SUPPLEMENTAL MATERIAL
Data S1.

Supplemental Methods

In creating multivariable Cox models in the primary analysis, we conducted a complete-case analysis only. However, several patients were missing one more of the covariates included. We therefore conducted a missing case analysis, comparing patients with one more missing covariates with those who are considered complete cases.

To explore the characteristics of patients who reversed pre-operative pulmonary hypertension (PH) and those who did not, we compared two groups with respect to baseline, operative, and other characteristics. The two groups were described using mean (SD) and compared t-test for continuous variables or $\chi^2$ test for categorical variables.

We additionally explored whether one of several complications in the immediate post-operative period (atrial fibrillation, myocardial infarction, stroke, infection, or renal failure) impacted overall survival. The immediate post-operative period is defined as the duration of the index hospitalization during which mitral valve surgery (MVS) occurred. Cohorts of patients with and without a significant complication were visualized with the Kaplan-Meier method and compared using a log-rank test.

Several exploratory analyses were performed examining the relation between other patient characteristics and survival. In the first analysis, we examined post-operative survival in patients stratified by both pre-operative PH status and type of MVS (repair, replacement). We then examined longitudinal mortality after stratification by post-operative PH status (reversed vs persistent PH) and type of MVS. Finally, we examined whether presence of atrial fibrillation on post-operative echocardiogram was associated with mortality by use of a minimally adjusted Cox model which included timing of echocardiogram and surgeon as covariates.
Supplemental Results

Table S1 shows results of the complete case analysis. The two groups were largely comparable. Serum creatinine represented the most commonly missing covariate.

Compared to patients who had reversal of pre-operative PH, patients who did not have reversal of PH had increased prevalence of mildly enlarged and dysfunctional right ventricles (Table S4). However, we note that post-operative assessment and high frequency of missing data limits interpretation of this finding, and those who did not. Patients with persistent and reversed PH were otherwise similar with respect to demographics, surgical characteristics, and degree of residual mitral regurgitation.

Detailed index hospital records were not available for 5 patients. Among the 483 patients with detailed hospital records, 202 (41%) had an immediate post-operative complication, and 281 (58%) did not. Patients without complications had lower overall mortality during longitudinal follow-up (p=0.04, Figure S1).

In exploratory analyses, we found that type of MVS (repair or replacement) had little relation to post-operative longitudinal outcomes (Figure S2). Patients without pre-operative PH who underwent valve repair had lower overall mortality than patients with PH who underwent either repair or replacement (p=0.003 for both), however other pairwise comparisons were not significant. Specifically, there was no difference in overall survival between patients without PH who underwent repair vs replacement (p=0.45), nor was there a difference between patients with PH who underwent repair vs replacement (p=0.70). When stratified both by MVS type and persistence of PH post-operatively, no differences were seen in overall survival, although the sample size may not be sufficient for such comparisons.
In an exploratory analysis of survival by atrial fibrillation status on post-operative echocardiogram, we did not find a significant relation between presence of atrial fibrillation and mortality in a basic model adjusting for timing of echocardiogram and surgeon (HR = 1.47, 95% CI 0.84-2.59, p=0.17).
Table S1. Missing covariate analysis.

| Missing N | Cases missing ≥1 covariate (N=100) | Complete cases (N=388) | P-value |
|-----------|----------------------------------|------------------------|---------|
| Age, years | 0 | 68.1 (11.7) | 66.9 (11.1) | 0.36 |
| Female | 0 | 45.0% | 44.8% | 1.0 |
| Body mass index, kg/m,² | 0 | 27.1 (5.2) | 28.3 (5.8) | 0.074 |
| Mitral valve replacement | 0 | 31.0% | 30.7% | 1.0 |
| Combined aortic valve surgery | 0 | 30.0% | 28.6% | 0.81 |
| Combined tricuspid valve surgery | 0 | 15.0% | 19.3% | 0.39 |
| Combined CABG | 0 | 44.0% | 43.5% | 1.0 |
| Diabetes | 0 | 24.0% | 30.2% | 0.27 |
| Hypertension | 0 | 69.0% | 80.9% | 0.014 |
| Prior heart failure | 0 | 43.0% | 54.9% | 0.043 |
| Pre-op ejection fraction, % | 0 | 49.2 (13.5) | 49.0 (14.3) | 0.90 |
| Serum creatinine, µmol/L | 94 | 76.0 (21.3) | 92.1 (62.9) | 0.54 |
| Platelets, 10⁹ L⁻¹ | 1 | 200.0 (60.1) | 195.2 (±72.4) | 0.54 |
| Serum albumin, g/L | 14 | 34.5 (±4.9) | 36.5 (±5.5) | 0.003 |

Values presented are column percentages for categorical variables or mean (SD) for continuous variables.

CABG=coronary artery bypass grafting
Table S2. Causes of death during follow-up.

|                          | Pre-operative mPAP ≤20 mmHg (N=75) | Pre-operative mPAP >20 mmHg (N=413) | Total (N=488) |
|--------------------------|-----------------------------------|-------------------------------------|---------------|
| Total deaths during follow-up | 8 (10.7%)                         | 126 (30.5%)                        | 134 (27.5%)   |
| Follow-up time, years (SD) | 4.6 (1.6)                          | 3.8 (2.0)                           | 3.9 (2.0)     |
| Cardiovascular deaths     | 0 (0%)                             | 39 (31%)                            | 39 (29%)      |
| Heart failure             | 0 (0%)                             | 17 (13%)                            | 17 (13%)      |
| Sudden cardiac death      | 0 (0%)                             | 13 (10%)                            | 13 (10%)      |
| Myocardial infarction     | 0 (0%)                             | 2 (2%)                              | 2 (1%)        |
| Cerebrovascular event     | 0 (0%)                             | 4 (3%)                              | 4 (3%)        |
| Other cardiovascular death| 0 (0%)                             | 3 (2%)                              | 3 (2%)        |
| Cancer                   | 1 (13%)                            | 4 (3%)                              | 5 (4%)        |
| Infectious causes         | 1 (13%)                            | 19 (15%)                            | 20 (15%)      |
| Other causes              | 0 (0%)                             | 9 (7%)                              | 9 (7%)        |
| Unknown causes            | 6 (75%)                            | 54 (43%)                            | 60 (45%)      |

Values shown are N (%) of all deaths in the column group, except for the first row, where percentage of all patients in column is shown.
Table S3. Comparison of patients with and without post-operative echocardiograms.

|                             | No echocardiogram (N=227) | Echocardiogram (N=231) | P-value |
|-----------------------------|----------------------------|------------------------|---------|
| Age, years                  | 67.1 (10.9)                | 67.1 (11.4)            | 0.95    |
| Female                      | 101 (44.5%)                | 108 (46.8%)            | 0.64    |
| Body mass index, kg/m²      | 27.7 (5.1)                 | 28.4 (6.2)             | 0.20    |
| Valve replacement (vs. repair) | 66 (29.1%)              | 72 (31.2%)             | 0.68    |
| Combined aortic valve surgery | 164 (72.2%)            | 166 (71.9%)            | 1.0     |
| Combined tricuspid valve surgery | 195 (85.9%)           | 179 (77.5%)            | 0.022   |
| Combined coronary artery bypass | 148 (65.2%)           | 162 (70.1%)            | 0.27    |
| Diabetes                    | 60 (26.4%)                 | 69 (29.9%)             | 0.47    |
| Hypertension                | 173 (76.2%)                | 188 (81.4%)            | 0.21    |
| Prior heart failure         | 111 (48.9%)                | 122 (52.8%)            | 0.45    |
| Pre-op ejection fraction, % | 51.1 (13.1)                | 47.8 (14.6)            | 0.01    |
| Follow-up time, years       | 4.3 (1.8)                  | 4.0 (1.8)              | 0.17    |
| Died during follow-up       | 39 (17.2%)                 | 65 (28.1%)             | 0.005   |
| Died during first year      | 16 (7.0%)                  | 21 (9.1%)              | 0.49    |

Values presented are column percentages for categorical variables or mean (SD) for continuous variables. Comparison of characteristics between patients with and without post-operative echocardiograms. Patients who died prior to the echocardiogram eligibility window (days 42-
365) are excluded from the table. Included in the “with echocardiogram” column are 24 patients who had an echocardiogram but did not have quantification of pulmonary hypertension.
| Characteristic                                | Persistent PH (N=102) | Reversed PH (N=82) | P-value |
|----------------------------------------------|-----------------------|--------------------|---------|
| Age, years                                   | 70.0 (10.3)           | 65.4 (13.1)        | 0.009   |
| Female                                       | 52.0%                 | 41.5%              | 0.18    |
| Body mass index, kg/m\(^2\)                  | 28.6 (6.4)            | 28.9 (6.4)         | 0.77    |
| Pre-operative ejection fraction, %           | 46.4 (14.4)           | 47.3 (16.0)        | 0.68    |
| Diabetes                                     | 41 (40.2%)            | 22 (26.8%)         | 0.063   |
| Hypertension                                 | 91 (89.2%)            | 67 (81.7%)         | 0.20    |
| Dyslipidemia                                 | 73 (71.6%)            | 55 (67.1%)         | 0.52    |
| Dialysis                                     | 4 (3.9%)              | 4 (4.9%)           | 1.0     |
| Current smoking                              | 18 (17.6%)            | 18 (22.0%)         | 0.58    |
| Hematocrit, %                                | 35.6 (4.9)            | 37.0 (5.3)         | 0.079   |
| Platelets, 10\(^9\) L\(^-1\)                | 199.5 (80.0)          | 195.1 (69.6)       | 0.70    |
| Serum creatinine, µmol/L                     | 92.4 (74.6)           | 100.1 (78.6)       | 0.53    |
| Serum albumin, g/L                           | 35.6 (5.4)            | 35.6 (5.3)         | 0.98    |
| Mitral valve replacement                     | 34.3%                 | 25.6%              | 0.26    |
| Primary mitral regurgitation                 | 50 (49.0%)            | 42 (51.2%)         | 0.88    |
| Days from catheterization to surgery, medial (IQR) | 9 (3, 38)            | 10 (4, 27)         | 0.58    |
| Right atrial pressure, mmHg                  | 9.8 (5.5)             | 9.7 (4.8)          | 0.99    |
| Mean pulmonary artery pressure, mmHg         | 34.4 (9.0)            | 34.3 (9.5)         | 0.93    |
| Pulmonary capillary wedge pressure, mmHg     | 21.5 (6.8)            | 22.3 (7.6)         | 0.47    |
| Transpulmonary gradient, mmHg                | 12.7 (6.5)            | 12.0 (7.4)         | 0.49    |
| Variable                                                                 | Study 1 (Mean, SD) | Study 2 (Mean, SD) | p-value |
|--------------------------------------------------------------------------|---------------------|--------------------|---------|
| Pulmonary vascular resistance, Wood units                               | 2.9 (1.9)           | 2.6 (2.0)          | 0.34    |
| Cardiac output, L/min                                                   | 4.8 (1.2)           | 5.1 (1.7)          | 0.25    |
| Cardiac index, L/min/m²                                                 | 2.5 (0.7)           | 2.5 (0.7)          | 0.90    |
| Days from surgery to echocardiogram, median (IQR)                       | 101 (69, 205)       | 86 (56, 176)       | 0.13    |
| Post-operative ejection fraction, %                                      | 46.4 (15.0)         | 48.1 (13.3)        | 0.42    |
| Post-operative LV end diastolic diameter, cm                           | 5.0 (0.9)           | 5.1 (0.8)          | 0.57    |
| Post-operative LV end systolic diameter, cm                            | 3.8 (1.1)           | 3.8 (1.0)          | 0.73    |
| Residual mitral regurgitation (≥moderate)                               | 16 (15.7%)          | 7 (8.5%)           | 0.18    |
| Tricuspid regurgitation (≥moderate)                                     | 41 (40.2%)          | 11 (13.4%)         | <0.0001 |
| Post-operative right ventricular size                                   |                     |                    | 0.043   |
| Normal                                                                  | 43 (42.2%)          | 39 (47.6%)         |         |
| Mildly enlarged                                                          | 15 (14.7%)          | 2 (2.4%)           |         |
| Moderately enlarged                                                     | 4 (3.9%)            | 3 (3.7%)           |         |
| Severely enlarged                                                       | 1 (1.0%)            | 0 (0.0%)           |         |
| Not assessed                                                            | 39 (38.2%)          | 38 (46.3%)         |         |
| Post-operative right ventricular function                               |                     |                    | 0.026   |
| Normal                                                                  | 44 (43.1%)          | 44 (53.7%)         |         |
| Mildly reduced                                                          | 13 (12.7%)          | 2 (2.4%)           |         |
| Moderately reduced                                                      | 4 (3.9%)            | 2 (2.4%)           |         |
| Severely reduced                                                        | 0.0%                | 0.0%               |         |
| Not assessed                                                            | 41 (40.2%)          | 34 (41.5%)         |         |

Values presented are column percentages for categorical variables or mean (SD) for continuous variables, except where otherwise noted. All patients described had pre-operative pulmonary...
hypertension by right heart catheterization. P-values are t-test or chi-squared test except when variable is described as medical (IQR); in such cases rank sum test is used. LV=left ventricular; PH=pulmonary hypertension.
Figure S1. Post-operative survival according to presence of post-operative complication.

A post-operative complication is defined as atrial fibrillation, myocardial infarction, stroke, infection, or renal failure occurring during index hospitalization after mitral valve surgery.
Figure S2. Longitudinal outcomes after mitral valve repair or replacement in patients with pulmonary hypertension.

**A**

Longitudinal survival after mitral valve surgery by type of procedure (valve repair or replacement) and pulmonary hypertension (PH). Patients are additionally stratified by (A)

**B**

Number at risk

|                | 0    | 1    | 2    | 3    | 4    |
|----------------|------|------|------|------|------|
| Repaired, no pre-op PH | 63   | 62   | 61   | 56   | 39   |
| Replaced, no pre-op PH  | 276  | 234  | 221  | 198  | 148  |
| Repaired, pre-op PH     | 12   | 11   | 11   | 8    | 6    |
| Replaced, pre-op PH     | 137  | 114  | 111  | 90   | 58   |

**p = 0.006**

**B**

|                | 0    | 1    | 2    | 3    | 4    |
|----------------|------|------|------|------|------|
| Repaired, persistent PH | 67   | 60   | 54   | 47   | 38   |
| Replaced, persistent PH  | 61   | 54   | 52   | 45   | 35   |
| Repaired, reversed PH    | 35   | 30   | 29   | 22   | 16   |
| Replaced, reversed PH    | 21   | 20   | 20   | 16   | 7    |

**p = 0.20**

*Longitudinal survival after mitral valve surgery by type of procedure (valve repair or replacement) and pulmonary hypertension (PH). Patients are additionally stratified by (A)*
presence of pre-operative PH, or (B) persistence of pre-operative PH after surgery. P-value is for overall heterogeneity.