohort Characteristics**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | VUMC | | | | UPMC | | | | DECAMP | | | | Denver | | | |
| Characteristic | Benign | | Cancer | | Benign | | Cancer | | Benign | | Cancer | | Benign | | Cancer | |
| Count, No. (%) | 51 | (30) | 120 | (70) | 59 | (60) | 40 | (40) | 49 | (50) | 50 | (50) | 40 | (45) | 48 | (55) |
| Age, median (IQR), y | 63 | (55-69) | 70 | (63-75) | 68 | (64-74) | 68 | (62-76) | 65 | (61-72) | 68 | (63-74) | 67 | (61-72) | 66 | (62 |
| Current/Former Smoker, No. (%) | 42 | (82) | 115 | (94) | 59 | (100) | 40 | (100) | 49 | (100) | 50 | (100) | 31 | (78) | 39 | (81) |
| Pack-years, median (IQR), y | 30 | (4-49) | 44 | (30-70) | 46 | (36-70) | 40 | (30-59) | 40 | (30-54) | 45 | (35-60) | 45 | (14-54) | 45 | (25-63 |
| Previous Cancer, No. (%) | 11 | (22) | 45 | (37) | 2 | (3) | 0 | (0) | 23 | (47) | 25 | (50) | 5 | (13) | 6 | (13) |
| Located in Upper Lobe, No. (%) | 26 | (51) | 77 | (63) | 25 | (42) | 29 | (73) | 29 | (59) | 26 | (52) | 24 | (60) | 38 | (79) |
| Size (mm), median (IQR), mm | 13 | (8-20) | 20 | (13-23) | 11 | (8-14) | 21 | (16-26) | 11 | (8-14) | 15 | (11-19) | 13 | (11-19) | 19 | (15-24) |
| Spiculated, No. (%) | 15 | (29) | 50 | (41) | 2 | (3) | 11 | (28) | 26 | (53) | 22 | (44) | 8 | (20) | 18 | (38) |
| Gender (Male), No. (%) | 29 | (57) | 70 | (57) | 37 | (63) | 21 | (53) | 37 | (76) | 39 | (78) | 27 | (68) | 33 | (69) |
| BMI, median (IQR)a | 28 | (23-33) | 27 | (23-31) | 29 | (25-32) | 27 | (22-30) | 25 | (23-28) | 25 | (23-30) | 28 | (26-32) | 28 | (24-31) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mayo Model Risk |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Risk, median (IQR) | 29 | (13-50) | 62 | (36-80) | 16 | (9-33) | 51 | (32-75) | 44 | (25-59) | 53 | (34-72) | 27 | (18-54) | 51 | (26-77) |
| Low Risk: <10%, No. (%) | 11 | (22) | 4 | (3) | 16 | (27) | 1 | (3) | 2 | (4) | 0 | (0) | 6 | (15) | 4 | (8) |
| Int. Risk: 10-70%, No. (%) | 33 | (65) | 73 | (61) | 43 | (73) | 27 | (68) | 35 | (71) | 36 | (72) | 31 | (78) | 30 | (63) |
| High Risk: >70%, No. (%) | 7 | (14) | 43 | (36) | 0 | (0) | 12 | (30) | 12 | (24) | 14 | (28) | 3 | (8) | 14 | (29) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cancer Histology, No. (%) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Adenocarcinoma |  |  | 70 | (58) |  |  | 21 | (53) |  |  | 26 | (52) |  |  | 34 | (71) |
| Squamous Cell |  |  | 22 | (18) |  |  | 7 | (18) |  |  | 11 | (22) |  |  | 7 | (15) |
| Small Cell |  |  | 14 | (12) |  |  | - |  |  |  | 5 | (10) |  |  | - |  |
| Large Cell |  |  | 2 | (2) |  |  | 3 | (8) |  |  | 2 | (4) |  |  | - |  |
| Carcinoid |  |  | 6 | (2) |  |  | - |  |  |  | 1 | (2) |  |  | - |  |
| Unspecified NSCLC |  |  | 2 | (2) |  |  | 7 | (18) |  |  | 2 | (4) |  |  | 2 | (4) |
| Other† |  |  | 4 | (3) |  |  | 2 | (5) |  |  | 3 | (6) |  |  | 5 | (10) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cancer Stage, No. (%) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| I |  |  | 79 | (65) |  |  | 15 | (38) |  |  | 26 | (52) |  |  | 33 | (69) |
| II |  |  | 13 | (11) |  |  | 4 | (10) |  |  | 3 | (6) |  |  | - |  |
| III |  |  | 11 | (9) |  |  | 9 | (23) |  |  | 12 | (24) |  |  | 4 | (8) |
| IV |  |  | 9 | (7) |  |  | 6 | (15) |  |  | 3 | (6) |  |  | 6 | (13) |
| Limited |  |  | 3 | (2) |  |  | - |  |  |  | - |  |  |  | - |  |
| Extensive |  |  | 6 | (5) |  |  | - |  |  |  | - |  |  |  | - |  |
| Missing |  |  | 1 | (1) |  |  | 6 | (15) |  |  | 6 | (12) |  |  | 5 | (10) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

†Other cancers include: adenosquamous (1), adenomatous hyperplasia (1), neuroendocrine (4), mucoepidermoid (1), schwannoma (1), adenocarcinoma and squamous cell carcinoma simultaneous primary (1), unknown (5).