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Titre: Optimizing prevention, diagnosis and treatment of intravascular catheter-related infections in critically ill patients.

Background: Catheter-related bloodstream infection (CRBSI) is a frequent event in intensive care unit (ICU) and are an important cause of septic shock. It is associated with high morbidity, mortality and resource utilization. The main objective of this PhD was to explore the principal determinants of intravascular catheter infections in order to optimize prevention and treatment of these severe ICU infections. First, we investigated the impact of several determinants potentially influencing *prevention* measures of intravascular catheter infections. In particular, we assessed the role of i) the ultrasound guidance (US) in central venous catheters (CVCs) and arterial catheters (ACs), ii) chlorhexidine-gluconate (CHG) impregnated dressings, iii) concurrent systemic antibiotics at catheter insertion, iv) insertion site in ACs, v) catheter type, and vi) Body Mass Index (BMI) in preventing intravascular catheter infections. Second, we investigated specific factors (vii and viii) that were supposed to influence *treatment* of intravascular catheter infections.

Methods: We created a large cohort (10'269 patients and 18'743 catheters overall) using individual patient data from five large Randomized Clinical Trials performed in France. We performed several analyses and, therefore, different statistical models were used (descriptive statistics, survival analyses and logistic regression models).

Results: i) We showed an increased infectious risk for US insertion in CVCs but not in ACs. ii) Comparing CHG-gel dressing with CHG-sponge dressing we observed a similar intravascular catheter infection risk. Geldressing exhibited fewer dressing disruptions. iii) We showed that systemic antibiotics at insertion did not reduce the risk of intravascular catheter infections. iv) We illustrated that the infectious risk was similar for ACs inserted in the femoral and in the radial artery. v) The infectious risk for short-term dialysis catheters was significantly higher than CVCs within the first 7 days of catheter maintenance. vi) Patients with BMI ≥40 had an increased risk for intravascular catheter infections. vii) In the first seven days of catheter maintenance, local signs increased the probability to observe CRBSI. viii) Among infected CVCs, the distribution of microorganisms was significantly different between femoral and radial site, with Gram-negative non-fermenters being more frequently identified in femoral insertions.

Conclusions: On one hand, we closed the knowledge gap for certain prevention measures (*e.g.*, use of CHG-dressings, utilization of systemic antibiotics as a preventive measure, selection of the insertion site for ACs). On the other hand, we open new challenges for future research in this field (correct utilization of US for intravascular catheter insertion or prevention measures for critically ill obese patients). Last but not least, this PhD allowed to optimize management of intravascular catheter infections.

Mots clefs: Intravascular catheter infections, colonization, bacteraemia, catheter, intensive care unit