



Obesity in critically ill patients is associated with increased need of mechanical ventilation but not with mortality



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Summary Worldwide incidence of obesity is increasing and impaired outcome in postoperative patients has been described. Antibiotic prescribing is complicated by different pharmacology in this population. This study evaluates mortality and morbidity of obese postoperative patients and explores possible relation to antibiotic therapy. Therefore, data obtained in a prospective study in 2009–2010 were analysed. Postoperative patients on 5 ICUs were included with >48 h of ICU treatment and documented body-mass-index (BMI). Altogether 451 non-obese patients (BMI < 30 kg/m²) were compared with 130 obese patients including propensity score matching. There was significant heterogeneity of baseline characteristics. ICU-mortality was 7.5% in non-obese and 7.7% in obese patients ($p > 0.999$), but 65.4% of obese patients required mechanical ventilation compared with only 53.2% of non-obese patients ($p = 0.016$). These findings were validated in multivariate regression analyses (adjusted OR for ICU-mortality for obese patients 0.53, 95%-CI 0.188–1.321, $p = 0.197$; adjusted OR for mechanical ventilation 1.841, 95%-CI 1.113–3.076, $p = 0.018$). Results were confirmed by propensity score matching. Therapeutic drug monitoring for vancomycin (TDM) showed that underdosing and overdosing occurred more often in obese patients and sufficient TDM levels were

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less often achieved. In conclusion, obesity is associated with increased morbidity but ICU mortality is equal compared with a non-obese population. Pharmacological differences might explain observed differences in antibiotic therapy and in obese patients TDM might be especially of importance.

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Introduction

In the intensive care unit (ICU) obesity is a common comorbidity in about 20% of patients and rising incidence is described worldwide [1]. In concordance with the World Health Organisation, obesity is most commonly defined as a body mass index (BMI) of $\geq 30 \text{ kg/m}^2$ [2,3]. Obesity is associated with increased morbidity of ICU patients but there remains uncertainty regarding the effect on mortality. Similar mortality rates were described by several authors comparing obese and non-obese ICU patients [4,5]. These findings were contrasted by a meta-analysis of Fezeu et al. [6] that described a significantly higher mortality in obese ICU patients with H1N1 influenza for death. A doubled mortality rate was also found in obese medical ICU patients admitted due to obstructive airway disease, pneumonia, and sepsis [7]. Similarly, in a cohort study of patients following trauma Byrnes et al. described an increased mortality rate for obese patients [8]. However, other authors described even lower mortality in obese patients [9]. Potential mechanisms to explain this variance are still under debate. There is evidence that obese patients experience higher postoperative pain intensity and are under higher risk to acquire postoperative infections [10–12]. Nosocomial infections and especially pneumonia and surgical site infections were found to occur more often in obese patients [13,14]. A recent study by Ferrada et al. focussing on patients following emergency surgery described higher rates for surgical site infections [15]. Other authors reported that weight-adapted dosing strategies for benzodiazepines and opioids were one factor altering outcome [16]. In this context, differences in pharmacokinetics and pharmacodynamics in obese patients were described for volume of distribution, changes in hepatic metabolism and renal function that may lead to antibiotic overdosing as well as underdosing [17,18]. Currently, there is a lack of evidence to guide an optimal dosing regimen for antibiotic agents [18]. Antibiotic dosing is most commonly based on weight together with renal or hepatic function and can be adapted using results from therapeutic drug monitoring for some

agents [19]. In summary, obese patients seem to experience increased morbidity following surgery but relation on overall outcome is not completely clear. Furthermore, there is currently no conclusive mechanism identified that might explain a potential protective effect on outcome [20]. Attention has been drawn to dosing of anti-infective agents in obese ICU patients as one potential contributing factor [18,21]. Against this background, we conducted this observational study in postoperative ICU patients. The aims of this study were to assess ICU mortality in obese patients and to compare outcome with non-obese patients; to describe perioperative morbidity and to relate outcome with antibiotic therapy including therapeutic drug monitoring.

Material and methods

Study design and setting

This study was conducted as secondary analysis of a prospective interventional study [22]. This initial trial was performed at Charité hospital, a tertiary university hospital in Berlin, Germany. The study evaluates an ICU stewardship program of the ABx Study Group (ISRCTN54598675) on infection management and included all consecutively admitted ICU patients [22]. Data used for the present analysis were obtained from August 2009 to April 2010 including patients predominantly following surgery or major trauma. The study wards comprised five surgical ICUs with a focus on postoperative patients from different surgical disciplines (neurosurgery, abdominal surgery, cardiac surgery, trauma, gynaecology) and patients with major trauma. The project was approved by the local Ethics Review Board and the data safety authorities. The Ethics Review Board waived the need for informed consent.

Patients and data collection

Patients older than 18 years admitted to one of the ICUs with at least two days of ICU

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