Study Protocol

Development of Pneumonia Due to Alveolar Glucose Levels in Systemic Hyperglycemia

Version: 2
Date: 08/01/2017

1. General study design:
   Monocentric prospective clinical observational study

2. Schedule:

Inclusion of the first patient:	08/01/2017
Inclusion last patient:	12/31/2018
Close the database:	01/31/2019
End of the statistical evaluation:	06/31/2019

3. Study endpoint, duration of study:
   The primary endpoint of the study is the incidence of pneumonia

4. Sample size calculation:
   The sample size estimate was based on the assumption that in the investigated patient population the occurrence of pneumonia could be expected in 10% of the patients. Thus, for an unconnected sample, a ratio (m) of 0.9 controls per incidence of pneumonia. In a previous study (Bacterial respiratory tract infections are promoted by systemic hyperglycemia after severe burn injury in pediatric patients, Kraft et al., Burns, 2014, May), it was found that the mean values (δ) of both groups for glucose differed by about 30 mg / dL in the mean with a standard deviation (σ) of 20 mg / dL. Under the same conditions, 14 controls and 16 patients with pneumonia are needed to reject the null hypothesis with a probability (power) of 0.9.
   The occurrence of the first type error (α) was set at 0.01. Design: Independent
   $\alpha = 0.01$; power = 0.9; $\delta = 30$; $\sigma = 20$; $m = 0.9$; $n = 16$;
   t-test confidence interval width = 40.68604
   Calculated with PS Power and Samplesize Calculator Version 3.0,
   http://biostat.mc.vanderbilt.edu/PowerSampleSize

5. Selection of the study population:
   Patients undergoing elective cardiac surgery matching inclusion and exclusion criteria

6. Subsequent exclusion of study patients:
   Reasons for a subsequent exclusion of the patient only apply if subsequently it is determined that not all inclusion criteria are met or exclusion criteria that were not initially recognized. These patients are also excluded from the documentation.

7. Documentation / Evaluation:
   All study-relevant data are recorded in the provided documentation sheets by the responsible study physicians and, if necessary, the study assistants. The study forms are digitized and stored in the in-house EDP system in compliance with the safety guidelines using the programs Microsoft Excel® and Access®. Radiological images are stored in digital form, preferably in TIFF or raw data format. The statistical analysis is carried out by means of the programs Sigmastat® and Sigmaplot®.
   The statistical evaluation is carried out on the one hand with regard to the cut-off value of the glucose threshold of the lung by means of Receiver Operating Characteristic (ROC). This is used to validate our findings in comparison to the already existing preliminary studies. The evaluation of dichotomous variables is performed by Chi Square Test or, if necessary, by Logistic Regression Analysis.

Constant features are compared using Student's t-test, analysis of variance between the groups. With regard to the presence of disturbing variables between the two groups, the formation of subgroups, possibly a matching by means of a propensity score, is planned.

8. Study plan:

Timepoint 1, preoperative: Obtaining informed consent and inclusion in the study, blood draw Preoperative chest X-ray (clinical routine)

Timepoint 2, Operative Intervention: Blood draw, asservation of alveolar secretions (endobronchial after intubation)

Timepoints 3.1 – 3.n, postoperative (daily): Blood draw, asservation of alveolar secretions (if ventilated) chest X-ray (if clinically needed)

Timepoint 4, Discharge: Final evaluation

Patients will be included in the study, if fulfilling the inclusion criteria and missing exclusion criteria. Written informed consent will be obtained from the patients. Patients will be pseudonymyised by assigning a sequential number. Anonymization of the patients cannot be considered in such a conceived study, since the change of personal data makes an assignment of essential clinical course data impossible.

Blood draws:
Blood will be collected by puncture or draw by venous or arterial catheter during the clinical routine for determination of leucocyte count, CRP value, and blood sugar. Blood samples will be analyzed in the in-house laboratory. Blood sugar levels are additionally measured in the intensive care unit using a blood gas analyzer.
In addition, one blood sample EDTA and one serum are collected (9 mL each). The centrifugation and aliquoting of the obtained plasma and serum samples will be spinned down and aliquoted. The samples are stored at -80 ° C in the laboratory rooms of the Cardiac Surgery Department for later analysis.

X-ray:
The evaluation of the radiological images of the chest is carried out as part of the clinical requirements. There is no additional requirements of radiological examinations due to the study.

Endobronchial sampling:

The endobronchial sampling of alveolar fluid will be performed by utilizing the inserted tube and aspiration with a suction catheter. Two samples are taken. The first sample is sent to the in-house laboratory immediately after sampling for microbiological analysis. The second sample is stored at -80 ° C in the premises of the cardiosurgical research department until later analysis.

Clinical evaluation/examination:
There is a daily clinical examination of the patients for signs of pneumonia.