

### *Data management and statistical analysis*

Study data were collected and managed using REDCap electronic data capture tools hosted at Clermont-Ferrand University Hospital<sup>[27]</sup>. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Statistical analysis was performed using Stata 13 software (StataCorp LP, College Station, TX, US). The tests were two-sided, with a type I error set at  $\alpha = 0.05$ . Subject's characteristics were presented as mean ( $\pm$  standard-deviation) or median [interquartile range] for continuous data (assumption of normality assessed using the Shapiro–Wilk test) and as the number of patients and associated percentages for categorical parameters. Comparisons between the independent groups were performed using the chi-squared or Fisher's exact tests for categorical variables, and using Student t-test or Mann-Whitney test for quantitative parameters (normality, assumption of homoscedasticity studied using Fisher-Snedecor test). Concerning the censored data, estimates were constructed using the Kaplan–Meier method. The log-rank test was used in a univariate analysis to test the prognostic value of patient characteristics for the occurrence of an event. Cox proportional hazards regression was used to investigate prognostic factors in a multivariate situation by backward and forward stepwise analysis of the factors considered significant in univariate analysis (entered into the model if  $P < 0.10$ ) and according to clinically relevant parameters. The proportional hazard hypotheses were verified using Schoenfeld's test and plotting residuals. The interactions between possible predictive factors were also tested. Results were expressed as hazard ratios (HRs) and 95% confidence intervals (CI<sub>95%</sub>).