RIPCOM 1

The right ventricular pulmonary circulation in mitral valve disease study 1

Statistical methods

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Statistical methods

Data are presented as mean ± SD for continuous numerical variables and as count and percentages for categorical variables. Normality was assessed with Lilliefors (Kolmogorov-Smirnov) normality test: for consistency in reporting the data we have reported the numerical variables as mean ± SD regardless their distribution. We compared the pre-operative characteristics, echocardiographic characteristics and CPET variables between class 1 and class 2 diagnosis with Student t-test for normally distributed numerical variables and Mann-Whitney (Wilcoxon) test for not normally distributed numerical variables. The comparison between categorical variables was conducted with Chi-square test or Fisher Exact test as appropriate. The CPET results before and after surgery have been compared using paired t-test or paired Wilcoxon test depending on the distribution.

Primary Outcome: reduced functional capacity at follow up

This was a per protocol analysis. To identify the predictors of reduced functional capacity we have run two different types of regression models. In the first model (linear regression) we have treated our outcome (VO2 % at follow up) as a numerical continuous variable. The predictors were evaluated trough a univariable analysis first and then a multiple model was run including those predictors that appeared to be significant at univariable analysis. The final model was obtained via a backward selection using AIC (Aikake Information Criterion) as criterion.

In the second model, the outcome was defined as a dichotomic variable that included a VO2% of ≤ 84% and/or LVEF ≤ 50% at follow up. To evaluate the predictors of

this outcome we have run univariable and multivariable logistic regression model. In consideration of the fact that the overall number of events for this outcome was limited, the final multiple model was a parsimonious model developed using a meaningful selection of the variables that were considered relevant in previous published research (preoperative LVEF ≤ 60 %, LVESD ≥ 40 mm and ppVO2 % <≤84%) plus the class of surgical indication.

Correlation between TTE parameters and MRI parameters

Linear models have been run to compare some TTE parameters with the same MRI models.

Comparing changes in quality of life between class of indication of surgery

Linear mixed effects models were fitted for longitudinal (repeated measures) outcomes (physical functioning and social functioning) adjusted for time, preoperative percentage predicted peak VO2, preoperative LVEDD and preoperative LVESD.

For each of the main outcomes a stepwise approach has been used to model the data: first, an unconditional means model was run to describe the data and to test the null hypothesis; then an Unconditional Growth Model to set up the slope has been run followed by a Conditional Growth model (to set up the intercept). The unconditional mean model determines if the intercept is different from zero and if there is subject-related variability. The unconditional growth model can have a fixed or a random slope: the fixed slope is based on the assumption that each individual in the dataset is following a similar pattern over time, while the random slope allows individual

variability. Both models have been run to find out the best fitting model. The Conditional growth model is the final step and it is the complete final model adjusted for the covariates. All models were fitted using maximum likelihood methods.