Establishing Normal Ranges for ECG Intervals in a Normal Healthy Population

J. Olbertz, R. Lester and M. Combs
1Celerion, Tempe, AZ, USA, 2Celerion, Lincoln NE USA

INTRODUCTION

The acquisition of ECGs as a screening tool for evaluation of normal healthy subjects is an essential component of qualifying subjects for early clinical research studies. Accurate assessment in this process is dependent upon comprehensive screening in a controlled phase I clinic. A secondary objective was to establish an ECG database to establish reference ranges for heart rate (HR), PR, QRS, QT, QTc, PT and JT intervals in a normal healthy population. This database was created using a standardized digital ECG acquisition and analysis. The use of manual interval measurements employing variable reader methodology. Results can also be difficult to interpret when the dataset used includes variation in age, ethnicity and other covariates. Other studies have used a heterogeneous subject population in order to assist the clinician with discerning differences between normal and abnormal ECG measurements. In addition, this is the first known large cohort evaluation of ECG-related inclusion and exclusion criteria for early clinical studies assuming no disease pathology in this latter category of individuals (Table 2).

METHODS

The data set for this exploratory analysis was created using screening digital ECG data from all healthy subjects accepted into early phase clinical studies in a controlled phase I clinic. Subjects were enrolled in these trials under the supervision of investigators affiliated with the clinic and diligent adherence to current standards for establishing reference ranges for laboratory testing and ambulatory subjects.» Journal of electrocardiology 40.3 (2007): 228-234.

RESULTS

The difference in QTcF between the genders in the overall database was not clinically significant.

Figure 2. Mean QTcF, QTcB, and QT interval measurements trend higher with both age and BMI with minimal changes in HR. Whereas the JT interval appears to increase with age but not BMI. Time of Day had minimal impact on interval measurements.

CONCLUSION

The normal ranges for ECG intervals established in this analysis are applicable to the screening of healthy subjects for entry into early clinical research studies. They may not reflect normal values in the geriatric population with similar disease pathology in this latter category of individuals (Table 2).

ACKNOWLEDGMENTS

The potential value of mortality deviating the QT interval, especially in situations where conduction abnormalities and bradycardia were noted. Only 60% of the QT interval was considered to be normal.

REFERENCES

3. Acknowledgments. The authors gratefully acknowledge the work of J. Olbertz for assistance with data programing and analysis.

Table 1: Table 1: Normal ranges for ECG interval measurements

Table 1: Normal ranges for ECG interval measurements (using ECG acquisition and analysis). In order to better determine which if any of the covariates listed might have a meaningful impact on normal range, the explorers were assigned to statistical analyses including linear regression analysis and multiple regression analysis in SAS to analyze each covariate. The least squares means and their standard errors were calculated for each covariate in the SAS general linear model procedure. From this exploratory analysis, an adjusted model was made for multiplicity.

Table 2: Observed normal ranges representing 2.5th and 97.5th percentiles and suggested inclusion criteria for healthy subjects based on these normal ranges.

Table 2: Observed normal ranges representing 2.5th and 97.5th percentiles and suggested inclusion criteria for healthy subjects based on these normal ranges.

Table 3: Impact of gender on ECG interval measurements (shown as 1S Mean (SE)).

Table 3: Impact of gender on ECG interval measurements (shown as 1S Mean (SE)).