University Hospital of Cologne | Department of Anesthesiology and Intensive Care Medicine

Enhancing preclinical research by a software supporting randomized, blinded and adaptive study designs.

Jens Hansen^{1,2}, Thorsten Annecke¹, Tobias Neumann¹

¹) University Hospital of Cologne, Department of Anesthesiology and Intensive Care Medicine

²) Krankenhaus Dueren gem. GmbH, Klinik fuer Anaesthesiologie, operative Intensivmedizin, Notfallmedizin und Schmerztherapie

Purpose of the study

Prospective randomized controlled trials are accepted as gold standard of clinical research. For the comparison of two defibrillation techniques in an animal model of cardiac arrest we aimed to transfer this standard to preclinical research.

Materials and methods

Our goals for randomization were its execution in a blinded manner that can be presented transparently in future publications. As primary variable we are interested in the first shock success rate. Following the 3R concept by Russel and Burch¹ we aimed to add an adaptive design to reduce sample size to the lowest statistically justifiable level for our primary variable².

Results

To setup a new study our newly developed software requests: number of treatment arms, maximum sample size, its allocation, number of interim looks, levels of error for the final look (Fig. 1). Blinded to the researchers our software creates based on these data a set of unique IDs for all cases. Each ID is assigned to one of the defibrillation techniques. When starting with a new animal the software randomly picks one of these IDs and hands the corresponding defibrillation technique over to the defibrillator that shows in “study mode” as sole option “defibrillation”. The number of shocks required is counted (Fig. 2) and transferred to our software’s database. First shock success rates are then compared on interim looks (Fig. 3). The software terminates the study when significant statistical differences between the groups are shown.

References

¹) Russell, W. M. S., Burch, R. L., & Hume, C. W. (1959). The principles of humane experimental technique.

²) Gaus, W. & Muche, R. (2014). Medizinische Statistik.

Modular Software Design

Conclusions

Our study is still ongoing and final results on the defibrillation technologies are pending. However, our software has yet shown its feasibility for the examination of medical technology. It facilitates randomization and interim looks and improves scientific impact and animal welfare at the same time. Currently it is limited to animal studies on medical technology.

Figure 1

Figure 2

Figure 3

Presenting and corresponding author

Dr. med. Tobias Neumann, MD

Uniklinik Koeln
 Klinik fuer Anaesthesiologie und
 Operative Intensivmedizin
 Kerpener Str. 62, 50937 Koeln
 tobias.neumann@uk-koeln.de