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Mortality, morbidity and special issues of obese ICU patients

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Mortalität, Morbidität und spezielle Probleme bei adipösen Intensivpatienten

Zusammenfassung. Adipositas ist in den westlichen Industrienationen auf dem Vormarsch und daher auch für die Intensivmedizin zunehmend von Bedeutung. Entgegen der landläufigen Meinung, dass adipöse Intensiv-Patienten wohl eine erhöhte Mortalität haben dürften, zeigen überzeugende Meta-Analysen dass dem nicht so ist. Nichtsdestotrotz sind adipöse Intensiv-Patienten eine Herausforderung. Insbesondere die Beatmung dieser Patienten ist erwähnenswert: neben den anatomischen Besonderheiten, die die Intubation adipöser Patienten erschweren können, sind obstruktive Schlafapnoe, das Adipositas-Hypoventilations-Syndrom und der erhöhte intraabdominale Druck in Hinblick auf Beatmung, Entwöhnung und erfolgreiche Extubation zu nennen. Auch das Risiko für Infektionen ist bei adipösen Intensivpatienten erhöht, wenngleich damit kein erhöhtes Sepsisrisiko einherzugehen scheint. Unabhängig davon ist die mögliche Interaktion von Adipositas und Sepsis faszinierend, wenngleich die Rolle der Adipokine in der Sepsis des adipösen Patienten noch nicht aufgeklärt ist.

Schlüsselwörter: Adipositas, Intensivmedizin, Mortalität, Infektion, mechanische Ventilation

Summary. Obesity is on the advance in western industrialised countries and is therefore increasingly relevant also to intensive care medicine. In contrast to the common prejudice that obese patients probably have a higher ICU mortality than lean patients, convincing meta-analyses have revealed that this is not the case. Nevertheless, obese ICU patients are challenging. Especially mechanic ventilation has to be addressed: besides obesity-related anatomical problems that may complicate intubation, obstructive sleep apnoea, obesity hypoventilation syndrome and increased intra-abdominal pressure are of major relevance concerning ventilation, weaning and successful extubation. Also the risk of infections is increased in obese ICU patients, although this does not seem to increase the risk of sepsis. Nevertheless, the interplay of obesity and sepsis is a fascinating field in that adipous tissue is not just a passive reservoir of energy but an active endocrine and immunomodulating organ. However, the way of how adipokines interact with inflammation and coagulation in sepsis has yet to be clarified.

Key words: Obesity, intensive care, mortality, infection, mechanic ventilation

Introduction

Overweight and obesity are increasing problems in western industrialised countries. In the United States 66% of adults are overweight or obese, a number which is expected to increase to 75% in the next decade [1]. Also in Europe the numbers give raise to concern: according to a multi-national European study 38% of Europeans are overweight and 15% are obese [2]. In Austria data of the most western province (Vorarlberg) show rates of overweight and obesity of 31% and 11%, respectively [3]. Similar frequencies are also found among patients admitted to intensive care units (ICUs). In a multinational European study (SOAP trial) 36% of ICU patients were overweight and 18% were obese or

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very obese [4]. Thus obesity is also of increasing relevance in intensive care medicine and therefore several specific issues concerning morbidity and care of obese patients need to be mentioned.

Obesity, ICU-mortality and ICU-morbidity

Although obesity is a well-known risk factor for mortality in various medical conditions like cardiovascular disease or malignancy, studies on the association between obesity and mortality in ICU patients have revealed conflicting data [reviewed in refs. 5 and 6]. The comparison of these studies has to be done with caution due to several methodological differences: some studies used a retrospective design whereas others were done prospectively and the studies differed with respect to medical, surgical, trauma or mixed patient populations. Also the assessment of obesity and body mass index (BMI) is matter of debate, because the measurement of the weight of ICU patients is technically often difficult to achieve and may be falsified by volume depletion or overload. Nevertheless, there is increasing evidence that overweight and obesity do not have that detrimental effect in ICU patients one would assume, but may even be of benefit. Two meta-analyses have been conducted to elucidate the impact of obesity on ICU mortality (Tab. 1): The meta-analysis by Oliveros and Villamor including 23 studies demonstrated that the risk of mortality was even decreased in overweight and obese patients and only increased in underweight (i.e. kachectic) patients [5]. The meta-analysis by Akinnusi et al. including a total of 62.045 subjects compared obese (BMI $\geq$ 30 kg/m^2, $n = 15.347$) *vs.* non-obese ICU patients (BMI < 30 kg/m^2, $n = 46.698$) [6]. There was no difference in ICU-mortality between the two groups (RR: 1.00; 95% CI: 0.86–1.16; $p = 0.97$; $I^2 = 75.6\%$). With respect to hospital survival there was even a benefit in the obese group (RR: 0.83; 95% CI: 0.74–0.92; $p < 0.001$).

Tab. 1 : Meta-analyses concerning mortality of overweight and obese ICU patients

	BMI (kg/m^2)	Pooled OR (95% CI)*	Mortality
Oliveros and Villamor	< 18.5	1.25 (1.02–1.48)	ICU
	18.5–24.9	Reference category	
	25–29.9	0.91 (0.84–0.98)	ICU
	30–34.9	0.92 (0.74–1.15)	ICU
	35–39.9	0.77 (0.68–0.98)	ICU
	≥40	0.94 (0.82–1.07)	ICU
Akinnusi et al. [6]	< 30	Reference category	
	≥30	1.00 (0.86–1.16)	ICU
	≥30	0.83 (0.74–0.92)	Hospital

* Random effects model

Tab. 2: Summary of usual problems and special issues of obese ICU patients

Morbidity/ complications	Related factors
frequent respiratory failure	COPD obstructive sleep apnoea obesity hypoventilation syndrome increased abdominal pressure
increased risk of infections	respiratory tract catheters/blood stream urinary tract
impaired wound healing	
decubitus ulcers	
deep venous thrombosis	
prolonged mechanic ventilation	weaning failure
prolonged ICU stay	
prolonged hospital stay	

Table 2 does not lay claim to completeness

Nevertheless, the experience of most intensivists that obese ICU patients have more complications, a higher morbidity and represent a "heavy" challenge for the nursing personnel is in line with the literature. Some of the problems of obese ICU patients that were reported from medical, surgical and trauma settings are summarised in Tab. 2 [4, 6, 7–9]. Some issues need to be discussed further.

Obesity and mechanic ventilation

One of the most important and challenging problems in the management of obese ICU patients is related to mechanic ventilation. Obese ICU patients require ventilation more often than their lean counterparts [7]. The challenge already starts at the time of intubation for several reasons [10]. On the one hand, there may be anatomical handicaps for intubation such as limited mouth opening, long tongue, excessive palatal and pharyngeal soft tissue, a high anterior larynx and/or restricted neck distension [11]. On the other hand, obesity-related restriction of residual capacity

may result in lower oxygen stores [12]. In addition, maintenance of airway patency during preoxygenation prior to intubation may be hindered due to the above-mentioned factors which in sum increases the risk of desaturation [13]. Once the patient is intubated further issues concerning mechanic ventilation need to be considered. First of all it needs to be stressed that obesity *per se* has a negative impact on lung function irrespective of critical illness and mechanic ventilation. It is not surprising that obesity leads to a restrictive ventilatory pattern due to decreased chest wall compliance and abdominal obesity with increased intra-abdominal pressure [14]. Interestingly it has also been demonstrated that metabolic syndrome and abdominal obesity in particular are independently associated with an obstructive ventilatory pattern [15]. The authors assumed that the immunomodulatory effects of adipokines could contribute to bronchiolar obstruction and might be responsible for this observation. When adjusting ventilator settings it needs to be remembered that with increasing weight the lung volume does not grow. That means the tidal volume with the usual goal of 6 ml/kg body weight has to be calculated on the basis of ideal body weight instead of the true body weight [16]. If this important concept is overlooked harmful excessive tidal volumes may be applied to the patient. Another issue is related to the total respiratory compliance because chest wall compliance is decreased in obesity. Thus the compliance of the whole respiratory system, which is usually displayed by modern ventilators, does not reflect lung compliance. The failure to take the chest wall component into account may lead to inappropriate ventilator settings [17].

Also the weaning from mechanic ventilation especially extubation needs to be considered. First of all, successful extubation is dependent on upper airway patency. In this respect it is necessary to remember that obstructive sleep apnoea is common in obese patients, a condition that might be aggravated by residual effects of analgesic and narcotic drugs [18]. Second, the obesity hypoventilation syndrome, a combination of obesity (BMI > 30 kg/m^2) and hypercapnia (>45 mmHg) during wakefulness in the absence of other known causes, has a prevalence of as high as 30% in obese patients [19]. In addition gas exchange may be hampered in obese patients by frequent atelectases in dependent lung zones and the increased intra-abdominal pressure (see above). To overcome these problems, especially a possible airway obstruction/collapse, use of non-invasive pressure ventilation and/or reverse Trendelenburg positioning has been recommended in obese patients after extubation [20–22].

Obesity, risk of infection and risk of sepsis

Although mortality is not increased among obese ICU patients, there is large agreement that obese patients are at higher risk for infections. In a secondary analysis of a large, dual-institutional, prospective observational study of critically ill surgical patients, Dossett et al. found a 2.2-fold increased risk for catheter-related infections and a 3.2-fold increased risk for other blood stream infections [23]. The authors hypothesised that the difficulty in obtaining vascular access in obese patients might lead to reluctance in changing catheters if signs of infection occur. In trauma patients Newell et al. showed that patients with severe obesity (BMI≥40 kg/m^2) had a 2.5-fold increased risk for pneumonia and a 2.3-fold increased risk for urinary tract infections [24]. Nevertheless, obese ICU patients with infections still do not have an increased mortality when compared to normal weight ICU patients, at least in the surgical/trauma setting [25].

Because obese patients are at increased risk for infections, the logical question is whether they are also at increased risk for sepsis. Recently the SOPA trial addressed this issue [4]. In this prospectively recruited cohort of 2878 patients who were admitted to ICU, 1206 patients had a normal BMI (18.5–24.9 kg/m^2), 120 patients were underweight, 1047 patients were overweight (25–29.9 kg/m^2), 424 patients were obese (BMI 30–39.9 kg/m^2) and 81 patients were very obese (BMI ≥ 40 kg/m^2). There were no differences concerning sepsis, severe sepsis and septic shock as reasons for admission to the ICU. Nevertheless, the morbidity at the ICU was higher among obese patients in agreement to other studies. Also in this study the risk of ICU acquired infections was significantly higher among obese and very obese patients when compared to patients with normal BMI. However, this actually did not increase the risk of developing sepsis, severe sepsis and septic shock during ICU stay.

Impact of obesity on sepsis

In contrast to the increasing frequencies of both obesity and sepsis in western countries, there is a relative paucity of clinical information regarding the interplay between obesity and sepsis. This may partly be explained by the exclusion of obese patients in landmark clinical studies in critical care and/or the lack of reported BMI [26, 27]. Considering that obesity may be seen as chronic inflammatory state one can imagine that obese patients might respond to sepsis differently

from patients with normal BMI [28]. In this respect it is necessary to recognise that adipous tissue is not just a passive reservoir of energy and lipid soluble nutrients but an active metabolic and endocrine organ [29]. These endocrine effects that are also immunomodulating are not totally understood up to now, there are conflicting data and some of the knowledge has to be adopted from animal models which are more or less appropriate to elucidate the interplay between obesity and sepsis. Leptin, for example, is an adipokine that is secreted by adipocytes and is known to have proinflammatory properties [30, 31]. Leptin levels are positively correlated to BMI [32]. In animal models high leptin levels were associated with improved bacterial clearance [33]. However, the role of leptin in sepsis of obese human patients is not clear and data are conflicting. On the one hand, high leptin levels have been associated with improved survival in sepsis [34]. In addition it has been shown that a low serum leptin level is an adverse prognostic marker in patients with peritonitis whereas the mechanisms involved are opposing in that leptin associated with IL-6 has a proinflammatory effect and in association with IL-10 mitigates the inflammatory response [35]. Unfortunately, these effects have not been reported with respect to BMI. On the other hand it was shown in paediatric patients mainly with meningococcal sepsis that patients with a high BMI who also had high leptin levels were at increased risk of mortality [36, 37].

Another example is adiponectin that has anti-inflammatory properties. Although secreted by adipocytes, adiponectin is negatively correlated with BMI [38]. In an animal model it has been shown that adiponectin knockout mice had a higher inflammatory response to sepsis induced by cecal ligation and puncture and had a higher mortality whereas wild-type mice had an improved mortality when adiponectin levels were increased after stimulation by PPAR-gamma [39]. The role of adiponectin in obese patients with sepsis is not known. To get to the point: adipous tissue exerts a lot of pleotropic endocrine and immunomodulatory functions that possibly influence sepsis and are therefore interesting players within the network of inflammation and coagulation. Nevertheless, future research is needed to clarify the way this game is played.

Conflict of interest

The author declares that there is no conflict of interest.

References

[1] Wang Y, Beydun M. The obesity epidemic in the United States – gender, age, socioeconomic, racial/ethnic and geographic characteristics: a systematic review and meta-regression analysis. Epidemiol Rev, 29: 6–28, 2007.

[2] Pischon T, Boeing H, Hoffmann K, et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med, 359: 2105–2120, 2008.

[3] Klenk J, Nagel G, Ulmer H, et al. Body mass index and mortality: results of a cohort of 184,697 adults in Austria. Europ J Epidemiol, 24: 83–91, 2009.

[4] Sakr Y, Madl C, Filipescu D, et al. Obesity is associated with increased morbidity but not mortality in critically ill patients. Intensive Care Med, 34: 1999–2009, 2008.

[5] Oliveros H, Villamor E. Obesity and mortality in critically ill adults: a systematic review and meta-analysis. Obesity, 16: 515–521, 2008.

[6] Akinnusi M, Pineda L, Solh A. Effect of obesity on intensive care morbidity and mortality: a meta-analysis. Crit Care Med, 36: 151–158, 2008.

[7] El-Solh A, Sikka P, Bozkanat E, et al. Morbid obesity in the medical ICU. Chest, 120: 1989–1997, 2001.

[8] Bochicchio G, Joshi M, Bochicchio K, et al. Impact of obesity in the critically ill trauma patient: a prospective study. J Am Coll Surg, 203: 533–538, 2006.

[9] Newell M, Bard M, Goettler C, et al. Body mass index and outcomes in critically injured blunt trauma patients: weighing the impact. J Am Coll Surg, 204: 1056–1061, 2007.

[10] Frat JP, Gissot V, Ragot S, et al. Impact of obesity in mechanically ventilated patients. Intensive Care Med, 34: 1991–1998, 2008.

[11] Malhotra A, Hillman D. Obesity and the lung: obesity, respiration and intensive care. Thorax, 63: 925–931, 2008.

[12] Ceylan E, Cömlekci A, Akkoclu A, et al. The effects of body fat distribution on pulmonary function tests in the overweight and obese. South Med J, 102: 30–35, 2009.

[13] Juvin P, Lavaut E, Dupont H, et al. Difficult tracheal intubation is more common in obese than in lean patients. Anesth Analg, 97: 595–600, 2003.

[14] Malbrain M, Cheatham M, Kirkpatrick A, et al. Results from the international Conference of experts on intra-abdominal hypertension and abdominal compartment syndrome. I. Definitions. Intensive Care Med, 32: 1453–1458, 2006.

[15] Leone N, Courbon D, Thomas F, et al. Lung function impairment and metabolic syndrom; the critical role of abdominal obesity. Am J Resp Crit Care Med, 179: 509–516, 2009.

[16] Marik P, Varon J. The obese patient in the ICU. Chest, 113: 492–498, 1998.

[17] Talmor D, Sarge T, O'Donnel C, et al. Esophageal and transpulmonary pressure in acute respiratory failure. Crit Care Med, 34: 1389–1394, 2006.

[18] Al Lawati N, Patel S, Ayas N. Epidemiology, risk factors, and consequences of obstructive sleep apnea and short sleep duration. Prog Cardiovasc Dis, 51: 285–293, 2009.

[19] Nowbar S, Burkart K, Gonzales R, et al. Obesity-associated hypoventilation in hospitalized patients: prevalence, effects and outcome. Am J Med, 116: 1–7, 2004.

[20] El-Solh A, Aquilina A, Pineda L, et al. Noninvasive ventilation for prevention of post-extubation respiratory failure in obese patients. Eur Resp J, 28: 588–595, 2006.

[21] Heinzer R, Stanchina M, Malhotra A, et al. Lung volume and continuous positive airway pressure requirements in obstructive sleep apnoea. Am J Resp Crit Care Med, 172: 114–117, 2005.

[22] Lee W, Mokhlesi B. Diagnosis and management of obesity hypoventilation syndrome in the ICU. Crit Care Clin, 24: 533–549, 2008.

[23] Dossett L, Dageforde L, Swenson B, et al. Obesity and site-specific nosocomial infection risk in the intensive care unit. Surg Infect, 10: 137–142, 2009.

[24] Newell M, Bard M, Goettler C, et al. Body mass index and outcome in critically injures blunt trauma patients: weighing the impact. J Am Coll Surg, 204: 1056–1064, 2007.

[25] Smith R, Chong T, Hedrick T, et al. Does body mass index affect infection-related outcomes in the intensive care unit? Surg Infect, 8: 581–588, 2007.

[26] Bernard G, Vincent J, Laterre P, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. N Engl J Med, 344: 699–709, 2001.

[27] The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med, 342: 1301–1308, 2000.
[28] Vachharajani V. Influence of obesity on sepsis. Pathophysiology, 15: 123–134, 2008.
[29] Hauner H. Secretory factors from human adipous tissue and their functional role. Proc Nutr Soc, 64: 163–169, 2005.
[30] Lord G, Matarese G, Howard J, et al. Leptin modulates the T-cell immune response and reverses starvation-induced immunosuppression. Nature, 394: 897–901, 1998.
[31] Rodriguez L, Graniel J, Ortitz R. Effect of leptin on activation and cytokine synthesis in peripheral blood lymphocytes of malnurishes infected children. Clin Exp Immunol, 148: 478–485, 2007.
[32] Considine R, Sinha M, Heiman M, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. N Engl J Med, 334: 292–295, 1996.
[33] Hsu A, Aronoff D, Phipps J, et al. Leptin improves pulmonary bacterial clearance and survival in ob/ob mice during pneumococcal pneumonia. Clin Exp Immunol, 150: 332–339, 2007.
[34] Bornstein S, Licinio J, Tauchnitz R, et al. Plasma leptin levels are increased in survivors of acute sepsis: associated loss of diurnal rhythm, in cortisol and leptin secretion. J Clin Endocrinol Metab, 83: 280–283, 1998.
[35] Bracho-Riquelme R, Reyes-Romero M, Pescador N, et al. A leptin serum concentration less than 10 ng/ml is a predictive marker of outcome in patients with moderate to severe secondary peritonitis. Eur Surg Res, 41: 238–244, 2008.
[36] Blanco-Quirós A, Casado-Flores J, Nieto-Moro M, et al. Meningococcal sepsis in pediatrics. Parameters associated with poor outcome. An Pediatr, 61: 305–313, 2004.
[37] Blanco-Quiros A, Casado-Flores J, Arranz E, et al. Influence of leptin levels and body weight in survival of children with sepsis. Acta Paediatr, 91: 626–631, 2002.
[38] Ouchi N, Kihara S, Arita Y, et al. Novel modulator for endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. Circulation, 100(25): 2473–2476, 1999.
[39] Uji Y, Yamamoto H, Tsuchihashi H, et al. Adiponectin deficiency is associated with severe polymicrobial sepsis, high inflammatory cytokine levels, and high mortality. Surgery, 145: 550–557, 2009.