ORIGINAL ARTICLE

The impact of body mass index and gender on the development of infectious complications in polytrauma patients

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Abstract

Purpose The aim was to test the impact of body mass index (BMI) and gender on infectious complications after polytrauma.

Methods A total of 651 patients were included in this retrospective study, with an Injury Severity Score (ISS) ≥ 16 and age ≥ 16 years. The sample was subdivided into three groups: BMI <25 kg/m^2, BMI 25–30 kg/m^2, and BMI >30 kg/m^2, and a female and a male group. Infectious complications were observed for 31 days after admission. Data are given as mean $\pm$ standard errors of the means. Analysis of variance, Kruskal–Wallis test, χ^2 tests, and Pearson's correlation were used for the analyses and the significance level was set at $P < 0.05$.

Results The overall infection rates were 31.0 % in the BMI <25 kg/m^2 group, 29.0 % in the BMI 25–30 kg/m^2 group, and 24.5 % in the BMI >30 kg/m^2 group ($P = 0.519$). The female patients developed significantly fewer infectious complications than the male patients (26.8 vs. 73.2 %; $P < 0.001$). The incidence of death was significantly decreased according to the BMI group (8.8 vs. 7.2 vs. 1.5 %; $P < 0.0001$) and the female population had a significantly lower mortality rate (4.1 vs. 13.4 %; $P < 0.0001$). Pearson's correlations between the Abbreviated Injury Scale (AIS) score and the corresponding infectious foci were not significant.

Conclusion Higher BMI seems to be protective against polytrauma-associated death but not polytrauma-associated infections, and female gender protects against both polytrauma-associated infections and death. Understanding gender-specific immunomodulation could improve the outcome of polytrauma patients.

Keywords Body mass index · Gender · Polytrauma · Infection · ISS

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Introduction

Different results have been reported for the association between body mass index (BMI) and polytrauma [1, 2]. BMI is an anthropometric index defining the weight-to-height relationship, and is expressed as the weight of the individual in kilograms divided by the square of his/her height in meters (kg/m^2). Individuals with normal weight have BMIs between 18.5 and 24.9 kg/m^2; overweight is defined as BMI ≥ 25 kg/m^2 and obesity as BMI ≥ 30 kg/m^2. BMI values are age- and sex-independent [3], and obesity is known to be one of the most significant risk factors for diseases such as cancer, heart disease, and diabetes mellitus in Western-oriented countries, called the metabolic syndrome [4]. To date, the association between

chronic diseases and obesity seems to be clear, but the impact of obesity on patients' immunity in critical care settings after polytrauma remains unclear [2, 5]. It is also a well-known fact that overweight people have a higher incidence in infectious viral diseases such as pandemic influenza A (H1N1), but the question remains as to whether it is caused by obesity itself or by its secondary effects, such as obstructive ventilation [6]. Obesity not only hinders nursing procedures, but also negatively affects airway management, and makes surgical exposure more difficult and radiographic imaging less feasible and less reliable [7]. However, one report claimed that overweight, obese, and severely obese patients in critical care showed reduced mortality and improved functional status after discharge from hospital—whether it was due to the energy storage of fatty tissue in a catabolic intensive care unit (ICU) stay remains speculative [8]. This seems to contradict data from population- and disease-based studies and a plethora of data from the critical care literature [9–13]. Those studies have shown that severely obese victims of blunt trauma deteriorate rapidly and are less responsive to interventions. Furthermore, obesity is recognized as an independent predictor of mortality in such patients, who are also reported to have an increased risk of multi-organ failure [2, 14]. BMI is reported to be a predictor of injury pattern and a BMI >30 kg/m^2 significantly predicted the development of pulmonary problems and rib and pelvic fractures in patients after blunt trauma [15]. On the other hand, there might be also some protective effect of the fatty tissue by its aromatase activity, converting the 4-androstenedione to estradiol-17β [16]. This might lead to a partial feminization of the obese patient and, thus, to a reduced incidence in infectious complications. There is high evidence that female patients are positively protected against infectious complications [17–20]. Whether this 'female advantage' in reality has an effect on the incidence of infectious complications in polytrauma patients has not yet been tested. However, the protective effect of estradiol-17β produced by female patients and possibly obese patients is a well-known fact [17–20]. In this study, the focus was placed on the gender- and BMI-specific incidence of infections in polytrauma patients.

Patients and methods

Patients and ethics

A total of 651 patients with polytrauma admitted to the emergency room of the University Hospital Zürich in the period 1996–2008 were included in this study. The inclusion criteria were an Injury Severity Score (ISS) ≥16 points, age ≥16 years, and admission within at least 24 h

of incurring polytrauma (ISS ≥16). The population was subdivided into three groups (Table 1a), BMI <25 kg/m^2, BMI 25–30 kg/m^2, and BMI >30 kg/m^2, and males and females. The minimal acceptable BMI was 18.5 kg/m^2. The observation period was 31 days. All patient data were collected retrospectively. All data were retrieved from patient records with the approval of the local institutional review board (IRB) according to the University of Zürich IRB guidelines, as well as the World Medical Association (WMA) Declaration of Helsinki and the study was conducted according to the guidelines for good clinical practice ("Retrospektive Analysen in der Chirurgischen Intensivmedizin" Nr. StV 01-2008).

Diagnostic protocol

All hemodynamically stable patients admitted to the trauma bay underwent an immediate whole-body computed tomography (CT) scan. Hemodynamically unstable patients underwent resuscitative procedures according to the Advanced Trauma Life Support® (ATLS®) standards, with a subsequent whole-body CT scan.

Primary care

The primary treatment of all patients admitted was according to the ATLS® guidelines and the previously assessed trauma management protocol after appropriate indications were identified [21, 22]. Briefly, after airway intubation, ventilation, and cardiovascular management, life-saving surgery was performed with decompression of the body cavities, control of any hemorrhage, and the identification of any contaminated tissues. The first surgical interventions were followed by the stabilization of major fractures and the radical debridement of necrotic tissues.

Trauma scoring systems

The ISS and the New Injury Severity Score (NISS) were used to define the severity of the trauma based on the Abbreviated Injury Scale (AIS) score [23–25]. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was used to evaluate the overall physiological impairment of the patient [26].

Definition of infection

Infection was defined as the invasion and multiplication of pathogenic microorganisms in a bodily part or tissue, such as bacteria, viruses, and parasites that are not normally present within the body, which may produce subsequent tissue injury and progress to overt disease through a variety of cellular or toxic mechanisms. An infection may cause no

Table 1 Characteristics of the patient sample at admission. **a** Patient sample divided by BMI. **b** Patient sample divided by gender

Characteristics	Total	BMI 18.5–25 kg/m^2	BMI 25–30 kg/m^2	BMI >30 kg/m^2	P-value
a					
Patients (N)	651	378	224	49	
Age (years)	42.9 ± 0.75	42.9 ± 1.0	43.4 ± 1.3	44.3 ± 2.4	0.715*
Sex male/female (N)	495/156	264/114	191/33	40/9	<0.0001[†]
BMI (kg/m^2)	24.7 ± 0.1	22.3 ± 0.1	27.0 ± 0.1	32.7 ± 0.6	<0.0001*
AIS head	3.9 ± 0.1	4.0 ± 0.1	4.0 ± 0.1	3.8 ± 0.3	0.841*
AIS face	2.1 ± 0.1	2.1 ± 0.1	2.2 ± 0.1	1.9 ± 0.3	0.568*
AIS thorax	3.2 ± 0.0	3.2 ± 0.1	3.2 ± 0.1	3.5 ± 0.2	0.131*
AIS abdomen	4.1 ± 0.1	4.1 ± 0.1	4.1 ± 0.1	4.3 ± 0.2	0.646*
AIS spine	3.1 ± 0.1	3.1 ± 0.1	3.1 ± 0.2	3.3 ± 0.3	0.825*
AIS extremities	2.7 ± 0.1	2.7 ± 0.1	2.6 ± 0.1	2.7 ± 0.1	0.876*
AIS pelvis	2.8 ± 0.1	2.8 ± 0.1	2.7 ± 0.1	2.5 ± 0.2	0.193*
AIS skin	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	2.0 ± 0.3	0.569*
ISS	29.6 ± 0.5	28.9 ± 0.7	30.1 ± 1.0	32.8 ± 1.8	0.147*
NISS	40.1 ± 0.6	39.2 ± 0.8	41.0 ± 1.1	43.4 ± 2.3	0.160*
APACHE II	16.9 ± 0.4	16.9 ± 0.5	17.0 ± 0.6	15.5 ± 1.2	0.583*
Hemoglobin (g/L)	10.6 0.1	10.8 ± 0.2	10.7 ± 0.3	9.4 ± 0.5	0.056*
Base excess (mmol/L)	−2.8 ± 0.4	−2.3 ± 0.6	−3.4 ± 0.6	−4.1 ± 1.6	0.276*
Lactate (mmol/L)	3.5 ± 0.3	3.5 ± 0.4	3.5 ± 0.2	3.5 ± 0.5	0.990*
pH	7.3 ± 0.0	7.2 ± 0.0	7.3 ± 0.0	7.3 ± 0.0	0.427*
Prothrombin time (%)	77.9 ± 1.0	76.1 ± 1.4	81.0 ± 1.6	76.5 ± 3.9	0.073*
Platelets (10^3/μL)	189.7 ± 3.9	189.8 ± 5.1	193.5 ± 6.7	171.7 ± 10.9	0.356*

Characteristics	Male		Female		P-value
b					
Patients (N)	495		156		<0.0001[†]
Age (years)	40.0 ± 0.8		45.7 ± 1.6		<0.0001*
BMI (kg/m^2)	25.3 ± 0.2		24.1 ± 0.3		<0.0001*
AIS head	3.6 ± 0.1		3.7 ± 0.1		0.352*
AIS face	2.2 ± 0.1		2.2 ± 0.1		0.254*
AIS thorax	3.2 ± 0.1		3.3 ± 0.1		0.657*
AIS abdomen	4.0 ± 0.1		4.2 ± 0.1		0.106*
AIS spine	3.1 ± 0.1		2.8 ± 0.1		0.211*
AIS extremities	2.8 ± 0.1		2.8 ± 0.1		0.739*
AIS pelvis	2.9 ± 0.1		2.7 ± 0.1		0.071*
AIS skin	1.6 ± 0.1		1.5 ± 0.1		0.486*
ISS	28.4 ± 0.5		28.3 ± 1.1		0.968*
NISS	38.1 ± 0.7		38.8 ± 1.3		0.668*
APACHE II	14.3 ± 0.4		15.5 ± 0.7		0.135*
Hemoglobin (g/L)	11.3 ± 0.2		10.1 ± 0.2		<0.0001*
Base excess (mmol/L)	−2.9 ± 0.4		−2.9 ± 0.4		0.989*
Lactate (mmol/L)	3.1 ± 0.1		2.8 ± 0.2		0.372*
pH	7.3 ± 0.2		7.3 ± 0.1		0.237*
Prothrombin time (%)	78.3 ± 1.1		79.5 ± 2.1		0.605*
Platelets (10^3/μL)	195.1 ± 4.1		199.5 ± 8.9		0.623*

All BMI values are in kg/m^2. Only 14 patients met the criterion for being underweight (BMI < 18.5) and were excluded. Data are given as mean ± SEM

AIS Abbreviated Injury Scale, *ISS* Injury Severity Score, *NISS* New Injury Severity Score, *APACHE II* Acute Physiology and Chronic Health Evaluation II

* ANOVA

[†] χ^2 test

symptoms and be subclinical, or it may cause symptoms and be clinically apparent. Microorganisms that live naturally in the body were not considered to constitute an infection. All infections had to be proved by a positive microbial culture.

Laboratory parameters

Lactate, pH, and hematocrit were measured at regular intervals with a blood–gas analyzer (ABL800 Flex; Radiometer Switzerland, GmbH, Thalwil, Switzerland). Platelets were measured with flow cytometry (FACSCalibur; Becton–Dickinson, Allschwil, Switzerland). The prothrombin time was measured with a standard method described previously [27].

Statistical analysis

Data are presented as the mean ± standard errors of the means (SEM) for continuous variables and as percentages for categorical variables. The data for the BMI groups were compared using the Kruskal–Wallis and χ^2 tests for categorical data and with analysis of variance (ANOVA) for continuous data. Pearson's correlation was used to determine the dependency of the data sets. $P < 0.05$ was to be considered significant. The data were analyzed using the SPSS statistical software (version 21.0; IBM, Armonk, NY, USA).

Results

Patient sample

All BMI data given below are reported in kg/m^2, but the units are not included for simplicity of presentation. A total of 651 patients met the inclusion criteria; 378 of them were non-obese, with a BMI <25; 224 were overweight, with a BMI 25–30; and 49 were obese, with a BMI >30. Of these patients, 495 were male and 156 were female, with significantly more men in all three groups ($P < 0.0001$; Table 1a). The overall mean BMI was 24.7 ± 0.1. The mean age was 42.9 ± 0.75 years, and did not differ significantly according to BMI (BMI <25, 42.9 ± 1.0 years; BMI 25–30, 43.4 ± 1.3 years; and BMI >30, 44.3 ± 2.4 years; $P = 0.715$; Table 1a). The female patients had a significantly lower BMI (25.3 ± 0.2 vs. 24.1 ± 0.3, male vs. female; $P < 0.0001$). The female sample was significantly older than the male sample (40.0 ± 0.8 vs. 45.7 ± 1.6 years, male vs. female; $P < 0.0001$). There were no other differences found except for significantly lower hemoglobin in the female sample on admission (Table 1b). Only 14 patients (four males and ten

females) met the criteria for being underweight (BMI <18.5) and were excluded from the study. All patients admitted to the trauma bay who met the inclusion criteria were included in the study.

Injury patterns

The analysis of the injury patterns according to the AIS revealed no significant differences between the BMI groups. In this patient sample, there were no differences between the three groups in the ISS, NISS, or APACHE II scores (Table 1a). The gender-specific analysis revealed no significant differences in the injury pattern or physiological parameters on admission (Table 1b).

Incidence of infection

There were no significant differences between the three BMI groups in the incidence of infection (Table 2a). However, the female sample revealed a significantly lower incidence of infectious complications in all anatomical region after polytrauma compared with the male population ($P < 0.001$) (Table 2b).

Correlation of injury pattern and infection

Pearson's correlation revealed no significant association between the injury pattern and the infectious focus. The correlation coefficient was always negative or below 0.1. There was absolutely no correlation between the severity of an injury in an anatomical region and the incidence of infection in that region (Table 3).

Outcomes

Patients with a higher BMI revealed a significantly lower mortality rate (BMI <25, 8.8 %; BMI 25–30, 7.2 %; and BMI >30, 1.5 %; $P < 0.0001$) (Table 4a). The female patients showed a significantly lower mortality compared to the male sample (13.4 vs. 4.1 %, male vs. female; $P < 0.0001$) (Table 4b). There were no significant differences found between hospitalization, intensive care stay, or ventilation in all BMI groups and in the male and female samples (Table 4a, b).

Discussion

This study was designed to evaluate the impact of BMI and gender on the development of infectious complications in patients with polytrauma. Understanding the altered physiology of obese patients with polytrauma can play a pivotal role in their multidisciplinary treatment. In

Table 2 **a** Patient sample divided by BMI. **b** Patient sample divided by gender

BMI group	Infection	CNS infection	Pneumonia	Abdominal infection	Urinary tract infection	Wound infection	Catheter infection	Male	Female
a									
18.5–25 kg/m^2	31.0 %	4.1 %	17.7 %	2.4 %	4.5 %	7.1 %	6.6 %	69.8 %	30.2 %
25–30 kg/m^2	29.0 %	3.5 %	15.6 %	0.4 %	3.5 %	7.1 %	4.9 %	85.3 %	14.7 %
>30 kg/m^2	24.5 %	4.0 %	12.2 %	2.0 %	10.2 %	4.1 %	6.1 %	81.6 %	18.4 %
Total	29.8 %	4.0 %	16.6 %	1.7 %	4.6 %	6.9 %	6.0 %	76.0 %	24 %
P-value	0.519*	0.924*	0.438*	0.172*	0.146*	0.667*	0.563*	<0.001*	<0.001*

Gender	Infection	CNS infection	Pneumonia	Abdominal infection	Urinary tract infection	Wound infection	Catheter infection
b							
Male	33.1 %	5.1 %	18.2 %	2.1 %	5.8 %	10.4 %	5.8 %
Female	29.3 %	3.5 %	16.5 %	0.6 %	4.2 %	5.9 %	4.4 %
Total	29.8 %	4.0 %	16.6 %	1.7 %	4.6 %	6.9 %	6.0 %
P-value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

Data represent the incidence of infectious complications in patients after polytrauma over an observation period of 31 days. Data are given as percentages of the respective groups

CNS central nervous system

* Kruskal–Wallis test within the BMI and gender groups

Table 3 Pearson's correlation between the incidence of infectious complications and the injury severity in the corresponding anatomical region

P-value* Pearson's correlation	AIS head	AIS face	AIS thorax	AIS abdomen	AIS spine	AIS extremities	AIS pelvis	AIS skin
Infection	0.476	0.588	0.351	0.345	0.966	0.734	0.775	0.079
	−0.029	−0.022	−0.037	−0.038	0.002	−0.014	0.011	−0.070
CNS infection	0.742	0.829	0.374	0.196	0.400	0.208	0.787	0.950
	0.013	−0.009	−0.036	−0.052	−0.034	0.050	0.011	0.003
Pneumonia	0.245	0.372	0.406	0.706	0.760	0.659	0.525	0.211
	−0.046	−0.036	−0.033	0.015	−0.012	0.018	0.025	−0.050
Abdominal infection	0.662	0.702	0.964	0.445	0.041	0.446	0.255	0.911
	−0.017	0.015	0.002	−0.031	0.082	0.030	−0.045	−0.004
Urinary tract infection	0.365	0.192	0.878	0.242	0.189	0.578	0.744	0.081
	−0.036	0.052	−0.006	0.047	−0.053	0.022	−0.013	−0.070
Wound infection	0.986	0.533	0.210	0.605	0.830	0.163	0.955	0.311
	0.001	−0.025	−0.050	0.021	0.009	−0.056	0.002	−0.041
Catheter infection	0.272	0.662	0.397	0.525	0.606	0.648	0.352	0.590
	−0.044	0.017	0.034	0.025	0.021	0.018	0.037	0.022

There was a significant correlation between spinal injury severity and abdominal infection, but the correlation coefficient was very low

* ANOVA, Pearson's correlation

AIS Abbreviated Injury Scale, *CNS* central nervous system

Western-oriented societies, the prevalence of obesity is a growing problem that appears to be altering current medical and surgical treatment strategies [28]. Female gender has a positive immunomodulatory effect on the development of infectious complications after trauma [17–20]. Overweight patients have significantly more comorbidities than normal-weight patients and face more post-traumatic complications [29, 30]. In this study, the incidence of infections was analyzed over a period of 31 days after polytrauma. The ISS did not differ between the study groups. The incidence of infectious complications also did not differ with increasing BMI scores over the observation period. On one hand, the production of estrogen by aromatase activity in adipocytes is a well-known phenomenon [16]. The steroid pathway then shifts from the production of 4-androstenedione and testosterone toward the

Table 4 Outcomes of the study sample. **a** Patient sample divided by BMI. **b** Patient sample divided by gender

Outcome	Total	BMI 18.5–25 kg/m^2	BMI 25–30 kg/m^2	BMI >30 kg/m^2	P-value
a					
Death [N, (% of all)]	114 (17.5 %)	57 (8.8 %)	47 (7.2 %)	10 (1.5 %)	<0.0001*
Hospitalization (days)	18.9 ± 1.1	20.0 ± 1.6	17.2 ± 1.3	18.5 ± 3.1	0.473[†]
Intensive care (days)	9.8 ± 0.5	9.9 ± 0.6	9.5 ± 0.7	10.7 ± 2.4	0.813[†]
Ventilation (days)	6.2 ± 0.4	6.3 ± 0.5	5.8 ± 0.5	7.5 ± 2.4	0.508[†]

Outcome	Total	Male	Female	P-value
b				
Death [N, (% of all)]	114 (17.5 %)	87 (13.4 %)	27 (4.1 %)	<0.0001**
Hospitalization (days)	18.9 ± 1.1	25.3 ± 1.4	26.3 ± 1.8	0.705[†]
Intensive care (days)	9.8 ± 0.5	11.7 ± 0.6	10.9 ± 0.9	0.485[†]
Ventilation (days)	6.2 ± 0.4	6.9 ± 0.5	5.8 ± 0.6	0.180[†]

The death rate was significantly lower in the higher BMI groups. Data are given as mean ± SEM

* Kruskal–Wallis

** χ^2 test

[†] ANOVA

production of estrone and estradiol-17β. Feminine steroids are highly protective against inflammatory reactions [27]. The data presented here indicate no difference in the incidence of infections in the overweight patients in this study. The production of estradiol-17β produced by the adipocytes seems not to be effective enough for the 'feminine protection' against infectious complications. However, the feminine gender was significantly protected against infectious complications without differences in injury severity or pre-existing diseases reflected by the ISS and APACHE II scores. The question as to whether the injury pattern correlates to a specific anatomical region seems to be negatively answered. There was no correlation between the injured anatomical region and an infection within that anatomical region, so the injury itself did not constitute an infectious focus. Only spinal injuries and abdominal infections correlated significantly, but with a low correlation coefficient. This may suggest a random association. On the other hand, polytrauma patients face a catabolic state early, with consumption of the body's energy reserves, decreasing the functionality of the immunity system. A slightly elevated BMI may provide enough energy in a polytrauma situation to keep the immunity system functional, which is mirrored in the better survival rate according to the increasing BMI. Taking all the findings together, the outcomes of the overweight patients were not better than those of the normal-weight patients, but the mortality rate decreased significantly in the overweight BMI group and in the female group. It can be stated definitively that females are protected against infectious complications in polytrauma conditions, whereas the overweight and obese patients are not. Further analyses that include the assessment of hormonal status and precise measurements of body fat might be more conclusive. The knowledge of hormonal immunomodulation could improve the outcome of severe infections and sepsis in polytrauma patients.

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