**Supplementary material - Table S1: Association of 3- and 12-month eGFR with death and non-death censored graft failure (including patient death)**

|  |  |  |
| --- | --- | --- |
|  | Single-center cohort | Multicenter cohort |
| Unadjusted | Adjusted\* | Unadjusted | Adjusted\*\* |
| HR (CI 95%) | p-value | HR (CI 95%) | p-value | HR (CI 95%) | p-value | HR (CI 95%) | p-value |
| Outcome: death |
| 3-month eGFR(for 10 mL/min/1.73m² increase) | 0.87 (0.76 - 1.01) | 0.064 | 1.09 (0.93 - 1.28) | 0.27 | 0.88 (0.83 - 0.95) | 0.0003 | 1.02 (0.94 - 1.11) | 0.60 |
| 3-month eGFR < 45 mL/min/1.73m² | 1.65 (1.09 - 2.50) | 0.018 | 1.01 (0.63 - 1.60) | 0.98 | 1.94 (1.52 - 2.46) | <0.0001 | 1.39 (1.03 - 1.88) | 0.031 |
| 12-month eGFR(for 10 mL/min/1.73m² increase) | 0.82 (0.70 - 0.96) | 0.014 | 1.05 (0.88 - 1.25) | 0.59 | 0.85 (0.79 - 0.91) | <0.0001 | 1.01 (0.92 - 1.11) | 0.80 |
| 12-month eGFR < 45 mL/min/1.73m² | 1.84 (1.20 - 2.83) | 0.005 | 1.03 (0.65 - 1.64) | 0.90 | 1.66 (1.29 - 2.13) | <0.0001 | 1.10 (0.81 - 1.50) | 0.54 |
| Outcome: graft failure (including patient death) |
| 3-month eGFR(for 10 mL/min/1.73m² increase) | 0.80 (0.73 - 0.88) | <0.0001 | 0.92 (0.83 - 1.02) | 0.13 | 0.77 (0.73 - 0.80) | <0.0001 | 0.82 (0.77 - 0.87) | <0.0001 |
| 3-month eGFR < 45 mL/min/1.73m² | 1.84 (1.43 - 2.38) | <0.0001 | 1.32 (0.99 - 1.76) | 0.060 | 2.39 (2.05 - 2.78) | <0.0001 | 2.01 (1.67 - 2.43) | <0.0001 |
| 12-month eGFR(for 10 mL/min/1.73m² increase) | 0.73 (0.66 - 0.81) | <0.0001 | 0.81 (0.73 - 0.91) | 0.0004 | 0.71 (0.68 - 0.75) | <0.0001 | 0.77 (0.72 - 0.82) | <0.0001 |
| 12-month eGFR < 45 mL/min/1.73m² | 2.05 (1.57 - 2.69) | <0.0001 | 1.53 (1.14 - 2.06) | 0.005 | 2.56 (2.18 - 2.99) | <0.0001 | 2.06 (1.70 - 2.51) | <0.0001 |

\* Adjusted for: recipient’s age, history of heart failure, donor type (living, standard criteria donor, expanded criteria donor), delayed graft function, immunization, number of A-B-DR-DQ HLA incompatibilities (<5, ≥5), induction treatment, graft rejection (prior to the considered variable, i.e. prior to 3 or 12 months).

\*\*Adjusted for: recipient’s age, cardiovascular history, type of donor (living, deceased), delayed graft function, anti-HLA immunization class I and/or II, number of A-B-DR HLA incompatibilities (<5, ≥5), induction treatment graft rejection (prior to the considered variable, i.e. prior to 3 or 12 months).

### Supplementary material - Table S2: Interaction between 3-month eGFR and the occurrence of graft rejection after 3 months for graft failure in the single-center cohort

|  |  |  |
| --- | --- | --- |
| **Effect of 3-month eGFR****(per 10mL/min/1.73m²)** | **Unadjusted** | **Adjusted\*** |
| **Nevents/N (%)** | **HR (CI 95%)** | **p-value** | **Nevents/N (%)** | **HR (CI 95%)** | **p-value** |
| Rejection after 3 months  |  |  |  |  |  |  |
| No | 70/558 (12.5%) | 0.51 (0.42 - 0.62) | <0.0001 | 69/552 (12.5%) | 0.56 (0.46 - 0.68) | <0.0001 |
| Yes | 75/196 (38.3%) | 1.04 (0.90 - 1.20) | 0.58 | 75/196 (38.3%) | 1.07 (0.92 - 1.25) | 0.36 |
|  |  | Interaction p-value | <0.0001 |  | Interaction p-value | <0.0001 |
| Rejection after 3 months (excluding borderline andundetermined rejections) |  |  |  |  |  |  |
| No | 88/634 (13.9%) | 0.61 (0.52 - 0.72) | <0.0001 | 87/628 (13.9%) | 0.67 (0.56 - 0.79) | <0.0001 |
| Yes | 57/120 (47.5%) | 1.08 (0.91 - 1.27) | 0.40 | 57/120 (47.5%) | 1.11 (0.94 - 1.32) | 0.21 |
|  |  | Interaction p-value | <0.0001 |  | Interaction p-value | <0.0001 |
| Humoral rejection after 3 months |  |  |  |  |  |  |
| No | 119/713 (16.7%) | 0.70 (0.62 - 0.80) | <0.0001 | 118/707 (16.7%) | 0.76 (0.66 - 0.88) | 0.0003 |
| Yes | 26/41 (63.4%) | 1.05 (0.80 - 1.39) | 0.72 | 26/41 (63.4%) | 1.15 (0.87 - 1.52) | 0.31 |
|  |  | Interaction p-value | 0.010 |  | Interaction p-value | 0.007 |

\* Adjusted for recipient’s age, history of heart failure, donor type (living, standard criteria donor, expanded criteria donor), delayed graft function, immunization, number of A-B-DR-DQ HLA incompatibilities ≥ 5, induction treatment, graft rejection (prior to the considered variable, i.e. prior to 3 or 12 months).

### Supplementary material - Table S3: Interaction between 3-month eGFR and risk factors of alloimmune damage for graft failure in the single-center cohort

|  |  |  |
| --- | --- | --- |
| **Effect of 3-month eGFR** **(per 10mL/min/1.73m²)**  | **Unadjusted** | **Adjusted\*** |
| **Nevents/N (%)** | **HR (CI 95 %)** | **p-value** | **Nevents/N (%)** | **HR (CI 95 %)** | **p-value** |
| HLA immunization positiveclass I or II |  |  |  |  |  |  |
| No | 112/629 (17.8%) | 0.79 (0.69 - 0.90) | 0.0004 | 112/627 (17.9%) | 0.82 (0.71 - 0.95) | 0.007 |
| Yes | 33/122 (27.0%) | 0.68 (0.51 - 0.90) | 0.008 | 32/121 (26.4%) | 0.75 (0.56 - 1.01) | 0.055 |
|  |  | Interaction p-value | 0.33 |  | Interaction p-value | 0.60 |
| HLA A-B-DRincompatibilities ≥ 4 |  |  |  |  |  |  |
| No | 77/399 (19.3%) | 0.74 (0.63 - 0.87) | 0.0002 | 77/398 (19.3%) | 0.79 (0.66 - 0.94) | 0.007 |
| Yes | 68/354 (19.2%) | 0.79 (0.66 - 0.94) | 0.007 | 67/351 (19.1%) | 0.82 (0.69 - 0.99) | 0.034 |
|  |  | Interaction p-value | 0.56 |  | Interaction p-value | 0.71 |
| HLA A-B-DR-DQincompatibilities ≥ 5 |  |  |  |  |  |  |
| No | 79/416 (19.0%) | 0.75 (0.64 - 0.88) | 0.0004 | 79/415 (19.0%) | 0.81 (0.68 - 0.96) | 0.014 |
| Yes | 66/336 (19.6%) | 0.77 (0.64 - 0.92) | 0.004 | 65/333 (19.5%) | 0.80 (0.66 - 0.96) | 0.019 |
|  |  | Interaction p-value | 0.87 |  | Interaction p-value | 0.94 |

\* Adjusted for: recipient’s age, history of heart failure, donor type (living, standard criteria donor, expanded criteria donor), delayed graft function, immunization, number of A-B-DR-DQ HLA incompatibilities (<5, ≥5), induction treatment, graft rejection (prior to the considered variable, i.e. prior to 3 or 12 months).

# Supplementary material - Table S4: Prognostic accuracy of eGFR and proteinuria at 3, 6 and 12 months for the risk of death-censored graft failure

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **C-index for baseline model** | **C-index for****baseline model + eGFR/Proteinuria** | **∆ C-index** | **NRI** |
|  | **Value (IC 95 %)** | **p-value** | **Value (IC 95 %)** | **p-value** |
| **eGFR variables** |  |  |  |  |  |  |
|  3-month eGFR (linear) | 63.9 | 68.3 | 4.4 (1.1 to 7.7) | 0.009 | 12.6 (0.8 to 24.0) | 0.040 |
|  3-month eGFR (<45) | 63.9 | 66.1 | 2.2 (0.1 to 4.3) | 0.038 | 19.9 (2.8 to 29.4) | 0.032 |
|  6-month eGFR (linear) | 62.8 | 66.2 | 3.4 (-0.2 to 7.0) | 0.061 | 13.9 (-0.9 to 23.7) | 0.070 |
|  6-month eGFR (<45) | 62.8 | 64.3 | 1.5 (-0.5 to 3.5) | 0.14 | 15.9 (-3.8 to 26.8) | 0.084 |
|  12-month eGFR (linear) | 63.9 | 72.1 | 8.3 (3.3 to 13.2) | 0.001 | 29.9 (13.5 to 38.6) | <0.0001 |
|  12-month eGFR (<45) | 63.9 | 67.3 | 3.4 (0.4 to 6.4) | 0.025 | 24.7 (9.5 to 35.3) | 0.008 |
| **Proteinuria variables** |  |  |  |  |  |  |
|  3-month proteinuria (linear) | 64.1 | 70.8 | 6.8 (2.1 to 11.5) | 0.005 | 24.5 (13.4 to 38.5) | <0.0001 |
|  3-month proteinuria (>0.5) | 64.1 | 66.7 | 2.7 (-0.8 to 6.2) | 0.14 | 17.5 (5.0 to 28.3) | 0.016 |
|  6-month proteinuria (linear) | 63.5 | 73.5 | 10.0 (4.6 to 15.4) | 0.0003 | 37.1 (23.0 to 48.1) | <0.0001 |
|  6-month proteinuria (>0.5) | 63.5 | 71.4 | 7.9 (3.2 to 12.6) | 0.001 | 29.9 (16.6 to 42.0) | <0.0001 |
|  12-month proteinuria (linear) | 64.5 | 75.0 | 10.5 (5.2 to 15.9) | 0.0001 | 39.2 (23.7 to 49.9) | <0.0001 |
|  12-month proteinuria (>0.5) | 64.5 | 73.3 | 8.8 (4.0 to 13.6) | 0.0003 | 31.5 (12.2 to 43.1) | <0.0001 |
| **eGFR and Proteinuria variables** |  |  |  |  |  |  |
|  3-month eGFR and proteinuria (linear) | 64.1 | 72.1 | 8.0 (3.4 to 12.7) | 0.0006 | 27.0 (13.5 to 39.6) | <0.0001 |
|  3-month eGFR and proteinuria (<45 and >0.5) | 64.1 | 67.5 | 3.5 (0.0 to 6.9) | 0.049 | 13.7 (4.7 to 29.1) | 0.012 |
|  6-month eGFR and proteinuria (linear) | 63.5 | 73.7 | 10.1 (4.4 to 15.8) | 0.0005 | 33.3 (20.2 to 47.3) | <0.0001 |
|  6-month eGFR and proteinuria (<45 and >0.5) | 63.5 | 71.4 | 7.8 (3.0 to 12.6) | 0.001 | 29.5 (14.1 to 41.5) | <0.0001 |
|  12-month eGFR and proteinuria (linear) | 64.4 | 77.0 | 12.6 (6.4 to 18.8) | <0.0001 | 34.2 (21.3 to 47.7) | <0.0001 |
|  12-month eGFR and proteinuria (<45 and >0.5) | 64.4 | 74.3 | 9.9 (4.3 to 15.5) | 0.0005 | 34.5 (19.1 to 44.8) | <0.0001 |

Baseline clinical model included the following variables: recipient's age, history of heart failure, donor type, delayed graft function, immunization, HLA incompatibilities, induction treatment, graft rejection (prior to the considered variable, i.e. prior to 3, 6 or 12 months).

# Supplementary material - Table S5: Association of 3- and 12-month eGFR and proteinuria with death-censored graft survival in the single-center and the multicenter cohorts

|  |  |  |
| --- | --- | --- |
|  | **Single-center local cohort** | **Multicenter validation cohort** |
| **Univariable** | **Adjusted\*** | **Univariable** | **Adjusted\*\*** |
| **HR (CI 95 %)** | **p-value** | **HR (CI 95 %)** | **p-value** | **HR (CI 95 %)** | **p-value** | **HR (CI 95 %)** | **p-value** |
| **3-months** | eGFR (for 10 mL/min/1.73m² increase) | 0.76 (0.67-0.85) | <0.0001 | 0.80 (0.70-0.92) | 0.001 | 0.69 (0.65 - 0.73) | <0.0001 | 0.70 (0.65 - 0.75) | <0.0001 |
| eGFR < 45 mL/min/m² | 1.98 (1.42-2.74) | <0.0001 | 1.66 (1.14-2.40) | 0.008 | 2.73 (2.25 - 3.33) | <0.0001 | 2.55 (2.00 - 3.25) | <0.0001 |
| Proteinuria (for 1 g/day increase) | 1.24 (1.14-1.34) | <0.0001 | 1.25 (1.14-1.36) | <0.0001 | 1.19 (1.14 - 1.24) | <0.0001 | 1.19 (1.14 - 1.25) | <0.0001 |
| Proteinuria > 0.5 g/day | 2.69 (1.84-3.94) | <0.0001 | 2.45 (1.65-3.63) | <0.0001 | 2.47 (1.98 - 3.09) | <0.0001 | 2.22 (1.69 - 2.90) | <0.0001 |
| **12-months** | eGFR (for 10 mL/min/1.73m² increase) | 0.67 (0.59-0.77) | <0.0001 | 0.69 (0.60-0.80) | <0.0001 | 0.62 (0.58 - 0.67) | <0.0001 | 0.63 (0.58 - 0.69) | <0.0001 |
| eGFR < 45 mL/min/m² | 2.21 (1.55-3.13) | <0.0001 | 1.95 (1.33-2.86) | 0.0006 | 3.41 (2.77 - 4.20) | <0.0001 | 3.09 (2.39 - 4.00) | <0.0001 |
| Proteinuria (for 1 g/day increase) | 1.60 (1.43-1.79) | <0.0001 | 1.57 (1.38-1.77) | <0.0001 | 1.57 (1.48 - 1.67) | <0.0001 | 1.54 (1.42 - 1.67) | <0.0001 |
| Proteinuria > 0.5 g/day | 4.04 (2.75-5.92) | <0.0001 | 3.39 (2.25-5.11) | <0.0001 | 2.98 (2.38 - 3.73) | <0.0001 | 3.21 (2.47 - 4.16) | <0.0001 |

*\* Adjusted for: recipient’s age, history of heart failure, donor type (living, standard criteria donor, expanded criteria donor), delayed graft function, immunization, number of A-B-DR HLA incompatibilities, induction treatment, graft rejection (prior to the considered variable, i.e. prior to 3 or 12 months).*

*\*\* Adjusted for: recipient’s age, cardiovascular history, type of donor (living, deceased), delayed graft function, anti-HLA immunization class I and/or II, number of A-B-DR HLA incompatibilities (<5, ≥5), induction treatment graft rejection (prior to the considered variable, i.e. prior to 3 or 12 months).*

### Supplemental material - Table S6: C-indices of eGFR at 3 and 12 months with the MDRD formula and the CKD-EPI formula for the risk of death-censored graft failure

|  |  |  |
| --- | --- | --- |
|  | **C-index (CI 95%)****Single-center cohort** | **C-index (CI 95%)****Multicenter cohort** |
| 3-month eGFR MDRD (linear) | 62.6 (57.2 - 68.1) | 69.3 (66.4 - 72.1) |
| 3-month eGFR CKD-EPI (linear) | 62.4 (56.9 - 67.9) | 69.2 (66.3 - 72.1) |
| 3-month eGFR MDRD < 45 mL/min/m² | 59.9 (55.6 - 64.2) | 63.7 (61.3 - 66.1) |
| 3-month eGFR CKD-EPI < 45 mL/min/m² | 60.5 (56.2 - 64.7) | 63.6 (61.2 - 66.0) |
| 12-month eGFR MDRD (linear) | 66.0 (60.1 - 71.9) | 71.7 (68.7 - 74.6) |
| 12-month eGFR CKD-EPI (linear) | 65.7 (59.7 - 71.6) | 71.4 (68.4 - 74.3) |
| 12-month eGFR MDRD < 45 mL/min/m² | 61.3 (56.8 - 65.8) | 65.6 (63.2 - 68.1) |
| 12-month eGFR CKD-EPI < 45 mL/min/m² | 61.6 (57.0 - 66.1) | 65.2 (62.7 - 67.6) |

### Supplementary material - Table S7: Association of 3- and 12-month eGFR with the MDRD formula and the CKD-EPI formula with death-censored graft failure

|  |  |  |
| --- | --- | --- |
|  | **Single-center cohort** | **Multicenter cohort** |
| **Unadjusted** | **Adjusted\*** | **Unadjusted** | **Adjusted\*\*** |
| **HR (CI 95%)** | **p-value** | **HR (CI 95%)** | **p-value** | **HR (CI 95%)** | **p-value** | **HR (CI 95%)** | **p-value** |
| 3-month eGFR MDRD(for 10 mL/min/1.73m² increase) | 0.76 (0.67 - 0.85) | <0.0001 | 0.80 (0.70 - 0.92) | 0.001 | 0.69 (0.65 - 0.73) | <0.0001 | 0.70 (0.65 - 0.75) | <0.0001 |
| 3-month eGFR CKD-EPI(for 10 mL/min/1.73m² increase) | 0.79 (0.71 - 0.88) | <0.0001 | 0.82 (0.73 - 0.93) | 0.002 | 0.71 (0.67 - 0.75) | <0.0001 | 0.71 (0.66 - 0.77) | <0.0001 |
| 3-month eGFR MDRD < 45 mL/min/m² | 1.98 (1.42 - 2.74) | <0.0001 | 1.66 (1.14 - 2.40) | 0.008 | 2.73 (2.25 - 3.33) | <0.0001 | 2.55 (2.00 - 3.25) | <0.0001 |
| 3-month eGFR CKD-EPI < 45 mL/min/m² | 2.02 (1.46 - 2.81) | <0.0001 | 1.74 (1.20 - 2.54) | 0.004 | 2.73 (2.24 - 3.32) | <0.0001 | 2.54 (1.98 - 3.25) | <0.0001 |
| 12-month eGFR MDRD(for 10 mL/min/1.73m² increase) | 0.67 (0.59 - 0.77) | <0.0001 | 0.69 (0.60 - 0.80) | <0.0001 | 0.62 (0.58 - 0.67) | <0.0001 | 0.63 (0.58 - 0.69) | <0.0001 |
| 12-month eGFR CKD-EPI(for 10 mL/min/1.73m² increase) | 0.71 (0.63 - 0.81) | <0.0001 | 0.72 (0.62 - 0.82) | <0.0001 | 0.65 (0.61 - 0.69) | <0.0001 | 0.65 (0.60 - 0.71) | <0.0001 |
| 12-month eGFR MDRD < 45 mL/min/m² | 2.21 (1.55 - 3.13) | <0.0001 | 1.95 (1.33 - 2.86) | 0.0006 | 3.41 (2.77 - 4.20) | <0.0001 | 3.09 (2.39 - 4.00) | <0.0001 |
| 12-month eGFR CKD-EPI < 45 mL/min/m² | 2.25 (1.59 - 3.20) | <0.0001 | 2.06 (1.41 - 3.02) | 0.0002 | 3.29 (2.68 - 4.04) | <0.0001 | 2.96 (2.28 - 3.83) | <0.0001 |

\* Adjusted for: recipient’s age, history of heart failure, donor type (living, standard criteria donor, expanded criteria donor), delayed graft function, immunization, number of A-B-DR-DQ HLA incompatibilities (<5, ≥5), induction treatment, graft rejection (prior to the considered variable, i.e. prior to 3 or 12 months).

\*\*Adjusted for: recipient’s age, cardiovascular history, type of donor (living, deceased), delayed graft function, anti-HLA immunization class I and/or II, number of A-B-DR HLA incompatibilities (<5, ≥5), induction treatment graft rejection (prior to the considered variable, i.e. prior to 3 or 12 months).