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Body mass index affects the short-term outcome of patients with intra-abdominal infections.

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Data Availability Statement: The data used to support the findings of this study are available from the corresponding author upon request.

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31 **Abstract**

32 **Objectives:** The aim of this study was to determine the relationship between body mass
33 index (BMI) and the short-term prognosis of patients with intra-abdominal infection
34 (IAI) by using the Medical Information Mart for Intensive Care (MIMIC-III) database.

35 **Methods:** We conducted a retrospective analysis with adult IAI ICU patients from 2001
36 to 2012 in the MIMIC-III database. Cox proportional hazards analyses were used to
37 evaluate the relationships between BMI and 90-day mortality.

38 **Results:** In total, 1161 patients with IAI were included. There were 399 (34.4%)
39 patients with a normal BMI ($< 25 \text{ kg/m}^2$), 357(30.8%) patients with an overweight BMI
40 ($25\text{-}30 \text{ kg/m}^2$) and 405(34.9%) patients with an obese BMI ($> 30 \text{ kg/m}^2$) who tended to
41 be younger ($P<0.001$) and have higher Sequential organ failure assessment (SOFA)
42 scores ($P<0.05$). The mortality of patients with an obese BMI at 90- days was lower
43 than that of patients with a normal BMI ($P<0.05$), but their length of stay in ICU was
44 higher ($P<0.001$); however, their rate of mechanical ventilation utilization was higher
45 ($P<0.05$), with a higher probability of sepsis, and septic shock ($P<0.005$, $P<0.005$,
46 respectively). In the Cox regression model, we also confirmed that BMI was a
47 protective factor for patients with IAIs, and the mortality rate of patients with a higher
48 BMI was 0.974- times lower than that of patients with a lower BMI ($P<0.005$,
49 $\text{OR}=0.974$, 95% CI 0.956-0.992).

50 **Conclusions:** IAI patients with an overweight or obese BMI have better short-term
51 clinical outcomes than patients with a normal BMI.

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53 **Strengths and limitations of this study:**

54 In this study, we confirmed that IAI patients with an overweight and obese BMI have
55 better short-term clinical outcomes than patients with a normal BMI. The limitations of
56 this study were: first, this study is essentially a retrospective single center study; second,
57 due to the characteristics of the database itself, a considerable number of patients' data
58 are missing, especially various laboratory test data, which may cause selection bias

59 **Key word:** Intra-abdominal infection; BMI; MIMIC-III; Big data; Mortality; ICU;

611. Introduction

IAIs are common surgical emergencies and have been reported as major contributors to non-trauma deaths in emergency departments worldwide and as a common complication of abdominal surgery¹. IAIs are the second most common cause of sepsis, and the second most common infectious disease among inpatients. The death rate of IAIs can reach 20%, indicating a commonly poor prognosis of patients^{2,3}. IAIs can be divided into uncomplicated and complicated types. Uncomplicated IAIs affect a single organ, and complicated IAIs describe an extension of the infection into the peritoneal space. The resultant physiologic response may develop into a systemic inflammatory response syndrome (SIRS)⁴. The most extensively studied biomarkers in the context of IAIs are C-reactive protein (CRP) and procalcitonin (PCT). In addition, there are some serum mediators, such as proadrenomedullin and cytokines, that are not commercially available for routine monitoring⁵. The role of those biomarkers remains limited.

BMI, calculated by dividing weight by the square of height, is used by most health organizations, including the WHO, as a screening tool for diagnosing obesity⁶. Overweight and obesity are uniformly associated with a substantially increased risk of death⁷. In patients who do not enter the ICU, such as endometrial and breast cancer patients, BMI can be used as a prognostic indicator^{8,9}. Similarly, in ICU patients, such as liver transplant patients, morbid obesity has an impact on patient survival and post-transplant complications¹⁰. Furthermore, at least a quarter of patients in U.S. ICUs have a BMI indicating overweight, obesity or morbid obese¹¹. As mentioned above, patients with IAIs also tend to develop severe conditions and enter the ICU. Previous studies have shown that obesity plays a protective role in some diseases (such as chronic kidney disease, AIDS), which is a special phenomenon called the obesity paradox^{12,13}. However, in ICU patients with IAIs, whether BMI is a risk factor or a protective factor, considering the obesity paradox, still needs further study.

The aim of this study was to determine the relationship between BMI and the prognosis of patients with IAIs by using the Medical Information Mart for Intensive Care (MIMIC-III) database¹⁴. The MIMIC-III database is a large, single-center database comprising information relating to patients admitted to critical care units at a large

tertiary care hospital. Data included vital signs, medications, laboratory measurements, diagnostic codes, hospital length of stay, survival data, and more. The data cover 53,423 distinct hospital admissions for adult patients admitted to critical care units between 2001 and 2012, and many studies have been launched to explore the clinical features of ICU patients using the database.

962. Methods and Materials

97 2.1 Database

In this article we used a publicly available critical care medicine database: Medical Information Mart for Intensive Care III (MIMIC-III). This database contains unidentified medical information from about 60000 patients who admitted to critical care units of the Beth Israel Deaconess Medical Center in Boston, Massachusetts, from 2001 to 2012. Researchers at MIT's computational Physiology Lab and the collaborative research group provided the database. In MIMIC database, all diagnostics correspond to International Classification of Diseases (ICD-9) codes. We got permission to access the database only after completing web-course provided by the National Institutes of Health.

107 2.2 Study population

There is not a specific diagnosis of IAI in ICD-9 coding, so we include all the possible diagnosis related to IAIs in ICD-9 into our study cohort, all ICD-9 codes and diagnostics are listed in Table S1. For patients who had multiple ICU admissions, only the first admission record was kept. The exclusion criterion included: (1) age under 18 years old (2) the weight or height data was missing. According to the BMI classification standard of the WHO, we divided the patients into five groups: underweight (BMI< 18.5 kg/m²), normal weight (BMI: 18.5 to <25 kg/m²), overweight (BMI: 25 to <30 kg/m²), obese (BMI 30 to <40 kg/m²), and morbid obese (BMI >40kg/m²), but in this grouping method, the number of patients in the underweight and morbid obese subgroups is not enough (shows in Figure 1).Finally, all patients are divided into three groups: normal BMI group (BMI < 25kg/m²), overweight BMI group(25-30 kg/m²) and obese BMI group (BMI > 25kg/m²).

120 2.3 Data extraction and management

We used the structure query language (SQL) in PostgreSQL (v9.5) to retrieve the data. The following data were extracted from the MIMIC-III database from the first day of ICU admission: age, sex, ethnicity, admission weight, admission height, admission diagnosis, admission type, SOFA score, Simplified Acute Physiology Score II (SAPSII), use of vasopressors, renal replacement therapy (RRT), mechanical ventilation, values of hemoglobin(HGB), white blood cell count(WBC), platelet count(PLT), albumin(ALB), sodium(Na), chlorine(Cl) , potassium(K), creatinine(CRE), blood urea nitrogen(BUN), glucose(GLU) , lactate(LAC) , and bilirubin(BIL) in the first 24 h of ICU admission, length of stay before ICU admission, length of stay (both ICU and hospital), intake and output. The SOFA score was calculated within the first 24 h after ICU admission. If a variable was measured more than once in the first 24 h, the value which indicated a worse prognosis was used. In addition, dates of birth for patients aged over 89 were shifted to obscure their true age and comply with HIPAA regulations: these patients appear in the database with ages of over 300 years, but the median age of these patients was 91.5 years old, so we shifted the age of these patients to 91.5 years old.

2.4 Outcomes

The primary endings were the 90- days mortality after ICU admission. The secondary endings were the long of stay (LOS) in ICU. The probability of sepsis and septic shock was also included in this study.

2.5 Patient and Public Involvement

No patient involved.

2.6 Statistical analysis

First, univariate analysis was used to compare all the variables. If the data satisfied a normal distribution and the variance was homogeneous, the data are expressed as the mean \pm standard deviation, and Student's t-test was used for comparisons. If the variance was not homogeneous, then one-way ANOVA was used for the comparisons. If none of the above requirements were met or the data were not continuous variables, then the data are described as the median and interquartile range, and the Wilcoxon rank-sum test was used for comparisons. Categorical variables are presented as

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numbers and percentages and were compared by Pearson’s chi-square test or Fisher’s exact test as appropriate. We used the log-rank test and 90-day Kaplan–Meier curves to carry out the survival analysis, and determined whether BMI affects 90-day mortality. In addition, we compared the 90-day survival curves between subgroups of patients with and without sepsis by log-rank test. The variables with $P < 0.15$ in univariate analysis were included in the Cox proportional hazards analyses as covariates to determine which variable was the independent risk factor affecting the 90-day survival rates. SPSS (v25.0; IBM, Armonk, NY) was used for all data analysis; a two-tailed $P < 0.05$ was considered statistically significant. R STUDIO was used for propensity score match to adjusting for confounding factors, and results was showed in Fig S1-S6.

Results

3.1 Population and baseline characteristics

The MIMIC-III database includes 2087 patients diagnosed with intra-abdominal infection according to the criteria we mentioned above. Among these patients, 917 lacked height or weight data and were excluded from the study. Finally, 9 patients with abnormal data records were excluded (e.g., height value > 300 meter, survival time < 0 day). A total of 1161 patients were finally included in the study (Figure 2). Table 1 shows the baseline characteristics of patients grouped by BMI. There were 399 patients with BMI < 25 kg/m², 357 patients with BMI 25-30 kg/m² and 405 patients with BMI > 30 kg/m², accounting for 34.37%, 30.75% and 34.88% of the patients, respectively. In the subgroup aged 45-64 years, the proportion of patients with an obese BMI was higher than that of patients with a normal and an overweight BMI (42.96% vs. 31.58%, 42.96% vs. 33.61%, respectively, $P < 0.05$), while in the subgroup of patients older than 90 years, the result was the opposite (1.73% vs. 8.02%, 1.73% vs. 5.32, respectively, $P < 0.05$). The proportion of females in the group of patients with an overweight BMI was lower than that in the other groups of patients ($P < 0.001$). There was no significant difference in ethnicity between the three groups ($P = 0.183$). However, there were significant differences between the three groups in regard to marital status and admission type ($P = 0.008$ and 0.009 , respectively). The group with BMI < 25 kg/m²

had lower SOFA scores on the first day of admission than the obese group ($P=0.039$). However, there was no significant difference between the two groups in regard to SAPS ii, SIRS, qSOFA and OASIS score ($P > 0.05$). Table S2 shows the baseline characteristics after adjustment of confounding factors. After adjusting for all clinical covariates listed, SOFA scores remained significant difference between groups ($P<0.05$).

3.2 Univariate analysis of outcomes

The mortality rate at different time of admission and the LOS of patients in different BMI group are shown in Table 2.

The mortality of patients with BMI $< 25 \text{ kg/m}^2$ was significantly higher than that of patients with an obese BMI at 30 days after entering the ICU (18.55% vs. 11.85%, $P=0.016$, respectively), which was the same at 90 days after entering the ICU (28.07% vs. 20.74%, $P=0.048$, respectively). In addition, the median LOS for patients with a BMI < 25 , 25-30 and $> 30 \text{ kg/m}^2$ in the ICU was 3.13 days, 3.59 days and 4.93 days, respectively ($P<0.001$), and the obese group spent significantly more time in ICU than the former two groups ($P<0.05$, respectively). After adjusting for confounding factors, the LOS in ICU of obese patients was still significantly longer than that of the other two groups ($P<0.001$, Table S3).

The K-M curve for 90-day survival by BMI is shown in Figure 3. This shows that the group with an overweight and obese BMI had a significant survival advantage. ($P<0.001$ by log-rank test).

The morbidity of sepsis and septic shock in the three groups is shown in Table 3. In the obese group, the incidence was significantly higher than that in the group with a normal BMI ($P=0.002$, $P=0.004$, respectively). Results after adjustment for confounding factors are shown in Table S4.

The 90-day survival curve stratified by BMI in patients with and without sepsis is shown in Figure 4. In different subgroups, patients with a BMI $> 25 \text{ kg/m}^2$ had significantly better survival than those with a BMI $< 25 \text{ kg/m}^2$ ($P<0.001$, $P<0.05$, respectively by log-rank test).

We also compared the use of mechanical ventilation, vasoactive drugs and dialysis

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between the three groups and showed them in Table 4. The proportion of patients with an obese BMI who needed mechanical ventilation was higher than patients with a normal BMI (61.48% vs. 52.38%, $P=0.034$). However, in regard to the use of vasoactive drugs and dialysis, there was no significant difference between the three groups. After adjusting for confounding factors, there was no significant difference in the use of mechanical ventilation (Table S5).
The results of several laboratory tests stratified by BMI are shown in Table 5. Significant differences were shown in the hemoglobin, WBC, chlorine, creatinine and glucose levels between the three groups ($P=0.048$, 0.035, 0.007, 0.001 and <0.001 , respectively). After adjusting for confounding factors, there was no significant difference in HGB level among the groups, but in sodium level there was a significant difference among the groups ($P=0.042$, Table S6).

3.3 Cox proportional hazards analyses of 90- day mortality

We imported variables with P values less than 0.15 in univariate analysis into Cox proportional hazards analyses, including gender, admission type, admission age, BMI, marital status, SOFA score, ventilation, sepsis, septic shock, LOS in the ICU and hospital, HGB, chloride, WBC, CRE, GLU (Table 6). Our analysis revealed the relationship between BMI and 90- day mortality, and the mortality rate of patients with a higher BMI was 0.972 times lower than that of patients with a lower BMI ($P=0.004$, $OR=0.974$, 95% CI 0.956-0.992). Moreover, admission age, admission type and SOFA score also showed a significant correlation with 90 day mortality. Sepsis was a risk factor for 90-day mortality ($P<0.001$, $OR=2.176$, 95% CI 1.543-3.067). HGB showed a significant correlation with 90 day mortality ($P=0.003$, $OR=0.905$, 95% CI 0.847-0.966). After adjusting for confounding factors, LOS in hospital was no longer included in our Cox regression model (Table S7).

364. Discussion

In this retrospective study, we used the MIMIC-III database to study the relationship between BMI and the short-term prognosis of patients with abdominal infection. By comparing the survival curve and 30- day and 90- day mortality of the three groups, we found that the short-term prognosis of the patients with an overweight (25-30 kg/m²)

and obese ($>30\text{kg/m}^2$) BMI was significantly better than that of the normal group.

By comparing the baseline characteristics of the three groups of patients, we found that there was significant difference in the overall age composition of the three groups, and in the subgroup with age 45-64 and > 90 had a significant difference between the three groups, and this statistical difference between subgroups still exists after adjusting for confounding factors. Second, in our study, patients with overweight BMI were more likely to be male. However, previous studies have shown that obese cohorts tend to be younger and have a higher female prevalence¹⁵. The possible cause of this discrepancy, as mentioned in previous studies, could be that male patients are more likely to develop abdominal infections such as appendicitis, and smoking is a probable element for this increased risk^{16, 17}.

Currently, the study of the association of obesity with the outcome of patients is mainly focused on sepsis, and the results are ambiguous and contradictory¹⁸. In this study, we expanded the scope of this relationship to study the effect of BMI on the short-term outcome of patients with IAI. In our results, patients with an obese BMI had a higher SOFA score at admission, indicating a worse organ failure degree than that of patients with a lower BMI, and the incidence of sepsis events was higher in patients with a higher BMI. Previous studies have shown that people who were overweight or obese had higher susceptibility to developing postsurgical infections, and respiratory tract infections and tended to develop more severe infections, which is consistent with the results of our study; however, the short-term outcome of those patients was better^{19, 20}.

The same contradiction exists in our laboratory test results. According to a previous study, serum creatinine was an independent risk factor for clinical failure, but in our cohort, obese patients had significantly higher creatinine values, which should lead to a worse clinical outcome²¹. Previous studies also showed creatinine minimums at baseline provide a predictor of short-term mortality²². However, some studies have reported that creatinine can predict multiple organ failure²³. This may be related to the baseline characteristics of the population under study. Creatinine no longer appears as an independent factor which affect the prognosis after adjust the baseline characteristics in our study. Among the laboratory tests included in our study, HGB was an

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independent protective factor in the Cox regression model. On the one hand, a higher hemoglobin value can provide more oxygen to tissues and reduce hypoxia, on the other hand, obese patients may originally have a higher HGB value ,while critically ill patients often develop anemia related to a low level of erythropoietin (EPO) in the presence of sepsis, that kind of anemia indicates malnutrition of critically IAI patients; however, obese patients rarely have malnutrition , so they are unlikely to develop anemia²⁴⁻²⁶. Furthermore, we found that patients without sepsis but with IAIs can also benefit from a higher BMI. This shows that BMI has a protective effect not only in patients with a sever condition such as sepsis patients but also in patients with a milder condition. However, once sepsis occurs in patients with abdominal infection, the short-term prognosis will be significantly worse. Therefore, we should spare no efforts to prevent the occurrence and development of sepsis in the treatment of patients with abdominal infection, especially those with low BMI.

Our study also found that patients with a higher BMI had a higher probability of receiving mechanical ventilation, which was also reported in previous studies²⁷.This may be related to the impact of obesity on the respiratory system, obese patients tend to have higher respiratory rates and lower tidal volumes, and lung volumes tend to be decreased, especially expiratory reserve volume²⁸. BMI was associated with an increased risk of ARDS in a weight-dependent manner but was not associated with mortality²⁹. As mentioned above, obese patients are also more likely to receive mechanical ventilation because of the attention of medical staff³⁰. To summarize, patients with a higher BMI have a poor health foundation and are more likely to progress to critical illness, but there are also some indicators, such as HGB that may prevent organ failure caused by critical illness in this process. In addition, they are more likely to receive advanced ventilation, dialysis, liver function support and medical resources.

In the final Cox regression model, BMI remained a protective factor after adjusting for confounding variables. This is a phenomenon called the obesity paradox, which means that overweight and obese people are recognized as they often have more basic diseases, such as hypertension, cardiovascular disease and diabetes. Their general health is also

301 worse than that of normal persons, and some studies have shown that BMI is associated
302 with the incidence rate of more than 20 kinds of cancers, but BMI still shows protective
303 effects and improves the prognosis of patients. The reasons and underlying mechanisms
304 have not been clarified³¹. Some studies have suggested that patients with obesity-
305 associated comorbidities, such as hypertension may require less vasoactive drugs and
306 fluid resuscitation in the treatment process; severe IAs can lead to sepsis that requires
307 fluid resuscitation, and a restrictive fluid strategy would reduce the burden of heart or
308 lung injuries to protect organ function^{32, 33}. Drugs that patients with cardiovascular
309 disease take in the long term, such as aspirin, might play a protective role in IAs,
310 antiplatelet drugs can inhibit coagulation and inflammatory reactions in models of
311 sepsis, reducing damage to organ function, and clinical studies also suggest that aspirin
312 may improve the prognosis of patients with sepsis³⁴.

313 The protective effect of diabetes may occur through an unidentified hormonal
314 intermediary, or it may be caused by antidiabetic drugs such as rosiglitazone taken by
315 diabetic patients, which increase the serum levels of adiponectin, thus resulting in a
316 better prognosis^{35, 36}. A recent study also indicated an association between metformin
317 use prior to admission and lower mortality in septic adult patients with diabetes mellitus,
318 metformin may supply higher amounts of lactate, serving as an energetic carbon source,
319 thus making energy available to ischemic tissue^{37, 38}. Second, in acute catabolic
320 reactions caused by IAs, stored fuel and nutritional reserves might be critical in obese
321 patients. In our study, the higher creatinine values of overweight and obese patients also
322 support that standpoint; however, in IAs, due to anorexia and acute gastrointestinal
323 dysfunction, the energy supply is frequently insufficient³⁹. Third, adipocytes can
324 release adipokines and inflammatory factors such as IL-10 and leptin, which can
325 regulate the immune response and improve the prognosis of patients with an acute
326 inflammatory response⁴⁰. A previous study indicated that lipopolysaccharide may be
327 sequestered in adipose tissue via the very-low-density lipoprotein receptor, and this
328 sequestration may contribute to improved sepsis survival; when BMI was greater than
329 25 kg/m², this effect was accentuated⁴¹. In addition, the difference in nursing level may
330 also affect the prognosis of obese patients. As mentioned above, obese patients often

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suffer from more basic diseases and complications, and they are more likely to receive the attention of nursing staff, receiving more active treatment³⁰. Finally, previous studies suggest that BMI is not the best indicator to accurately evaluate obesity, which leads to the obesity paradox^{42, 43}.

This study still has several limitations. First, this study is essentially a retrospective single center study. Like other observational studies, it is difficult to completely exclude the influence of residual confounding factors. Second, due to the characteristics of the database itself, a considerable number of patients' data are missing, especially various laboratory test data, which may cause selection bias; however, we did not introduce the missing indicators into the final Cox regression model. Third, in this study, we only obtained the baseline characteristic information of patients and some laboratory examination results of patients within 24 hours after admission, but did not specifically study the infection and treatment process of patients (such as the use of antibiotics, etc.), and the disparate interventions in the two groups in regard to these factors may lead to deviations in our results. Finally, the total sample size of the database was very large, but the number of subgroups in our study was relatively small, which may also affect the reliability of our results.

Conclusion

IAI patients with an overweight and obese BMI have better short-term clinical outcomes than patients with a normal BMI; this difference is manifested in 90- day survival conditions, with obvious advantages observed in the higher BMI group. The protective effect of BMI not only exists in patients with severe conditions, such as sepsis patients, but also in patients with milder conditions.

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Authors' contributions

Li QL participated in the research design, data analysis and writing of the paper; **Tong YM** participated in the data collecting; **Liu SN** participated in data analysis and revising

of the paper; **Yang KB** participated in the data cleaning; **Li QL, Tong YM and Liu SN** contributed equally to this work. **Liu C and Zhang JY** provided substantial advice in designing the study and assisting in the division of labor, writing and revising the paper.

Competing interests

The authors declare that they have no competing interests.

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None.

Availability of supporting data

Data were fully available at <https://mimic.physionet.org/>.

Ethical Approval and Consent to participate

The patients' information was anonymised, and thus the need for patients' informed consent was not required in this study. All data were extracted by the corresponding author (Record ID: 28572693).

Consent for publication

Not applicable.

Reference

1. Sartelli M, Chichom-Mefire A, Labricciosa FM, Hardcastle T, Abu-Zidan FM, Adesunkanmi AK, et al. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections. *World J Emerg Surg* 2017; 12 29. doi: 10.1186/s13017-017-0141-6.
2. Hecker A, Reichert M, Reuss CJ, Schmoch T, Riedel JG, Schneck E, et al. Intra-abdominal sepsis: new definitions and current clinical standards. *Langenbecks Arch Surg* 2019; 404 (3): 257-271. doi: 10.1007/s00423-019-01752-7.
3. Eggimann P, Pittet D. Infection control in the ICU. *Chest* 2001; 120 (6): 2059-2093.
4. Shirah GR, O'Neill PJ. Intra-abdominal Infections. *Surg Clin North Am* 2014; 94 (6): 1319-1333. doi: 10.1016/j.suc.2014.08.005.
5. Montravers P, Tashk P, Tran Dinh A. Unmet needs in the management of intra-abdominal infections. *Expert Rev Anti Infect Ther* 2017; 15 (9): 839-850. doi: 10.1080/14787210.2017.1372750.
6. Gonzalez MC, Correia MITD, Heymsfield SB. A requiem for BMI in the clinical setting. *Curr Opin Clin Nutr Metab Care* 2017; 20 (5): 314-321. doi: 10.1097/MCO.0000000000000395.
7. Flegal KM, Ioannidis JPA, Doehner W. Flawed methods and inappropriate conclusions for

1
2
3 396 health policy on overweight and obesity: the Global BMI Mortality Collaboration meta-analysis.
4 397 J Cachexia Sarcopenia Muscle 2019; 10 (1): doi: 10.1002/jcsm.12378.
5
6 398 8. Heetun A, Cutress RI, Copson ER. Early breast cancer: why does obesity affect prognosis? Proc
7 399 Nutr Soc 2018; 77 (4): 369-381. doi: 10.1017/S0029665118000447.
8
9 400 9. Secord AA, Hasselblad V, Von Gruenigen VE, Gehrig PA, Modesitt SC, Bae-Jump V, et al. Body
10 401 mass index and mortality in endometrial cancer: A systematic review and meta-analysis.
11 402 Gynecol Oncol 2016; 140 (1): 184-190. doi: 10.1016/j.ygyno.2015.10.020.
12 403 10. Barone M, Viggiani MT, Losurdo G, Principi M, Leandro G, Di Leo A. Systematic review with
13 404 meta-analysis: post-operative complications and mortality risk in liver transplant candidates
14 405 with obesity. Aliment Pharmacol Ther 2017; 46 (3): 236-245. doi: 10.1111/apt.14139.
15 406 11. Wang Y, Beydoun MA. The obesity epidemic in the United States--gender, age, socioeconomic,
16 407 racial/ethnic, and geographic characteristics: a systematic review and meta-regression
17 408 analysis. Epidemiol Rev 2007; 29 6-28. doi: 10.1093/epirev/mxm007.
18 409 12. Kalantar-Zadeh K, Abbott KC, Salahudeen AK, Kilpatrick RD, Horwich TB. Survival advantages
19 410 of obesity in dialysis patients. Am J Clin Nutr 2005;81(3):543-54 2005.
20 411 13. Chlebowski RT, Grosvenor M, Lillington L, Sayre J, Beall G. Dietary Intake and Counseling,
21 412 Weight Maintenance, and the Course of HIV Infection. Journal of the American Dietetic
22 413 Association 1995; 95 (4): 428-435. doi: 10.1016/s0002-8223(95)00115-8.
23 414 14. Johnson AE, Pollard TJ, Shen L, Lehman LW, Feng M, Ghassemi M, et al. MIMIC-III, a freely
24 415 accessible critical care database. Sci Data 2016; 3 160035. doi: 10.1038/sdata.2016.35.
25 416 15. Li S, Hu X, Xu J, Huang F, Guo Z, Tong L, et al. Increased body mass index linked to greater short-
26 417 and long-term survival in sepsis patients: A retrospective analysis of a large clinical database.
27 418 Int J Infect Dis 2019; 87 109-116. doi: 10.1016/j.ijid.2019.07.018.
28 419 16. Ferris M, Quan S, Kaplan BS, Molodecky N, Ball CG, Chernoff GW, et al. The Global Incidence
29 420 of Appendicitis: A Systematic Review of Population-based Studies. Ann Surg 2017; 266 (2): 237-
30 421 241. doi: 10.1097/SLA.0000000000002188.
31 422 17. Montgomery SM, Pounder RE, Wakefield AJ. Smoking in adults and passive smoking in children
32 423 are associated with acute appendicitis. Lancet 1999; 353 (9150): 379.
33 424 18. Trivedi V, Bavishi C, Jean R. Impact of obesity on sepsis mortality: A systematic review. J Crit
34 425 Care 2015; 30 (3): 518-524. doi: 10.1016/j.jcrc.2014.12.007.
35 426 19. Maccioni L, Weber S, Elgizouli M, Stoehliker A-S, Geist I, Peter H-H, et al. Obesity and risk of
36 427 respiratory tract infections: results of an infection-diary based cohort study. BMC Public Health
37 428 2018; 18 (1): 271. doi: 10.1186/s12889-018-5172-8.
38 429 20. Dhurandhar NV, Bailey D, Thomas D. Interaction of obesity and infections. Obes Rev 2015; 16
39 430 (12): 1017-1029. doi: 10.1111/obr.12320.
40 431 21. White BP, Wagner JL, Barber KE, King ST, Stover KR. Risk Factors for Failure in Complicated
41 432 Intraabdominal Infections. South Med J 2018; 111 (2): 125-132. doi:
42 433 10.14423/SMJ.0000000000000770.
43 434 22. Thongprayoon C, Cheungpasitporn W, Kittanamongkolchai W, Srivali N, Ungprasert P, Kashani
44 435 K. Optimum methodology for estimating baseline serum creatinine for the acute kidney injury
45 436 classification. Nephrology (Carlton) 2015; 20 (12): 881-886. doi: 10.1111/nep.12525.
46 437 23. Dewar DC, Tarrant SM, King KL, Balogh ZJ. Changes in the epidemiology and prediction of
47 438 multiple-organ failure after injury. J Trauma Acute Care Surg 2013; 74 (3): 774-779. doi:
48 439 10.1097/TA.0b013e31827a6e69.

- 440 24. Vuong J, Qiu Y, La M, Clarke G, Swinkels DW, Cembrowski G. Reference intervals of complete
441 blood count constituents are highly correlated to waist circumference: should obese patients
442 have their own "normal values?". *American journal of hematology* 2014; 89 (7): 671-677. doi:
443 10.1002/ajh.23713.
- 444 25. Rogiers P, Zhang H, Leeman M, Nagler J, Neels H, Mélot C, et al. Erythropoietin response is
445 blunted in critically ill patients. *Intensive care medicine* 1997; 23 (2): 159-162.
- 446 26. Zhang Z, Pereira SL, Luo M, Matheson EM. Evaluation of Blood Biomarkers Associated with
447 Risk of Malnutrition in Older Adults: A Systematic Review and Meta-Analysis. *Nutrients* 2017;
448 9 (8): doi: 10.3390/nu9080829.
- 449 27. Sakr Y, Alhussami I, Nanchal R, Wunderink RG, Pellis T, Wittebole X, et al. Being Overweight Is
450 Associated With Greater Survival in ICU Patients: Results From the Intensive Care Over Nations
451 Audit. *Crit Care Med* 2015; 43 (12): 2623-2632. doi: 10.1097/CCM.0000000000001310.
- 452 28. Littleton SW. Impact of obesity on respiratory function. *Respirology* 2012; 17 (1): 43-49. doi:
453 10.1111/j.1440-1843.2011.02096.x.
- 454 29. Gong MN, Bajwa EK, Thompson BT, Christiani DC. Body mass index is associated with the
455 development of acute respiratory distress syndrome. *Thorax* 2010; 65 (1): 44-50. doi:
456 10.1136/thx.2009.117572.
- 457 30. O'Brien JM, Philips GS, Ali NA, Aberegg SK, Marsh CB, Lemeshow S. The association between
458 body mass index, processes of care, and outcomes from mechanical ventilation: a prospective
459 cohort study. *Critical care medicine* 2012; 40 (5): 1456-1463. doi:
460 10.1097/CCM.0b013e31823e9a80.
- 461 31. Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and
462 risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *The*
463 *Lancet* 2014; 384 (9945): 755-765. doi: 10.1016/s0140-6736(14)60892-8.
- 464 32. Wacharasint P, Boyd JH, Russell JA, Walley KR. One size does not fit all in severe infection:
465 obesity alters outcome, susceptibility, treatment, and inflammatory response. *Critical care*
466 (London, England) 2013; 17 (3): R122. doi: 10.1186/cc12794.
- 467 33. Stewart RM, Park PK, Hunt JP, McIntyre RC, McCarthy J, Zarzabal LA, et al. Less is more:
468 improved outcomes in surgical patients with conservative fluid administration and central
469 venous catheter monitoring. *J Am Coll Surg* 2009; 208 (5): doi:
470 10.1016/j.jamcollsurg.2009.01.026.
- 471 34. Wang Y, Ouyang Y, Liu B, Ma X, Ding R. Platelet activation and antiplatelet therapy in sepsis: A
472 narrative review. *Thromb Res* 2018; 166 28-36. doi: 10.1016/j.thromres.2018.04.007.
- 473 35. Kuperman EF, Showalter JW, Lehman EB, Leib AE, Kraschnewski JL. The impact of obesity on
474 sepsis mortality: a retrospective review. *BMC Infect Dis* 2013; 13 377. doi: 10.1186/1471-2334-
475 13-377.
- 476 36. Uji Y, Yamamoto H, Tsuchihashi H, Maeda K, Funahashi T, Shimomura I, et al. Adiponectin
477 deficiency is associated with severe polymicrobial sepsis, high inflammatory cytokine levels,
478 and high mortality. *Surgery* 2009; 145 (5): 550-557. doi: 10.1016/j.surg.2009.01.010.
- 479 37. Liang H, Ding X, Li L, Wang T, Kan Q, Wang L, et al. Association of preadmission metformin use
480 and mortality in patients with sepsis and diabetes mellitus: a systematic review and meta-
481 analysis of cohort studies. *Critical care (London, England)* 2019; 23 (1): 50. doi:
482 10.1186/s13054-019-2346-4.
- 483 38. Hui S, Ghergurovich JM, Morscher RJ, Jang C, Teng X, Lu W, et al. Glucose feeds the TCA cycle

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via circulating lactate. *Nature* 2017; 551 (7678): 115-118. doi: 10.1038/nature24057.

39. Niedziela J, Hudzik B, Niedziela N, Gąsior M, Gierlotka M, Wasilewski J, et al. The obesity paradox in acute coronary syndrome: a meta-analysis. *Eur J Epidemiol* 2014; 29 (11): 801-812. doi: 10.1007/s10654-014-9961-9.

40. McLaughlin T, Deng A, Yee G, Lamendola C, Reaven G, Tsao PS, et al. Inflammation in subcutaneous adipose tissue: relationship to adipose cell size. *Diabetologia* 2010; 53 (2): 369-377. doi: 10.1007/s00125-009-1496-3.

41. Shimada T, Topchiy E, Leung AKK, Kong HJ, Genga KR, Boyd JH, et al. Very Low Density Lipoprotein Receptor Sequesters Lipopolysaccharide Into Adipose Tissue During Sepsis. *Critical care medicine* 2020; 48 (1): 41-48. doi: 10.1097/CCM.0000000000004064.

42. Xing Z, Tang L, Chen J, Pei J, Chen P, Fang Z, et al. Association of predicted lean body mass and fat mass with cardiovascular events in patients with type 2 diabetes mellitus. *CMAJ* 2019; 191 (38): E1042-E1048. doi: 10.1503/cmaj.190124.

43. Xing Z, Peng Z, Wang X, Zhu Z, Pei J, Hu X, et al. Waist circumference is associated with major adverse cardiovascular events in male but not female patients with type-2 diabetes mellitus. *Cardiovasc Diabetol* 2020; 19 (1): 39. doi: 10.1186/s12933-020-01007-6.

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529 **Table1. Univariate analysis of baseline characteristics by BMI category**

	BMI<25	BMI 25-30	BMI>30	P
	kg/m ²	kg/m ²	kg/m ²	value
	(n=399)	(n=357)	(n=405)	
Age, n (%)	66.56(50.16	66.79(52.43-	62.97(51.94-	<0.00
	-80.25) ^a	77.63) ^b	72.92) ^b	1
<45	64(16.04)	47(13.17)	60(14.81)	
45-64	126(31.58) ^a	120(33.61) ^a	174(42.96) ^b	
65-89	177(44.36)	171(47.90)	164(40.49)	
>90	32(8.02) ^a	19(5.32) ^a	7(1.73) ^b	
Female, n (%)	207(51.88) ^a	141(39.50) ^b	206(50.86) ^a	0.001
Ethnicity, n (%)				0.183
White	297(74.43)	255(71.43)	305(75.31)	
Black	40(10.03)	36(10.08)	38(9.38)	
Hispanic or latino	11(2.76)	14(3.92)	11(2.72)	
Asian	7(1.75)	11(3.08)	1(0.25)	
Other	44(11.03)	41(11.49)	50(12.35)	
Marital status, n (%)				0.008
Married	169(42.36) ^a	196(54.90) ^b	196(48.40) ^{a,b}	
Single/divorced/separated/unknow	161(40.35)	121(33.89)	156(38.52)	
n				
Widowed	69(17.29)	40(11.20)	53(13.09)	
Admission type, n (%)				0.009
Elective	35(8.77) ^a	50(14.01) ^{a,b}	64(15.80) ^b	
Emergency/urgent	364(91.23) ^a	307(86.00) ^{a,b}	341(84.20) ^b	
Insurance type, n (%)				0.604
Medicare/Medicaid	261(65.41)	236(66.11)	250(61.73)	
Private	125(31.33)	109(30.53)	144(35.56)	
Other	13(3.26)	12(3.36)	11(2.72)	

SOFA	5(2-7) ^a	5(3-7) ^{a,b}	5(3-8) ^b	0.039
SAPS II	40(30-50)	39(29-50)	38(28-49)	0.473
SIRS	3(3-4)	3(3-4)	3(3-4)	0.786
qSOFA	2(1-2)	2(1-2)	2(1-2)	0.185
oasis	34(27-40)	33(28-41)	34(27-41)	0.941

Abbreviations: BMI: Body mass index; SOFA: sepsis-related organ failure assessment; SAPSII: Simplified Acute Physiology Score II; SIRS: systemic inflammatory response syndrome; OASIS: Oxford Acute Severity of Illness Score. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

Table 2. Univariate analysis of clinical outcome by gender category

Mortality, n (%)	BMI<25kg/m ² (n=399)	BMI25–30kg/m ² (n=357)	BMI>30 kg/m ² (n=405)	P
total Mortality, n (%)	241(60.40) ^a	168(47.06) ^b	178(43.95) ^b	<0.001
Hospital mortality	78(19.55)	65(18.21)	57(14.07)	0.102
30-day mortality	74(18.55) ^a	46(12.89) ^{a,b}	48(11.85) ^b	0.016
90-day mortality	112(28.07) ^a	83(23.25) ^{a,b}	84(20.74) ^b	0.048
Length of stay (day)				
Hospital LOS	14.8993(8.3479-28.6014)	15.3896(7.8535-27.0305)	16.1667(9.1011-29.8226)	0.137
ICU LOS	3.1343(1.7964-7.8206) ^a	3.5927(1.8996-8.9135) ^a	4.9257(2.1882-13.5617) ^b	<0.001

Abbreviations: BMI: Body mass index; LOS: length of stay. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

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Table 3. Univariate analysis of sepsis by BMI category

	BMI<25kg/m ² (n=399)	BMI25–30kg/m ² (n=357)	BMI>30 kg/m ² (n=405)	P
sepsis	78(19.55) ^a	81(22.69) ^{a,b}	121(29.88) ^b	0.002
sepsis shock	36(9.02) ^a	51(14.29) ^{a,b}	68(16.79) ^b	0.004

Abbreviations: BMI: Body mass index. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

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645 **Table 4. Univariate analysis of requirement of organ support therapy by BMI category**

	BMI <25kg/m ² (n=399)	BMI 25–30kg/m ² (n=357)	BMI >30 kg/m ² (n=405)	P
Ventilation , n(%)	209(52.38) ^a	203(56.86) ^{a,b}	249(61.48) ^b	0.034
Dialysis, n (%)	24(6.01)	30(8.40)	32(7.90)	0.409
Vasoactive agent, n (%)	138(34.59)	123(34.45)	143(35.31)	0.964

Abbreviations: BMI: Body mass index; The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

Table 5. Univariate analysis of laboratory examination by BMI category

	BMI<25kg/m ²	BMI25-30kg/m ²	BMI>30kg/m ²	P
		9.66±	9.84±	
HGB (g/dL)	9.50±1.85 ^a ,n=396	1.96 ^{a,b} ,n=355	1.92 ^b ,n=403	0.048
	10.10(6.20-14.85)	9.70(6.50-13.80) ^a ,	10.85(7.13-15.20)	
WBC (K/uL)	^{a,b} , n=396	n=355	^b ,n=404	0.035
	184.5(112.25-	182.0(124.00-	190.00(126.00-	
PLT (K/uL)	268.00), n=396	252.00), n=355	273.50), n=405	0.402
	1.10(0.80-1.80) ^a ,	1.20(0.9-2.20) ^b ,	1.30(0.90-2.20) ^b ,	
CRE (mg/dL)	n=396	n=355	n=405	0.001
	24.00(16.00-	25.00(16.00-	25.00(16.00-	
BUN (mg/dL)	39.00), n=396	41.00), n=355	44.00), n=405	0.61
		2.7(2.2-3.2),	2.7(2.3-3.1),	
ALB (g/dL)	2.6(2.2-3.1), n=234	n=215	n=228	0.463
	109(105-113) ^a ,	109(105-112) ^a ,	108(104-111) ^b ,	
Cl (mEq/L)	n=396	n=356	n=405	0.007
	3.60(3.20-4.00),	3.70(3.30-4.00),	3.70(3.40-4.10),	
K (mEq/L)	n=396	n=356	n=405	0.168
	136.0(132.0-	136.0(133.0-	136.0(133.5-	
Na (mEq/L)	139.0), n=396	139.0), n=356	139.0), n=405	0.235
	153.00(122.00-	154.00(125.00-	170.00(136.5-	
GLU (mg/dL)	194.00) ^a , n=396	195.75) ^a , n=356	226.00) ^b , n=405	<0.001
	2.50(1.6-4.5),	2.70(1.5-4.425),	2.30(1.4-4.2),	
LAC (mmol/L)	n=312	n=286	n=325	0.324
	1.10(0.5-3.05),	1.20(0.6-2.43),	1.00(0.5-2.5),	
BIL (mg/dL)	n=262	n=255	n=284	0.528

Abbreviations: BMI: Body mass index; HGB: hemoglobin; WBC: white blood cell count; PLT: platelet count; ALB: albumin; CRE: creatinine; BUN: urea nitrogen; GLU: glucose; LAC: lactate; BIL: bilirubin; Na: sodium; Cl: chlorine; K: potassium. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

Table 6. Result of the Cox proportional hazard regression analysis

	OR	95.0% CI		P value
BMI	0.974	0.956	0.992	0.004
Gender	1.116	0.857	1.454	0.415
Admission age	1.029	1.021	1.038	0.000
Admission type	1.876	1.121	3.138	0.017
Marital status	1.025	0.865	1.214	0.776
LOS in hospital	0.983	0.973	0.994	0.002
LOS in icu	1.012	0.999	1.025	0.078
Sepsis	2.124	1.514	2.979	0.000
Septic shock	0.704	0.481	1.029	0.070
WBC	1.006	0.991	1.022	0.441
Hemoglobin	0.905	0.847	0.966	0.003
Creatinine	0.999	0.931	1.073	0.987
Chloride	1.002	0.982	1.021	0.871
Glucose	1.000	0.999	1.001	0.515
SOFA score	1.109	1.065	1.155	0.000
Ventilation	0.939	0.696	1.266	0.678

Abbreviations: BMI: Body mass index; SOFA: sepsis-related organ failure assessment; LOS: length of stay; ICU: intensive care unit; WBC: white blood cell counting.

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Legends for the figures

Figure 1. Kaplan–Meier curve for 90-days survival stratified by BMI.
Abbreviations: BMI: Body mass index; Fig. 1 represents 90-days Kaplan–Meier curves, $P<0.001$ by log-rank test.

Figure 2. Flowchart of study cohort selection.

Figure 3. Kaplan–Meier curve for 90-days survival stratified by BMI.
Abbreviations: BMI: Body mass index; Fig. 3 represents 90-days Kaplan–Meier curves stratified by BMI in three groups, $P<0.001$ by log-rank test.

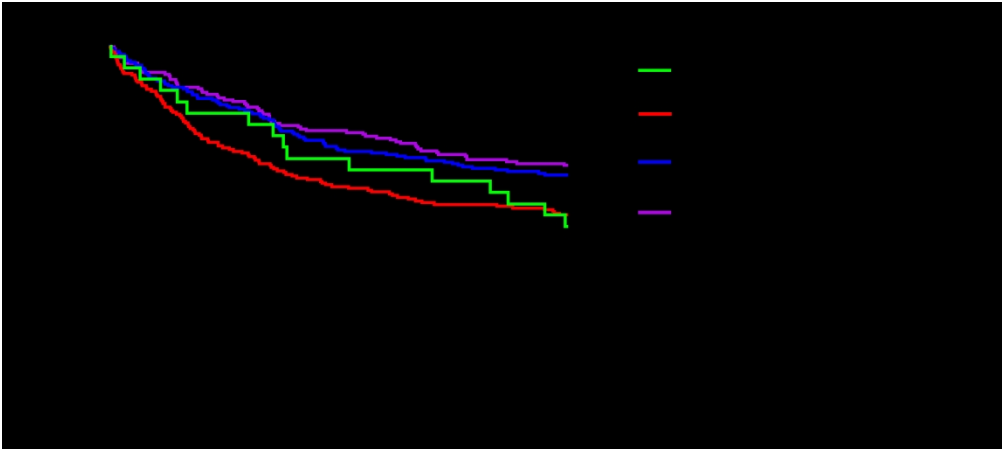
Figure 4. 90-days Kaplan–Meier curve of patients without (A) and with(B) sepsis stratified by BMI. Abbreviations: BMI: Body mass index; Fig. 4(A) and 4(B) represents 90-days Kaplan–Meier curves of patients without and with sepsis respectively. In log rank test $P<0.001$, $P<0.05$, respective.

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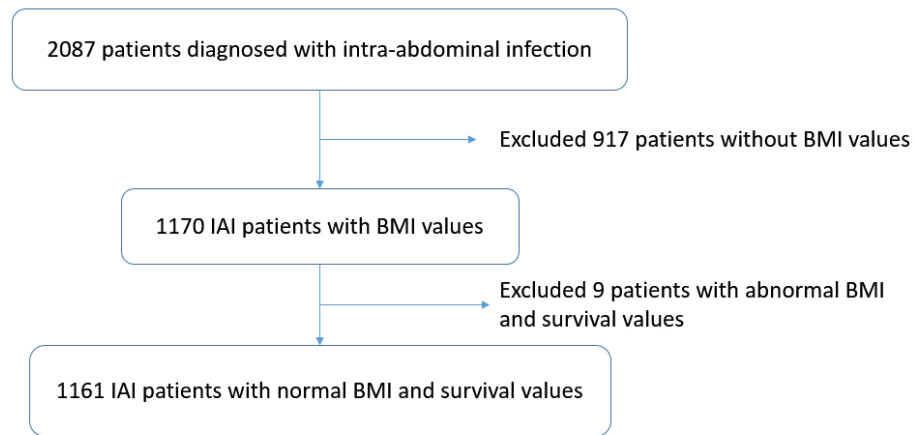
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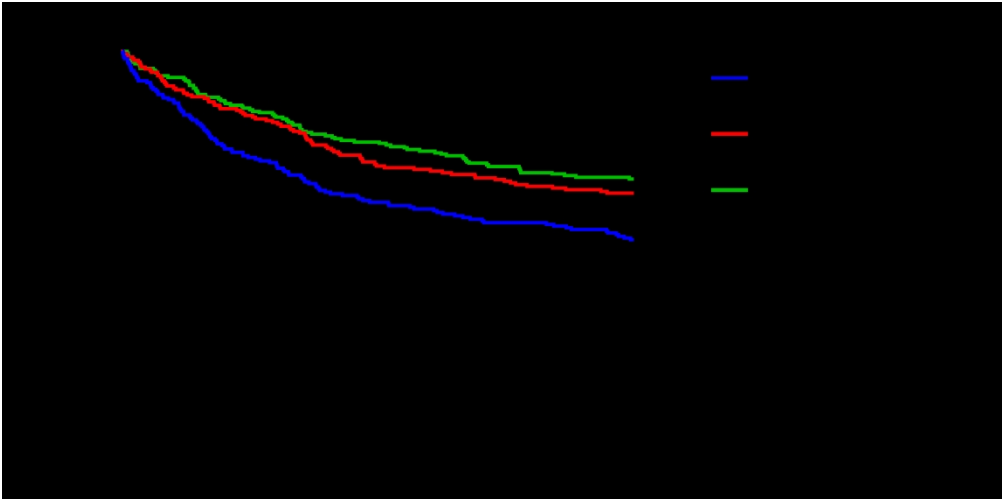
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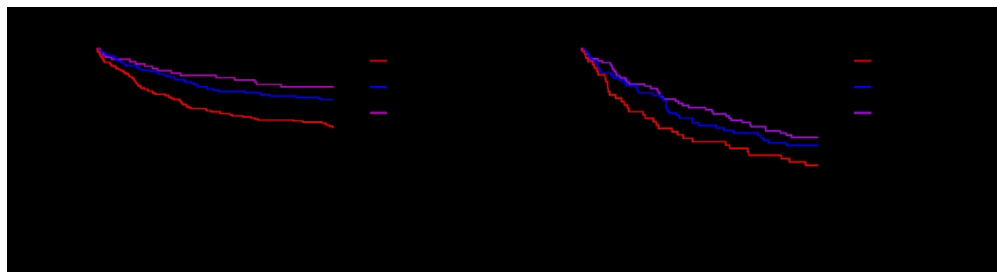
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Supplementary material:

Table S1.ICD-9 codes and diagnostics in study cohort

ICD-9 code	diagnostics
53110	Acute gastric ulcer with perforation, without mention of obstruction
53111	Acute gastric ulcer with perforation, with obstruction
53120	Acute gastric ulcer with hemorrhage and perforation, without mention of obstruction
53121	Acute gastric ulcer with hemorrhage and perforation, with obstruction
53150	Chronic or unspecified gastric ulcer with perforation, without mention of obstruction
53151	Chronic or unspecified gastric ulcer with perforation, with obstruction
53160	Chronic or unspecified gastric ulcer with hemorrhage and perforation, without mention of obstruction
53161	Chronic or unspecified gastric ulcer with hemorrhage and perforation, with obstruction
53210	Acute duodenal ulcer with perforation, without mention of obstruction
53211	Acute duodenal ulcer with perforation, with obstruction
53220	Acute duodenal ulcer with hemorrhage and perforation, without mention of obstruction
53221	Acute duodenal ulcer with hemorrhage and perforation, with obstruction
53250	Chronic or unspecified duodenal ulcer with perforation, without mention of obstruction
53251	Chronic or unspecified duodenal ulcer with perforation, with obstruction
53260	Chronic or unspecified duodenal ulcer with hemorrhage and perforation, without mention of obstruction
53261	Chronic or unspecified duodenal ulcer with hemorrhage and perforation, with obstruction
53310	Acute peptic ulcer of unspecified site with perforation, without mention of obstruction
53311	Acute peptic ulcer of unspecified site with perforation, with obstruction
53320	Acute peptic ulcer of unspecified site with hemorrhage and perforation, without mention of obstruction
53321	Acute peptic ulcer of unspecified site with hemorrhage and perforation, with obstruction
53350	Chronic or unspecified peptic ulcer of unspecified site with perforation, without mention of obstruction
53351	Chronic or unspecified peptic ulcer of unspecified site with perforation, with obstruction
53360	Chronic or unspecified peptic ulcer of unspecified site with hemorrhage and perforation, without mention of obstruction
53361	Chronic or unspecified peptic ulcer of unspecified site with hemorrhage and perforation, with obstruction
53410	Acute gastroduodenal ulcer with perforation, without mention of obstruction
53411	Acute gastroduodenal ulcer with perforation, with obstruction

53420	Acute gastrojejunal ulcer with hemorrhage and perforation, without mention of obstruction
53421	Acute gastrojejunal ulcer with hemorrhage and perforation, with obstruction
53430	Acute gastrojejunal ulcer without mention of hemorrhage or perforation, without mention of obstruction
53450	Chronic or unspecified gastrojejunal ulcer with perforation, without mention of obstruction
53451	Chronic or unspecified gastrojejunal ulcer with perforation, with obstruction
53460	Chronic or unspecified gastrojejunal ulcer with hemorrhage and perforation, without mention of obstruction
53461	Chronic or unspecified gastrojejunal ulcer with hemorrhage and perforation, with obstruction
53641	Infection of gastrostomy
53901	Infection due to gastric band procedure
53981	Infection due to other bariatric procedure
5400	Acute appendicitis with generalized peritonitis
5401	Acute appendicitis with peritoneal abscess
5511	Umbilical hernia with gangrene
55120	Ventral hernia, unspecified, with gangrene
55121	Incisional ventral hernia, with gangrene
55129	Other ventral hernia with gangrene
5513	Diaphragmatic hernia with gangrene
5518	Hernia of other specified sites, with gangrene
5519	Hernia of unspecified site, with gangrene
56081	Intestinal or peritoneal adhesions with obstruction (postoperative) (postinfection)
56722	Peritoneal abscess
56729	Other suppurative peritonitis
56738	Other retroperitoneal abscess
56739	Other retroperitoneal infections
56789	Other specified peritonitis
5679	Unspecified peritonitis
5680	Peritoneal adhesions (postoperative) (postinfection)
56961	Infection of colostomy or enterostomy
56981	Fistula of intestine, excluding rectum and anus
56983	Perforation of intestine
5754	Perforation of gallbladder
5755	Fistula of gallbladder
5763	Perforation of bile duct
5764	Fistula of bile duct
5770	Acute pancreatitis

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TableS2. Univariate analysis of baseline characteristics by BMI category after adjustment of confounding factors

	BMI<25	BMI 25-30	BMI>30	P
	kg/m ²	kg/m ²	kg/m ²	value
	(n=357)	(n=357)	(n=357)	
Age,n(%)				0.137
<45	51(14.29)	47(13.17)	43(12.04)	
45-64	116(32.49) a	120(33.61) ^a b	150(42.02) ^b	
65-89	161(45.10)	171(47.90)	157(43.98)	
>90	29(8.12) ^a	19(5.32) ^a	7(1.96) ^b	
Female, n (%)	167(46.78)	141(39.50)	162(45.38)	0.115
Ethnicity, n (%)				0.199
White	264(73.95)	254(71.15)	268(75.07)	
Black	37(10.36)	36(10.08)	34(9.52)	
Hispanic or latino	10(2.80)	14(3.92)	8(2.24)	
Asian	6(1.68)	11(3.08)	1(0.28)	
Other	40(11.20)	42(11.76)	46(12.89)	
Marital status, n (%)				0.303
Married	167(46.78)	196(54.90)	183(51.26)	
Single/divorced/separated/unknow				
n	142(39.78)	121(33.89)	128(35.85)	
Widowed	48(11.20)	40(11.20)	46(12.89)	
Admission type, n (%)				0.036
Elective	33(9.24) ^a	50(14.01) ^{a,b}	55(15.41) ^b	
Emergency/urgent	324(90.76) a	307(85.99) ^a b	302(84.59) ^b	
Insurance type, n (%)				0.550
Medicare/Medicaid	237(66.39)	236(66.11)	224(62.75)	
Private	108(30.25)	109(30.53)	125(35.01)	
Other	12(3.36)	12(3.36)	8(2.24)	

SOFA	5(3-8) ^a	5(3-7) ^{a,b}	5(3-9) ^b	0.014
SAPS II	40(30-50)	39(29-50)	39(29.5-50)	0.794
SIRS	3(3-4)	3(3-4)	3(3-4)	0.805
qSOFA	2(1-2)	2(1-2)	2(1-2)	0.122
oasis	34(27-40)	33(28-41)	34(27-41)	0.943

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44 **Table S3. Univariate analysis of clinical outcome by gender category after adjustment of**
45 **confounding factors**

Mortality,n(%)	BMI<25 kg/m ² (n=357)	BMI25–30kg/m ² (n=357)	BMI>30 kg/m ² (n=357)	P
total Mortality , n (%)	213(59.66) ^a	168(47.06) ^b	164(45.94) ^b	<0.001
Hospital mortality	69(19.33)	65(18.21)	51(14.29)	0.174
30-day mortality	65(18.21)	47(13.17)	45(12.61)	0.066
90-day mortality	99(27.73)	83(23.25)	76(21.29)	0.119
Length of stay (day)				
Hospital LOS	14.9771(8.5299-28.5330)	15.3896(7.8535-27.0305)	16.1667(9.1997-29.8719)	0.16
ICU LOS	3.1343(1.8290-7.8076) ^a	3.5927(1.8996-8.9135) ^a	4.9747(2.2122-13.4524) ^b	<0.001

Table S4. Univariate analysis of sepsis by BMI category after adjustment of confounding factors

	BMI<25kg/m ² (n=357)	BMI25–30kg/m ² (n=357)	BMI>30 kg/m ² (n=357)	P
sepsis	67(18.77) ^a	81(22.69) ^{a,b}	109(30.53) ^b	0.001
sepsis shock	30(8.40) ^a	51(14.29) ^b	62(17.37) ^b	0.002

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Table S5. Univariate analysis of requirement of organ support therapy by BMI category after adjustment of confounding factors

	BMI<25kg/m ² (n=357)	BMI25–30kg/m ² (n=357)	BMI>30 kg/m ² (n=357)	P
Ventilation , n(%)	188(52.66)	203(56.86)	219(61.34)	0.064
Dialysis, n (%)	21(5.9)	30(8.4)	28(7.8)	0.4
Vasoactive agent, n(%)	123(34.45)	123(34.45)	129(36.13)	0.863

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Table S6. Univariate analysis of laboratory examination by BMI category

	BMI<25kg/m ²	BMI25-30kg/m ²	BMI>30kg/m ²	P
HGB	9.50(8.30-10.70)n=354	9.60(8.4-10.80)n=355	9.70(8.6-11.2)n=356	0.053
WBC	10(6.1-14.525)n=354	9.7(6.5-13.8)n=355	10.7(6.825-14.575)n=356	0.145
PLT	184.5(114.5-269.5)n=354	182.0(124.0-252.0)355	187(123.5-269.5)357	0.732
CRE	1.1(0.8-1.8) ^a ,n=354	1.2(0.9-2.2) ^b ,n=355	1.4(0.9-2.3) ^b ,n=357	<0.001
BUN	25(16-39)n=354	25(16-41)n=355	26(16-44.5)n=357	0.57
ALB	2.6476±0.7267 n=208	2.7070±0.6912 n=215	2.7090±0.6789 n=201	0.597
Cl	108(105-113) ^{a,b} ,n=354	109(105-112) ^a ,n=356	108(104-112) ^b ,n=357	0.021
K	3.6(3.2-4.0)n=354	3.7(3.3-4.0)n=356	3.7(3.4-4.1)n=357	0.124
Na	135(132-139) ^a ,n=354	136(133-139) ^{a,b} ,n=356	137(134-139) ^b ,n=357	0.042
GLU	152(122.75-194) ^a ,n=354	154(125-195.75) ^a ,n=356	168(136.5-224) ^b ,n=357	0.001
LAC	2.6(1.6-4.6)n=279	2.7(1.5-4.425)n=286	2.4(1.4-4.2)n=287	0.329
BIL	1(0.5-2.85)	1.2(0.6-2.425)	1.1(0.6-2.5)	0.397

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Table S7.Result of the Cox proportional hazard regression analysis after adjustment of confounding factors

	OR	95.0% CI		P value
BMI	0.972	0.959	0.985	0.000
gender	1.025	0.856	1.227	0.789
Admission age	1.027	1.021	1.033	0.000
Admission type	1.417	1.071	1.875	0.015
SOFA	1.111	1.075	1.149	0.000
Ventilation	0.915	0.750	1.116	0.380
LOS in icu	1.000	0.992	1.007	0.950
Sepsis	2.250	1.739	2.911	0.000
Septic shock	0.807	0.589	1.105	0.181
Hemoglobin	0.913	0.868	0.960	0.000
WBC	1.006	0.997	1.015	0.185
Creatinine	0.993	0.940	1.048	0.789
Chloride	0.985	0.968	1.002	0.089
Potassium	1.156	0.976	1.369	0.094
Sodium	1.020	1.000	1.041	0.050
Glucose	1.000	1.000	1.001	0.548
qSOFA	0.935	0.811	1.077	0.351

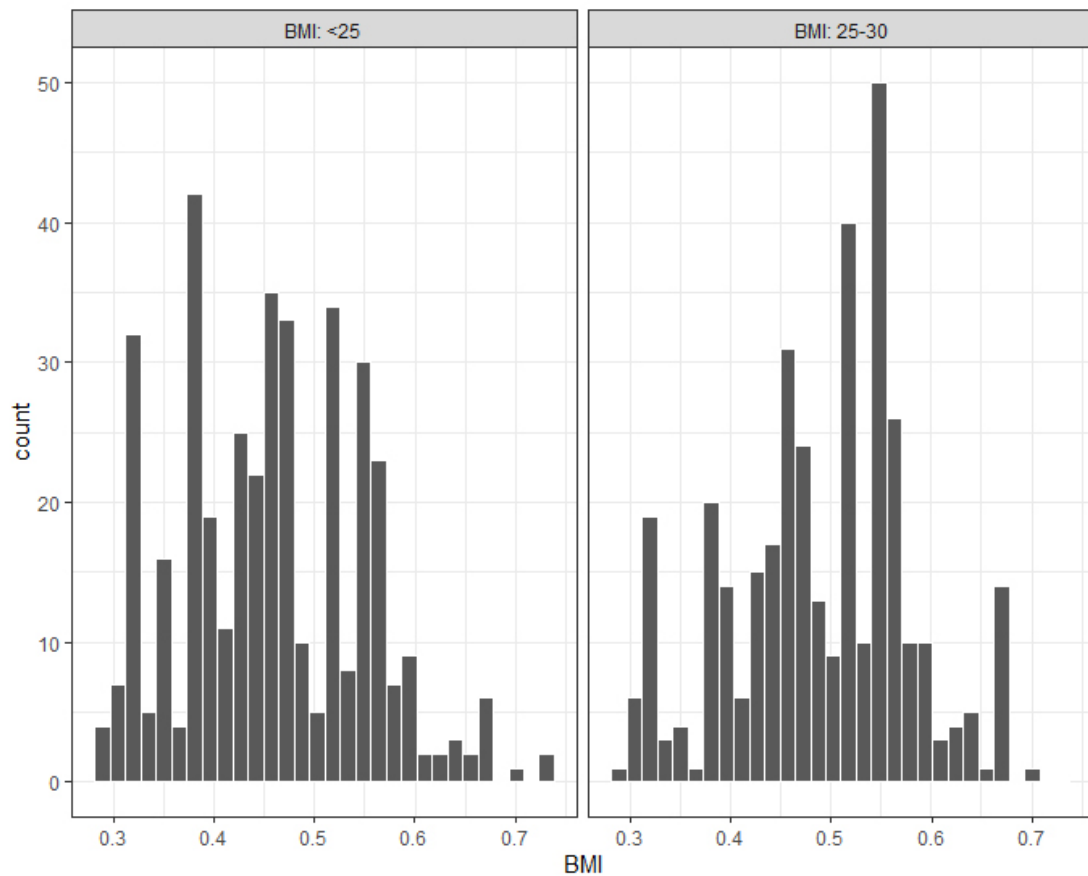


Figure S1. Propensity score counting of normal and overweight patients.

Abbreviations: BMI: Body mass index;

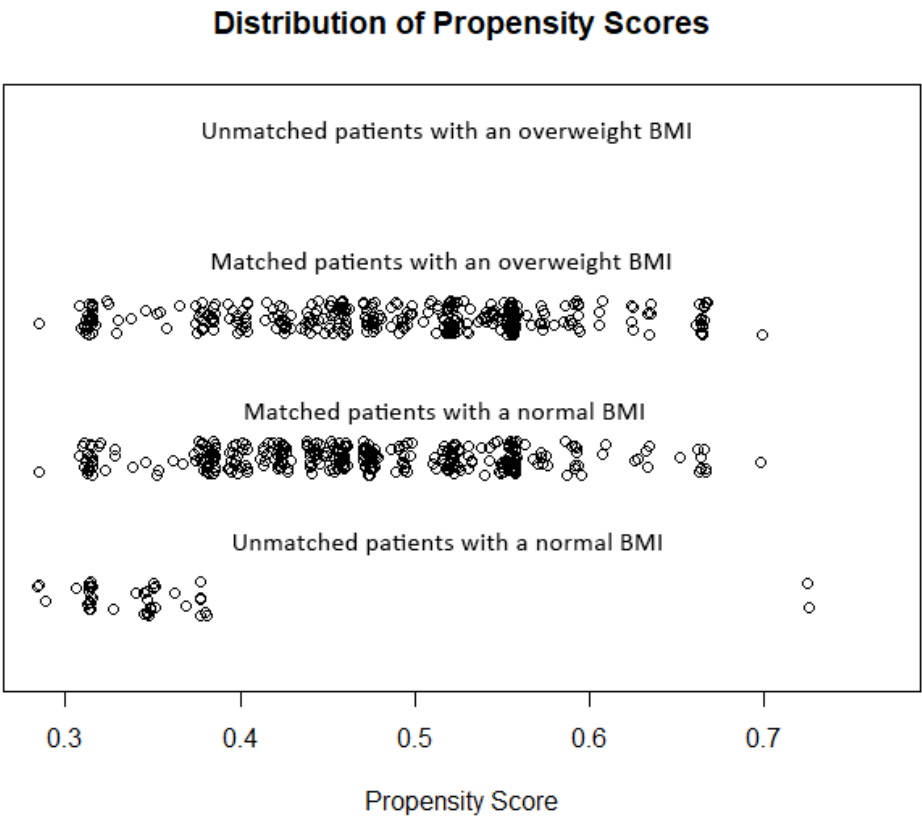


Figure S2. Distribution of propensity scores between normal and overweight patients. Abbreviations: BMI: Body mass index;

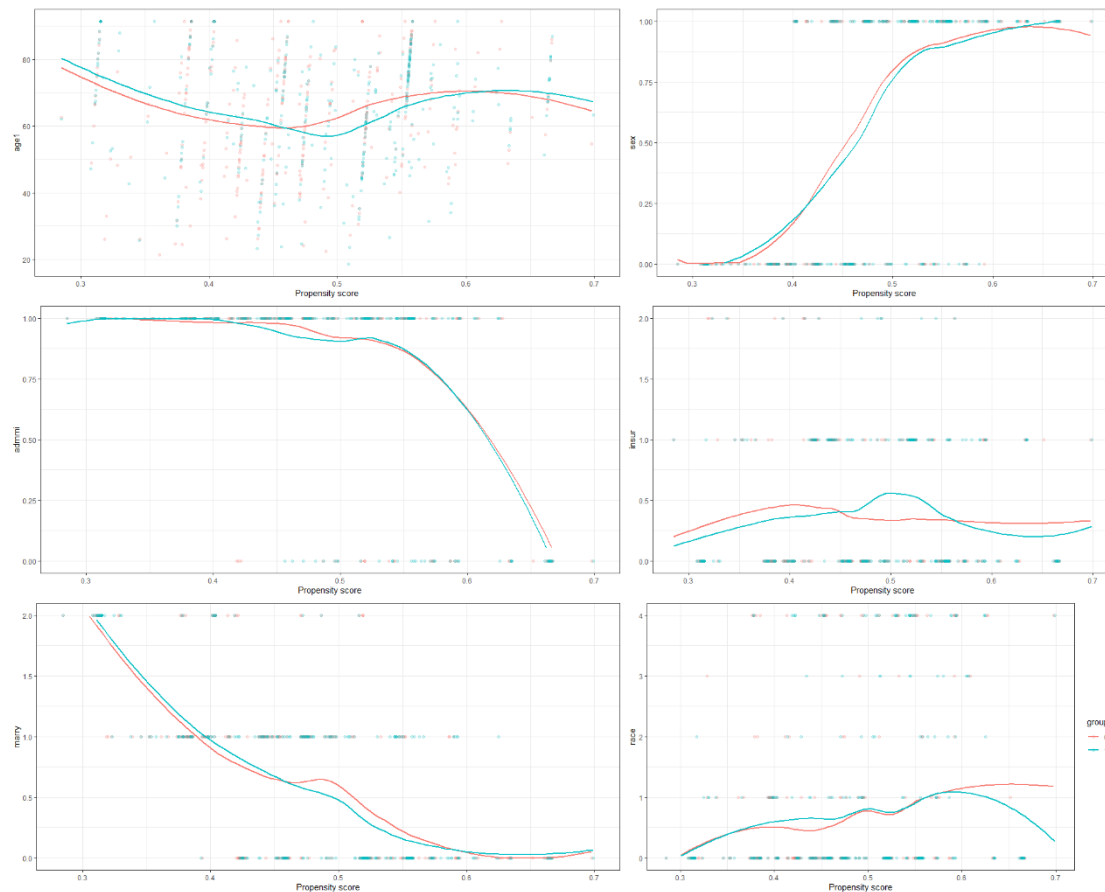


Figure S3. Trend of baseline characteristics after adjustment for confounding factors. Abbreviations: BMI: Body mass index; age1: Admission age of patients; sex: gender of patients; admmt: Admission type of patients; insur: Insurance type of patients; marry: Marital status of patients; race: Ethnicity of patients; group 0: patients with an overweight BMI; group 1: patients with a normal BMI;

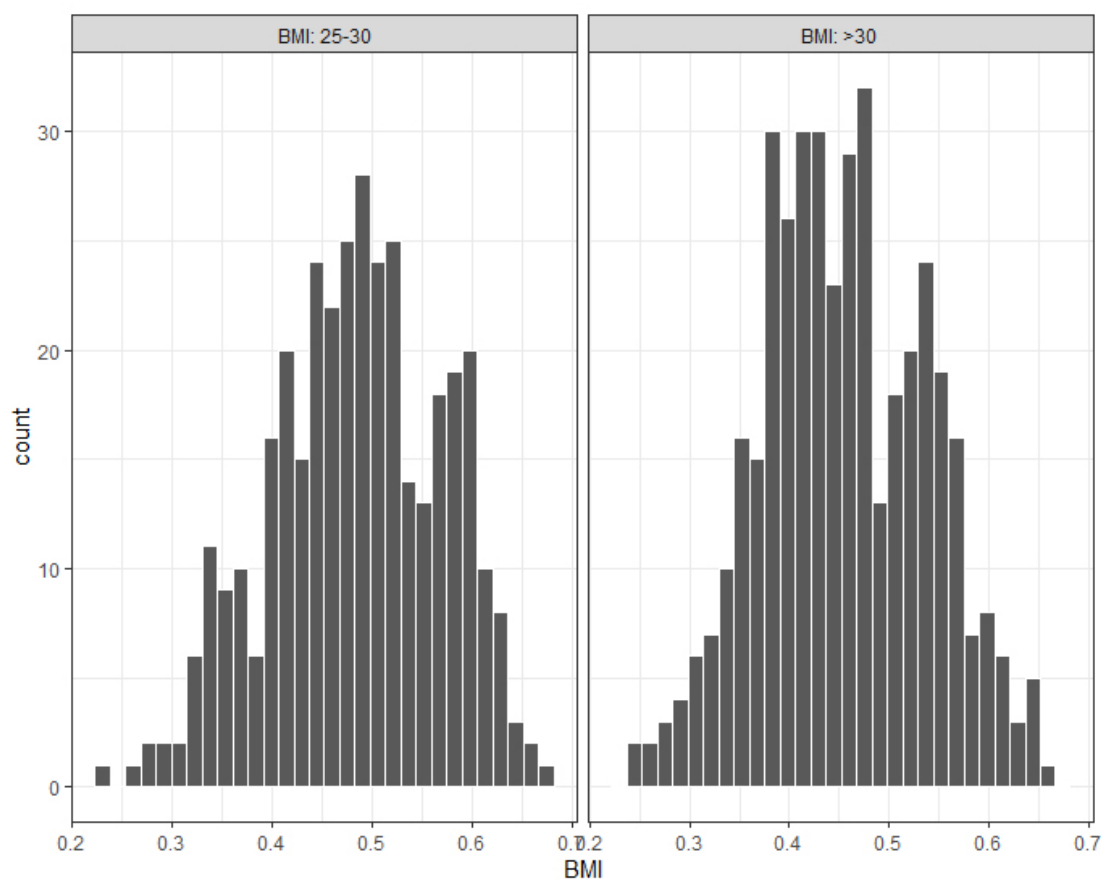


Figure S4. Propensity score counting of obese and overweight patients.

Abbreviations: BMI: Body mass index;

Distribution of Propensity Scores

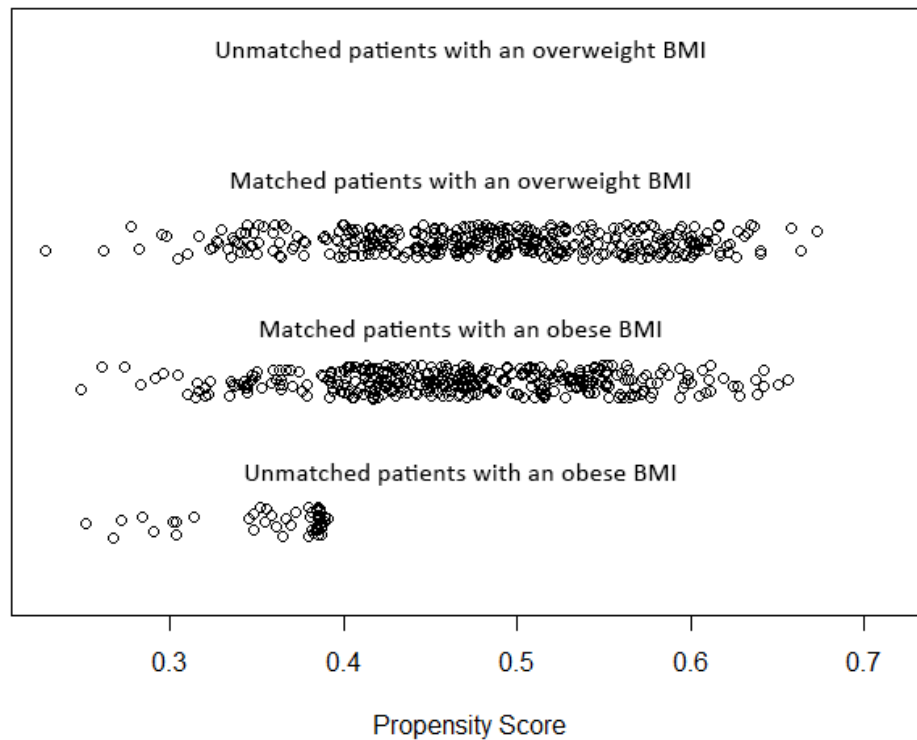


Figure S5. Distribution of propensity scores between obese and overweight patients. Abbreviations: BMI: Body mass index;

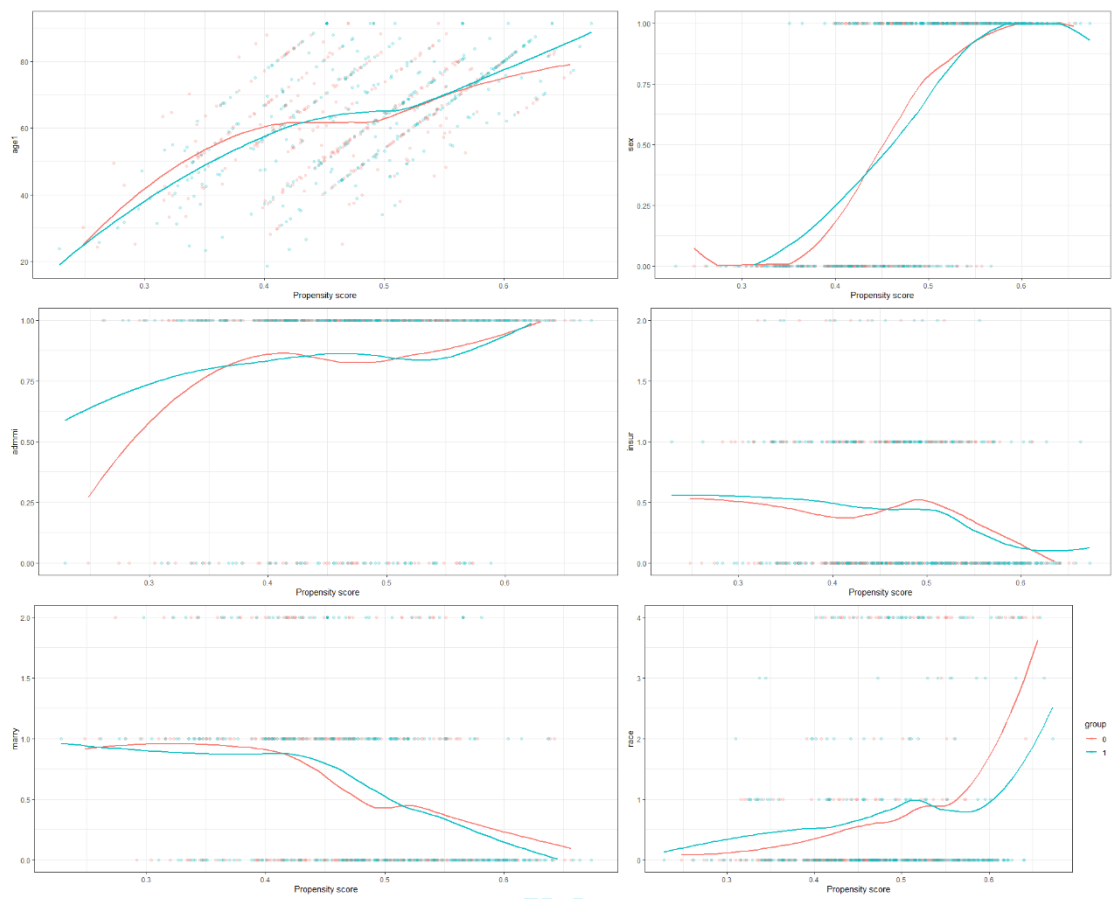


Figure S6. Trend of baseline characteristics after adjustment for confounding factors. Abbreviations: BMI: Body mass index; age1: Admission age of patients; sex: gender of patients; admmt: Admission type of patients; insur: Insurance type of patients; marry: Marital status of patients; race: Ethnicity of patients; group 0: patients with an overweight BMI; group 1: patients with a obese BMI;

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Body mass index affects the short-term mortality of patients with intra-abdominal infections: a retrospective study using the Medical Information Mart for Intensive Care database.

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31 **Abstract**

32 **Objectives:** This study aimed to determine the relationship between the body mass
33 index (BMI) and short-term mortality of patients with intra-abdominal infection (IAI)
34 using the Medical Information Mart for Intensive Care (MIMIC-III) database.

35 **Design:** Retrospective cohort study.

36 **Setting:** Adult intensive care units (ICUs) at tertiary hospitals.

37 **Participants:** Adult IAI ICU patients from 2001 to 2012 in the MIMIC-III database.

38 **Interventions:** In univariate analysis, we compared the differences in the
39 characteristics of patients in each BMI group. Cox regression models were used to
40 evaluate the relationships between BMI and short-term prognosis.

41 **Primary and secondary outcome measures:** 90-day survival.

42 **Results:** In total, 1161 patients with IAI were included. There were 399 (34.4%)
43 patients with a normal BMI ($< 25 \text{ kg/m}^2$), 357(30.8%) overweight patients (25-30
44 kg/m^2), and 405(34.9%) obese patients ($> 30 \text{ kg/m}^2$) who tended to be younger (p
45 <0.001) and had higher Sequential Organ Failure Assessment (SOFA) scores ($p <0.05$).
46 The mortality of obese patients at 90 days was lower than that of patients with a normal
47 BMI ($p <0.05$), but their length of stay(LOS) in the ICU was higher ($p <0.001$); however,
48 their rate of mechanical ventilation utilisation was higher ($p <0.05$). In the Cox
49 regression model, we also confirmed that BMI was a protective factor in patients with
50 IAIs, and the adjusted mortality rate of patients with a higher BMI was 0.97- times
51 lower than that of patients with a lower BMI ($p <0.001$, hazard ratio[HR] =0.97, 95%
52 CI 0.96-0.99).

53 **Conclusions:** IAI patients with an overweight or obese status might have lower 90-day
54 mortality than patients with a normal BMI.

55 **Strengths and limitations of this study**

- 56
- 57 • To our knowledge, this is the first study to evaluate the effects of BMI on the
58 short-term mortality of patients with abdominal infection.
 - 59 • Multiple imputation was used to handle the missing values.
 - 60 • This study is essentially a retrospective single-centre study, which makes it
difficult to completely exclude the influence of residual confounding factors.

- A considerable number of patients' data are missing, especially various laboratory test data, which may cause selection bias.

Key word: Intra-abdominal infection; BMI; MIMIC-III; Big data; Mortality; ICU;

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911. INTRODUCTION

Intra-abdominal infections (IAIs) are common surgical emergencies and have been reported as major contributors to non-trauma deaths in emergency departments worldwide and a common complication of abdominal surgery ¹. IAIs are the second most common cause of sepsis, and the second most common infectious disease among inpatients. The death rate of IAIs can reach 20%, indicating a commonly poor prognosis in patients ^{2 3}. IAIs can be divided into uncomplicated and complicated types. Uncomplicated IAIs affect a single organ, and complicated IAIs describe an extension of the infection into the peritoneal space. The resultant physiologic response may develop into a systemic inflammatory response syndrome (SIRS)⁴. The most extensively studied biomarkers in the context of IAIs are C-reactive protein and procalcitonin. In addition, some serum mediators, such as proadrenomedullin and cytokines, are not commercially available for routine monitoring⁵. The role of these biomarkers remain limited.

The body mass index(BMI), calculated as the weight divided by the square of the height, is used by most health organizations, including the World Health Organization (WHO), as a screening tool for diagnosing obesity⁶. Overweight and obesity are uniformly associated with a substantially increased risk of death⁷. In patients not admitted to the intensive care unit (ICU), such as endometrial and breast cancer patients, BMI can be used as a prognostic indicator ^{8 9}. Similarly, in ICU patients, such as liver transplant patients, morbid obesity has an impact on patient survival and post-transplant complications¹⁰. Furthermore, at least a quarter of patients in U.S. ICUs have a BMI indicating overweight, obesity or morbid obesity status ¹¹. As mentioned above, patients with IAIs also tend to develop severe conditions and were admitted in the ICU. Previous studies have shown that obesity plays a protective role in some diseases (such as chronic kidney disease, AIDS), which is a special phenomenon called the obesity paradox ¹² ¹³.However, in ICU patients with IAIs, whether BMI is a risk factor or a protective factor, considering the obesity paradox , still needs further study.

This study was aimed to determine the relationship between BMI and the 90-day mortality of patients with IAIs using the Medical Information Mart for Intensive Care

(MIMIC-III) database¹⁴. The MIMIC-III database is a large, single-centre database comprising information related to patients admitted to critical care units at a large tertiary care hospital. Data included vital signs, medications, laboratory measurements, diagnostic codes, hospital length of stay, survival data, etc. The data cover 53,423 distinct hospital admissions for adult patients admitted to critical care units between 2001 and 2012, and many studies have been conducted to explore the clinical features of ICU patients using the database.

2. MATERIALS AND METHODS

2.1. Database

In this article, we used a publicly available critical care medicine database, MIMIC-III. This database contains unidentified medical information from about 60000 patients admitted to the critical care units of the Beth Israel Deaconess Medical Center in Boston, Massachusetts, from 2001 to 2012. The database maintained by the Laboratory for Computational Physiology at the Massachusetts Institute of Technology (MIT). In MIMIC database, all diagnostics correspond to International Classification of Diseases (ICD-9) codes. The use of MIMIC-III database was under the approval from the review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center¹⁵. The database is freely available, in that any researcher who accepts the data-use agreement and has completed the “protecting human subjects” training can apply for permission to access the data. We did not need patient consent or ethics approval, as all of the data were de-identified. All authors completed the “protecting human subjects” training.

2.2. Study population

There is no specific IAI diagnosis in ICD-9 coding; therefore, we included all the possible diagnoses related to IAIs in ICD-9 into our study cohort, and all ICD-9 codes, diagnostics and numbers of specific diagnoses are listed in Table S1. For patients who had multiple ICU admissions, only the first admission record was kept. The exclusion criteria were as follows: (1) those under 18 years old and (2) missing weight data. According to the BMI classification standard of the WHO, we divided the patients into five groups: underweight ($BMI < 18.5 \text{ kg/m}^2$), normal weight ($BMI: 18.5 \text{ to } < 25 \text{ kg/m}^2$),

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overweight (BMI: 25 to <30 kg/m²), obese (BMI 30 to <40 kg/m²), and morbidly obese (BMI > 40kg/m²). However, in this grouping method, the number of patients in the underweight and morbidly obese subgroups was not sufficient (n = 27 and 54, respectively, as shown in Figure S1). Finally, all patients were divided into three groups: normal BMI group (BMI < 25kg/m²), overweight BMI group (25-30 kg/m²) and obese BMI group (BMI > 30kg/m²).

2.3. Data extraction and management

We used the structure query language (SQL) in PostgreSQL (version 9.5) to retrieve the data. The following data were extracted from the MIMIC-III database on the first day of ICU admission: age; sex; ethnicity; admission weight; admission height; admission diagnosis; admission type; Sequential Organ Failure Assessment (SOFA) score; Simplified Acute Physiology Score II (SAPSII); Charlson Comorbidity Index; use of vasopressors; renal replacement therapy (RRT); mechanical ventilation use; values of hemoglobin(HGB); white blood cell(WBC); platelet count(PLT); albumin(ALB); sodium(Na); chlorine(Cl) ; potassium(K); creatinine(CRE);blood urea nitrogen(BUN); glucose(GLU) ; lactate(LAC) , and bilirubin(BIL) levels in the first 24 h of ICU admission; length of stay(LOS) before ICU admission; length of stay (both ICU and hospital); intake and output. The SOFA score was calculated within the first 24 h after ICU admission. If a variable was measured more than once in the first 24 h, the value that indicated a worse prognosis was used. In addition, dates of birth for patients aged over 89 years were moved to obscure their true age and comply with HIPAA regulations: these patients appear in the database with ages of over 300 years, but the median age of these patients was 91.5 years, so we modified their age to 91.5 years.

2.4. Outcomes

The primary endings was the 90-day mortality after ICU admission.

2.5. Patient and public involvement

We did not need patient consent or ethics approval, as all data were de-identified. The use of MIMIC-III database was approved by the review boards of the MIT and Beth Israel Deaconess Medical Centre.

2.6. Statistical analysis

First, univariate analysis was used to compare all variables. If the data satisfied a normal distribution and the variance was homogeneous, the data were expressed as the mean \pm standard deviation, and Student's t-test was used for comparisons. If the variance was not homogeneous, one-way ANOVA was used for the comparisons. If none of the above requirements were met or the data were not continuous variables, then the data were described as the median and interquartile range, and the Wilcoxon rank-sum test was used for comparisons. Categorical variables were presented as numbers and percentages and compared using Pearson's chi-square test or Fisher's exact test as appropriate. We used the log-rank test and 90-day Kaplan–Meier(K-M) curves to carry out the survival analysis, and determined whether BMI affects 90-day mortality. In addition, we compared the 90-day survival curves between subgroups of patients with and without sepsis using log-rank test.

Propensity score matching (PSM) was performed to minimize the influence of confounding factors on selection bias. The propensity scores were elicited from matched patients in a 1:1 ratio with greedy matching algorithms without replacement. We adjusted for age, gender, admission type, ethnicity, marital status and insurance type.

We used multiple imputation (MI), based on five replications and a chained equation approach method in the R STUDIO MI procedure, to account for missing data on height and the missing laboratory test¹⁶. Multivariate analyses were adjusted for the possible variables that may affect the prognosis of patients to determine the relationship between BMI and 90- day mortality.

We tested the collinearity of the variables included in the statistical analysis, and found that the variance inflation factor (VIF) of all variables was < 3 ; hence, there was no statistical collinearity in the included variables.

Variables with $p < 0.10$ in univariate analysis were included in the Cox regression model as confounders to determine whether BMI was the independent risk factor of the 90-day survival rates. However, since SOFA scores included BIL and CRE level, PLT count, mechanical ventilation use, and vasoactive drug use, and Charlson

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comorbidity index includes comorbidity, to avoid instability of the model caused by collinearity among variables, we did not adjust these variables in the statistical analysis. SPSS (version 25.0; IBM, Armonk, NY) and EmpowerStats (version 2018-05-05, copyright 2009 X&Y Solutions, Inc) were used for data analysis; a two-tailed $p<0.05$ was considered statistically significant. R STUDIO was used for PSM to adjusting for confounding factors, and the PSM results was showed in Figures S2-S7.

RESULTS

3.1. Population and baseline characteristics

The MIMIC-III database includes 2,087 patients diagnosed with IAI according to the criteria mentioned above. Among these patients, 233 lacked weight data and were excluded from the study, and 14 patients with abnormal data records were excluded (e.g., height value> 300 m, survival time < 0 day). MI was used to account for missing data on height in the remaining 1840 patients. Finally, after excluding 679 patients without height measurements, a total of 1,161 patients were finally included in the study (Figure 1).

Table 1 shows the baseline characteristics of patients grouped according to their BMI. There were 399 patients with BMI < 25 kg/m², 357 patients with BMI 25-30 kg/m² and 405 patients with BMI > 30 kg/m², accounting for 34.37%, 30.75% and 34.88% of the patients, respectively. In the subgroup aged 45-64 years, the proportion of patients with an obese status was higher than that of patients with a normal and an overweight BMI (42.96% vs. 31.58% and, 42.96% vs. 33.61%, respectively, $p<0.05$), while in the subgroup of patients older than 90 years, the result was the opposite (1.73% vs. 8.02% and 1.73% vs.5.32, respectively, $p<0.05$). The proportion of females in the group of patients with an overweight status was lower than that in the other groups ($p<0.001$). There was no significant difference in ethnicity between the three groups ($p=0.183$). However, there were significant differences between the three groups in regard to marital status and admission type ($p= 0.008$ and 0.009 , respectively). The group with BMI < 25 kg/m² had lower SOFA scores on the first day of admission than the obese group ($p=0.039$). However, there was no significant difference between the two groups with regard to SAPS II, SIRS, qSOFA score, OASIS score and Charlson Comorbidity

Index ($p > 0.05$). Table S2 shows the baseline characteristics after adjusting for confounding factors. After adjusting for confounding factors listed above, SOFA scores remained significantly different between groups ($p < 0.05$).

3.2. Univariate analysis of outcomes

The mortality rates at different times of admission and the LOS of patients in the different BMI groups are shown in Table 2.

The mortality of patients with BMI $< 25 \text{ kg/m}^2$ was significantly higher than that of obese patients at 30 days after admission to the ICU (18.55% vs. 11.85%, respectively, $p=0.016$), which was the same at 90 days after admission to the ICU (28.07% vs. 20.74%, respectively, $p=0.048$). In addition, the median LOS for patients with a BMI < 25 , 25-30 and $> 30 \text{ kg/m}^2$ in the ICU was 3.13, 3.59 and 4.93 days, respectively ($p < 0.001$), and the obese group spent significantly more time in the ICU than the former two groups ($p < 0.05$). However, in the subgroup analysis, only those patients who did not die in the ICU showed significant differences, while those who died did not ($p < 0.001$ and $p=0.166$, respectively). After adjusting for confounding factors, the LOS in the ICU of obese patients was still significantly longer than that of the other two groups ($p < 0.001$, Table S3). In subgroup analysis, the conclusion was the same as above, which may be due to the bias caused by the number of deceased patients. The K-M curve for the 90-day survival by BMI is shown in Figure 2. This shows that the group with an overweight and obese BMI had a significant survival advantage ($p < 0.001$ by log-rank test). After excluding patients with BMI $< 18.5 \text{ kg/m}^2$, the K-M curve was rebuilt (Figure S8), and the result did not change ($p < 0.001$ by log-rank test). The 90-day survival curve stratified according to the BMI in patients with and without sepsis is shown in Figure 3. In different subgroups, patients with a BMI $> 25 \text{ kg/m}^2$ had significantly better survival than those with a BMI $< 25 \text{ kg/m}^2$ ($p < 0.001$ and $p < 0.05$, respectively, by log-rank test).

We also compared the use of mechanical ventilation, vasoactive drugs and dialysis between the three groups as shown in Table 3. The proportion of patients with an obese BMI who needed mechanical ventilation was higher than that in patients with a normal BMI (61.48% vs. 52.38%, $p=0.034$). However, in regard to the use of vasoactive drugs

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and dialysis, there was no significant difference between the three groups. After adjusting for confounding factors, there was no significant difference in the use of mechanical ventilation (Table S4).

The results of several laboratory tests stratified by BMI are shown in Table 4. Significant differences were observed in the HGB, WBC, Cl, CRE and GLU levels between the three groups ($p=0.048, 0.035, 0.007, 0.001$ and <0.001 , respectively). After adjusting for confounding factors, there was no significant difference in HGB levels among the groups, but there was a significant difference in Na levels ($p=0.042$, Table S5).

3.3. Cox proportional hazards analyses of 90- day mortality

We imported variables with p values < 0.10 in univariate analysis into Cox proportional hazards analyses after testing the collinearity of the variables. When BMI was employed as a continuous variable, the adjusted HR values in the four models were 0.98 (0.97, 0.99), 0.97 (0.96, 0.99), 0.97 (0.96, 0.99), and 0.96(0.95, 0.98). When BMI was applied as a classification variable, it was also associated with the 90-day mortality of patients with IAIs(Table 5). However, in the multi-factor regression analysis of the subgroup analysis of acute pancreatitis and other patients, when BMI was employed as a continuous variable, the adjusted HR values were 0.98(0.95,1.00) and 0.97(0.95,0.99) for acute pancreatitis patients and other patients, respectively (Table S6), while both before and after the adjustment, the HR values were almost the same, and the p value were close to 0.05,which may be due to the sample size($n=321$ and $n=355$,respectively after adjustment).

Considering the high proportion of missing height value in the patient group, we conducted MI with height values, and calculated the BMI with weight values and imputed height values. Whether BMI was employed as a continuous variable or a classification variable, the adjusted HR value in the models showed that BMI was a protective factor of the 90-day mortality in patients with IAIs (Table S7). The results in the Table S8 shows that in the imputed data, BMI was not a protective factor in patients with acute pancreatitis, but it was still a protective factor in other IAI patients.

Excluding acute pancreatitis patients from the analysis did not affect the results.

3014. Discussion

302 In this retrospective study, we used the MIMIC-III database to study the relationship
303 between BMI and the short-term mortality of patients with abdominal infection. By
304 comparing the survival curve and 90-day mortality of the three groups, it was found
305 that the short-term prognosis of overweight (25-30 kg/m²) and obese (>30kg/m²)
306 patients was significantly better than that in the normal group.

307 By comparing the baseline characteristics of the three groups of patients, a significant
308 difference was observed in the overall age composition of the three groups and in the
309 45-64 and >90 age subgroups between the three groups, and this statistical difference
310 between subgroups still exists after adjusting for confounding factors. Subsequently, in
311 our study, overweight patients were more likely to be males. However, previous studies
312 have shown that obese cohorts tend to be younger and have a higher female prevalence
313 ¹⁷. The possible cause of this discrepancy, as mentioned in previous studies, could be
314 that male patients are more likely to develop abdominal infections such as appendicitis,
315 and smoking is a probable cause for this increased risk^{18 19}.

316 Currently, studies on the association of obesity with patients outcomes are mainly
317 focused on sepsis, and the results are ambiguous and contradictory²⁰⁻²². In this study, we
318 expanded the scope of this relationship to study the effect of BMI on the short-term
319 outcomes of patients with IAIs. Our finding shows that obese patients had a higher
320 SOFA score at admission, indicating a worse degree of organ failure than that in
321 patients with a lower BMI, and the incidence of sepsis events was higher in patients
322 with a higher BMI. Previous studies have shown that people who were overweight or
323 obese had higher susceptibility to developing postsurgical infections, and respiratory
324 tract infections and tended to develop more severe infections, which is consistent with
325 the results of our study; however, the short-term outcome of these patients was better
326 ^{23 24}. The same contradiction exists in our laboratory test results. According to a
327 previous study, serum CRE was an independent risk factor for clinical failure, but in
328 our cohort, obese patients had significantly higher CRE values, which should lead to a
329 worse clinical outcome²⁵. Previous studies also showed that CRE minimums at baseline
330 were considered a predictor of short-term mortality²⁶. However, some studies have

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reported that CRE can predict multiple organ failure²⁷. This may be related to the baseline characteristics of our study population, and CRE level no longer appears as an independent factor that affects the prognosis after adjusting for the baseline characteristics. Among the laboratory tests included in our study, the HGB in the obese and overweight group was higher than that in the other groups. Contrarily, a higher HGB value can provide more oxygen to tissues and reduce hypoxia, whereas obese patients may originally have a higher HGB value ,while critically ill patients often develop anemia related to a low level of erythropoietin level in the presence of sepsis, a kind of anemia indicates malnutrition of critically IAI patients. However, obese patients rarely have malnutrition, so they are unlikely to develop anemia²⁸⁻³⁰. Furthermore, it was found that patients without sepsis but with IAIs can also benefit from a higher BMI. This shows that BMI has a protective effect not only in patients with severe conditions, such as sepsis patients but also in patients with a milder condition. However, once sepsis occurs in patients with abdominal infection, the short-term prognosis will be significantly worse.

Our study also found that patients with a higher BMI had a higher probability of receiving mechanical ventilation, which was also reported in previous studies³¹.This may be related to the impact of obesity on the respiratory system, obese patients tend to have higher respiratory rates and lower tidal volumes, and lung volumes tend to be decreased, especially the expiratory reserve volume³². BMI was associated with an increased risk of acute respiratory distress syndrme (ARDS) in a weight-dependent manner but was not associated with mortality³³. As mentioned above, obese patients are also more likely to receive mechanical ventilation as well as the attention of medical staff³⁴. In summarize, patients with a higher BMI have a poor health foundation and are more likely to progress to critical illness, but there are also some indicators, such as HGB level that may prevent organ failure caused by critical illness in this process. In addition, they are more likely to receive advanced modes of mechanical ventilation, dialysis, liver function support and medical resources.

In the final Cox regression model, BMI remained a protective factor after adjusting for confounding variables. This is a phenomenon called the obesity paradox, which means

that overweight and obese patients are recognised as they often have more basic diseases, such as hypertension, cardiovascular disease and diabetes. Their general health is also worse than that of patients with a normal BMI, and some studies have shown that BMI is associated with an incidence rate of more than 20 types of cancers, but BMI still shows protective effects and improves the prognosis of patients. The reasons and underlying mechanisms have not been clarified³⁵. Some studies have suggested that patients with obesity-associated comorbidities, such as hypertension may require less vasoactive drugs and fluid resuscitation in the treatment process; severe IAs can lead to sepsis that requires fluid resuscitation, and a restrictive fluid strategy would reduce the burden of heart or lung injuries to protect organ function^{36 37}. Drugs that patients with cardiovascular disease take in the long term, such as aspirin, might play a protective role in IAs, antiplatelet drugs can inhibit coagulation and inflammatory reactions in models of sepsis, reducing damage to organ function; and clinical studies also suggest that aspirin may improve the prognosis of patients with sepsis³⁸.

The protective effect of diabetes may occur through an unidentified hormonal intermediary, or it may be caused by antidiabetic drugs such as rosiglitazone taken by diabetic patients, which increases the serum levels of adiponectin, thus resulting in a better prognosis^{39 40}. A recent study also indicated an association between metformin use prior to admission and lower mortality in septic adult patients with diabetes mellitus. Metformin may supply higher amounts of LAC, serving as an energetic carbon source, thus making energy available to ischaemic tissue^{41 42}. Second, in acute catabolic reactions caused by IAs, stored fuel and nutritional reserves might be critical in obese patients. In our study, the higher CRE values of overweight and obese patients also support this standpoint; however, in IAs, due to anorexia and acute gastrointestinal dysfunction, the energy supply is frequently insufficient⁴³. Third, adipocytes can release adipokines and inflammatory factors such as Interleukin-10 and leptin, which can regulate the immune response and improve the prognosis of patients with an acute inflammatory response⁴⁴. A previous study indicated that lipopolysaccharides may be sequestered in adipose tissue via the very-low-density lipoprotein receptor, and this

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sequestration may contribute to improved sepsis survival; when BMI was greater than 25 kg/m², this effect was accentuated⁴⁵. In addition, the difference in nursing level may also affect the prognosis of obese patients. As mentioned earlier, obese patients often suffer from more basic diseases and complications, and they are more likely to receive the attention of nursing staff, receiving more active treatment³⁴. Finally, previous studies suggest that BMI is not the best indicator to accurately evaluate obesity, which leads to the obesity paradox^{46 47}.

This study has several limitations. First, this was a retrospective single centre study. Similar to other observational studies, it is difficult to completely exclude the influence of residual confounding factors. Second, due to the characteristics of the database itself, a considerable number of patients' data were missing, especially various laboratory test data, which may cause selection bias; however, we did not introduce the missing indicators into the final Cox regression model. Third, in this study, we only obtained the baseline characteristic information of patients and some of their laboratory examination results within 24 h after admission, but did not specifically study their infection and treatment process (such as the use of antibiotics), and the disparate interventions in the two groups with regard to these factors may lead to deviations in our results. Finally, the total sample size of the database was very large, but the number of subgroups in our study was relatively small, which may also affect the reliability of our results.

5.CONCLUSION

IAI patients with an overweight and obese status have lower 90-day mortality than patients with a normal BMI. The protective effect of BMI exists not only in patients with severe conditions, such as sepsis patients, but also in patients with milder conditions.

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Authors' contributions

Li QL participated in the research design, data analysis and writing of the paper; **Tong YM** participated in the data collecting; **Li QL, Tong YM** contributed equally to this work. **Liu SN** participated in data analysis and revising of the paper; **Yang KB** participated in the data cleaning; **Liu C and Zhang JY** provided substantial advice in designing the study and assisting in the division of labor, writing and revising the paper.

Competing interests

The authors declare that they have no competing interests.

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Data Availability Statement

MIMIC-III, a freely accessible critical care database. Johnson AEW, Pollard TJ, Shen L, Lehman L, Feng M, Ghassemi M, Moody B, Szolovits P, Celi LA, and Mark RG. Scientific Data (2016). DOI: 10.1038/sdata.2016.35. Available from: <http://www.nature.com/articles/sdata201635>

Patient consent for publication

Not required.

Consent for publication

Not applicable.

Reference

1. Sartelli M, Chichom-Mefire A, Labricciosa FM, et al. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections. *World J Emerg Surg* 2017;12:29. doi: 10.1186/s13017-017-0141-6 [published Online First: 2017/07/14]
2. Hecker A, Reichert M, Reuss CJ, et al. Intra-abdominal sepsis: new definitions and current clinical standards. *Langenbecks Arch Surg* 2019;404(3):257-71. doi: 10.1007/s00423-019-01752-7 [published Online First: 2019/01/28]
3. Eggimann P, Pittet D. Infection control in the ICU. *Chest* 2001;120(6):2059-93.
4. Shirah GR, O'Neill PJ. Intra-abdominal Infections. *Surg Clin North Am* 2014;94(6):1319-33. doi: 10.1016/j.suc.2014.08.005
5. Montravers P, Tashk P, Tran Dinh A. Unmet needs in the management of intra-abdominal infections. *Expert Rev Anti Infect Ther* 2017;15(9):839-50. doi: 10.1080/14787210.2017.1372750
6. Gonzalez MC, Correia MITD, Heymsfield SB. A requiem for BMI in the clinical setting. *Curr Opin Clin*

- 455 *Nutr Metab Care* 2017;20(5):314-21. doi: 10.1097/MCO.0000000000000395
- 456 7. Flegal KM, Ioannidis JPA, Doehner W. Flawed methods and inappropriate conclusions for health
457 policy on overweight and obesity: the Global BMI Mortality Collaboration meta-analysis. *J*
458 *Cachexia Sarcopenia Muscle* 2019;10(1) doi: 10.1002/jcsm.12378
- 459 8. Heetun A, Cutress RI, Copson ER. Early breast cancer: why does obesity affect prognosis? *Proc Nutr*
460 *Soc* 2018;77(4):369-81. doi: 10.1017/S0029665118000447
- 461 9. Secord AA, Hasselblad V, Von Gruenigen VE, et al. Body mass index and mortality in endometrial
462 cancer: A systematic review and meta-analysis. *Gynecol Oncol* 2016;140(1):184-90. doi:
463 10.1016/j.ygyno.2015.10.020
- 464 10. Barone M, Viggiani MT, Losurdo G, et al. Systematic review with meta-analysis: post-operative
465 complications and mortality risk in liver transplant candidates with obesity. *Aliment Pharmacol*
466 *Ther* 2017;46(3):236-45. doi: 10.1111/apt.14139
- 467 11. Wang Y, Beydoun MA. The obesity epidemic in the United States--gender, age, socioeconomic,
468 racial/ethnic, and geographic characteristics: a systematic review and meta-regression
469 analysis. *Epidemiol Rev* 2007;29:6-28. doi: 10.1093/epirev/mxm007 [published Online First:
470 2007/05/19]
- 471 12. Kalantar-Zadeh K, Abbott KC, Salahudeen AK, et al. Survival advantages of obesity in dialysis patients.
472 *Am J Clin Nutr* 2005;81(3):543-54 2005
- 473 13. Chlebowski RT, Grosvenor M, Lillington L, et al. Dietary Intake and Counseling, Weight Maintenance,
474 and the Course of HIV Infection. *Journal of the American Dietetic Association* 1995;95(4):428-
475 35. doi: 10.1016/s0002-8223(95)00115-8
- 476 14. Johnson AE, Pollard TJ, Shen L, et al. MIMIC-III, a freely accessible critical care database. *Sci Data*
477 2016;3:160035. doi: 10.1038/sdata.2016.35 [published Online First: 2016/05/25]
- 478 15. Johnson AEW, Pollard TJ, Shen L, et al. MIMIC-III, a freely accessible critical care database. *Scientific*
479 *data* 2016;3:160035. doi: 10.1038/sdata.2016.35
- 480 16. Park S-Y, Freedman ND, Haiman CA, et al. Association of Coffee Consumption With Total and Cause-
481 Specific Mortality Among Nonwhite Populations. *Ann Intern Med* 2017;167(4):228-35. doi:
482 10.7326/M16-2472
- 483 17. Li S, Hu X, Xu J, et al. Increased body mass index linked to greater short- and long-term survival in
484 sepsis patients: A retrospective analysis of a large clinical database. *Int J Infect Dis*
485 2019;87:109-16. doi: 10.1016/j.ijid.2019.07.018 [published Online First: 2019/07/30]
- 486 18. Ferris M, Quan S, Kaplan BS, et al. The Global Incidence of Appendicitis: A Systematic Review of
487 Population-based Studies. *Ann Surg* 2017;266(2):237-41. doi:
488 10.1097/SLA.0000000000002188 [published Online First: 2017/03/14]
- 489 19. Montgomery SM, Pounder RE, Wakefield AJ. Smoking in adults and passive smoking in children are
490 associated with acute appendicitis. *Lancet* 1999;353(9150):379.
- 491 20. Trivedi V, Bavishi C, Jean R. Impact of obesity on sepsis mortality: A systematic review. *J Crit Care*
492 2015;30(3):518-24. doi: 10.1016/j.jcrc.2014.12.007
- 493 21. Wang S, Liu X, Chen Q, et al. The role of increased body mass index in outcomes of sepsis: a
494 systematic review and meta-analysis. *BMC Anesthesiol* 2017;17(1):118. doi: 10.1186/s12871-
495 017-0405-4
- 496 22. Wang H, Shi Y, Bai Z-H, et al. Higher body mass index is not a protective risk factor for 28-days
497 mortality in critically ill patients with acute kidney injury undergoing continuous renal
498 replacement therapy. *Ren Fail* 2019;41(1):726-32. doi: 10.1080/0886022X.2019.1650767

23. Maccioni L, Weber S, Elgizouli M, et al. Obesity and risk of respiratory tract infections: results of an infection-diary based cohort study. *BMC Public Health* 2018;18(1):271. doi: 10.1186/s12889-018-5172-8
24. Dhurandhar NV, Bailey D, Thomas D. Interaction of obesity and infections. *Obes Rev* 2015;16(12):1017-29. doi: 10.1111/obr.12320
25. White BP, Wagner JL, Barber KE, et al. Risk Factors for Failure in Complicated Intraabdominal Infections. *South Med J* 2018;111(2):125-32. doi: 10.14423/SMJ.0000000000000770
26. Thongprayoon C, Cheungpasitporn W, Kittanamongkolchai W, et al. Optimum methodology for estimating baseline serum creatinine for the acute kidney injury classification. *Nephrology (Carlton)* 2015;20(12):881-86. doi: 10.1111/nep.12525
27. Dewar DC, Tarrant SM, King KL, et al. Changes in the epidemiology and prediction of multiple-organ failure after injury. *J Trauma Acute Care Surg* 2013;74(3):774-79. doi: 10.1097/TA.0b013e31827a6e69
28. Vuong J, Qiu Y, La M, et al. Reference intervals of complete blood count constituents are highly correlated to waist circumference: should obese patients have their own "normal values?". *American journal of hematology* 2014;89(7):671-7. doi: 10.1002/ajh.23713 [published Online First: 2014/03/20]
29. Rogiers P, Zhang H, Leeman M, et al. Erythropoietin response is blunted in critically ill patients. *Intensive care medicine* 1997;23(2):159-62.
30. Zhang Z, Pereira SL, Luo M, et al. Evaluation of Blood Biomarkers Associated with Risk of Malnutrition in Older Adults: A Systematic Review and Meta-Analysis. *Nutrients* 2017;9(8) doi: 10.3390/nu9080829 [published Online First: 2017/08/05]
31. Sakr Y, Alhussami I, Nanchal R, et al. Being Overweight Is Associated With Greater Survival in ICU Patients: Results From the Intensive Care Over Nations Audit. *Crit Care Med* 2015;43(12):2623-32. doi: 10.1097/CCM.0000000000001310 [published Online First: 2015/10/03]
32. Littleton SW. Impact of obesity on respiratory function. *Respirology* 2012;17(1):43-9. doi: 10.1111/j.1440-1843.2011.02096.x [published Online First: 2011/11/02]
33. Gong MN, Bajwa EK, Thompson BT, et al. Body mass index is associated with the development of acute respiratory distress syndrome. *Thorax* 2010;65(1):44-50. doi: 10.1136/thx.2009.117572
34. O'Brien JM, Philips GS, Ali NA, et al. The association between body mass index, processes of care, and outcomes from mechanical ventilation: a prospective cohort study. *Critical care medicine* 2012;40(5):1456-63. doi: 10.1097/CCM.0b013e31823e9a80
35. Bhaskaran K, Douglas I, Forbes H, et al. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *The Lancet* 2014;384(9945):755-65. doi: 10.1016/s0140-6736(14)60892-8
36. Wacharasint P, Boyd JH, Russell JA, et al. One size does not fit all in severe infection: obesity alters outcome, susceptibility, treatment, and inflammatory response. *Critical care (London, England)* 2013;17(3):R122. doi: 10.1186/cc12794
37. Stewart RM, Park PK, Hunt JP, et al. Less is more: improved outcomes in surgical patients with conservative fluid administration and central venous catheter monitoring. *J Am Coll Surg* 2009;208(5) doi: 10.1016/j.jamcollsurg.2009.01.026
38. Wang Y, Ouyang Y, Liu B, et al. Platelet activation and antiplatelet therapy in sepsis: A narrative review. *Thromb Res* 2018;166:28-36. doi: 10.1016/j.thromres.2018.04.007
39. Kuperman EF, Showalter JW, Lehman EB, et al. The impact of obesity on sepsis mortality: a

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4 543 retrospective review. *BMC Infect Dis* 2013;13:377. doi: 10.1186/1471-2334-13-377
5 544 40. Uji Y, Yamamoto H, Tsuchihashi H, et al. Adiponectin deficiency is associated with severe
6 545 polymicrobial sepsis, high inflammatory cytokine levels, and high mortality. *Surgery*
7 546 2009;145(5):550-57. doi: 10.1016/j.surg.2009.01.010
8 547 41. Liang H, Ding X, Li L, et al. Association of preadmission metformin use and mortality in patients with
9 548 sepsis and diabetes mellitus: a systematic review and meta-analysis of cohort studies. *Critical*
10 549 *care (London, England)* 2019;23(1):50. doi: 10.1186/s13054-019-2346-4
11 550 42. Hui S, Ghergurovich JM, Morscher RJ, et al. Glucose feeds the TCA cycle via circulating lactate.
12 551 *Nature* 2017;551(7678):115-18. doi: 10.1038/nature24057 [published Online First:
13 552 2017/10/19]
14 553 43. Niedziela J, Hudzik B, Niedziela N, et al. The obesity paradox in acute coronary syndrome: a meta-
15 554 analysis. *Eur J Epidemiol* 2014;29(11):801-12. doi: 10.1007/s10654-014-9961-9
16 555 44. McLaughlin T, Deng A, Yee G, et al. Inflammation in subcutaneous adipose tissue: relationship to
17 556 adipose cell size. *Diabetologia* 2010;53(2):369-77. doi: 10.1007/s00125-009-1496-3
18 557 45. Shimada T, Topchiy E, Leung AKK, et al. Very Low Density Lipoprotein Receptor Sequesters
19 558 Lipopolysaccharide Into Adipose Tissue During Sepsis. *Critical care medicine* 2020;48(1):41-48.
20 559 doi: 10.1097/CCM.0000000000004064
21 560 46. Xing Z, Tang L, Chen J, et al. Association of predicted lean body mass and fat mass with
22 561 cardiovascular events in patients with type 2 diabetes mellitus. *CMAJ* 2019;191(38):E1042-E48.
23 562 doi: 10.1503/cmaj.190124
24 563 47. Xing Z, Peng Z, Wang X, et al. Waist circumference is associated with major adverse cardiovascular
25 564 events in male but not female patients with type-2 diabetes mellitus. *Cardiovasc Diabetol*
26 565 2020;19(1):39. doi: 10.1186/s12933-020-01007-6
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Table1. Univariate analysis of baseline characteristics by BMI category

	BMI<25	BMI 25-30	BMI>30	P value
	kg/m ²	kg/m ²	kg/m ²	
	(n=399)	(n=357)	(n=405)	
Age, n (%)	66.56(50.16-80.25) ^a	66.79(52.43-77.63) ^b	62.97(51.94-72.92) ^b	<0.001
<45	64(16.04)	47(13.17)	60(14.81)	
45-64	126(31.58) ^a	120(33.61) ^a	174(42.96) ^b	
65-89	177(44.36)	171(47.90)	164(40.49)	
>90	32(8.02) ^a	19(5.32) ^a	7(1.73) ^b	
Female, n (%)	207(51.88) ^a	141(39.50) ^b	206(50.86) ^a	0.001
Ethnicity, n (%)				0.183
White	297(74.43)	255(71.43)	305(75.31)	
Black	40(10.03)	36(10.08)	38(9.38)	
Hispanic or latino	11(2.76)	14(3.92)	11(2.72)	
Asian	7(1.75)	11(3.08)	1(0.25)	
Other	44(11.03)	41(11.49)	50(12.35)	
Marital status, n (%)				0.008
Married	169(42.36) ^a	196(54.90) ^b	196(48.40) ^{a,b}	
Single/divorced/separated/unknown	161(40.35)	121(33.89)	156(38.52)	
n				
Widowed	69(17.29)	40(11.20)	53(13.09)	
Admission type, n (%)				0.009
Elective	35(8.77) ^a	50(14.01) ^{a,b}	64(15.80) ^b	
Emergency/urgent	364(91.23) ^a	307(86.00) ^{a,b}	341(84.20) ^b	
Insurance type, n (%)				0.604

Medicare/Medicaid	261(65.41)	236(66.11)	250(61.73)	
Private	125(31.33)	109(30.53)	144(35.56)	
Other	13(3.26)	12(3.36)	11(2.72)	
SOFA	5(2-7) ^a	5(3-7) ^{a,b}	5(3-8) ^b	0.039
SAPS II	40(30-50)	39(29-50)	38(28-49)	0.473
SIRS	3(3-4)	3(3-4)	3(3-4)	0.786
qSOFA	2(1-2)	2(1-2)	2(1-2)	0.185
OASIS	34(27-40)	33(28-41)	34(27-41)	0.941
Charlson comorbidity index	1(0-3)	2(1-3)	1(0-3)	0.719

Abbreviations: BMI: Body mass index; SOFA: sepsis-related organ failure assessment; SAPSII: Simplified Acute Physiology Score II; SIRS: systemic inflammatory response syndrome; OASIS: Oxford Acute Severity of Illness Score. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

Table 2. Univariate analysis of mortality and length of stay by BMI category

	BMI <25 kg/m ² (n=399)	BMI 25–30 kg/m ² (n=357)	BMI >30 kg/m ² (n=405)	<i>p</i>
Mortality, n (%)				
Hospital mortality	78(19.55)	65(18.21)	57(14.07)	0.102
30-day mortality	74(18.55) ^a	46(12.89) ^{a,b}	48(11.85) ^b	0.016
90-day mortality	112(28.07) ^a	83(23.25) ^{a,b}	84(20.74) ^b	0.048
Length of stay, day (IQR)				
Hospital LOS	14.9(8.4–28.6)	15.4(7.9–27.0)	16.2(9.1–29.8)	0.137
Living patients(n=962)	15.0(8.7–28.6)	14.3(7.9–24.9)	16.4(9.3–29.8)	0.059
Dead patients(n=201)	13.9(5.4–29.3)	17.9(7.1–33.3)	13.7(6.2–30.7)	0.412
ICU LOS	3.1(1.8–7.8) ^a	3.6(1.9–8.9) ^a	4.9(2.2–13.6) ^b	<0.001
Living patients(n=1036)	3.1(1.7–6.7) ^a	3.3(1.8–7.7) ^a	4.7(2.2–13.2) ^b	<0.001
Dead patients(n=125)	7.2(2.2–14.1)	11.7(3.7–31.1)	8.8(2.2–17.7)	0.166

Abbreviations: BMI: Body mass index; LOS: length of stay. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

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Table 3. Univariate analysis of requirement of organ support therapy by BMI category

	BMI<25kg/m ² (n=399)	BMI25–30kg/m ² (n=357)	BMI>30 kg/m ² (n=405)	<i>p</i>
Ventilation , n(%)	209(52.38) ^a	203(56.86) ^{a,b}	249(61.48) ^b	0.034
Dialysis, n (%)	24(6.01)	30(8.40)	32(7.90)	0.409
Vasoactive agent, n (%)	138(34.59)	123(34.45)	143(35.31)	0.964

Abbreviations: BMI: Body mass index; The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

Table 4. Univariate analysis of laboratory examination by BMI category

	BMI<25kg/m ²	BMI25-30kg/m ²	BMI>30kg/m ²	<i>p</i>
HGB (g/dL)	9.5(8.3-10.7) ^a , n=396	9.60(8.4-10.8) ^{a,b} , n=355	9.7(8.5-11.2) ^b , n=403	0.048
WBC (K/uL)	10.1(6.2-14.9) ^{a,b} , n=396	9.7(6.5-13.8) ^a , n=355	10.9(7.1-15.2) ^b , n=404	0.035
PLT (K/uL)	184.5(112.3-268), n=396	182 (124-252), n=355	190(126-273.5), n=405	0.402
CRE (mg/dL)	1.1(0.8-1.8) ^a , n=396	1.2(0.9-2.2) ^b , n=355	1.3(0.9-2.2) ^b , n=405	0.001
BUN (mg/dL)	24(16-39), n=396	25(16-41), n=355	25(16-44), n=405	0.610
ALB (g/dL)	2.6(2.2-3.1), n=234	2.7(2.2-3.2), n=215	2.7(2.3-3.1), n=228	0.463
Cl (mEq/L)	109(105-113) ^a , n=396	109(105-112) ^a , n=356	108(104-111) ^b , n=405	0.007
K (mEq/L)	3.6(3.2-4.0), n=396	3.7(3.3-4.0), n=356	3.7(3.4-4.1), n=405	0.168
Na (mEq/L)	136(132-139), n=396	136(133-139), n=356	136(133.5-139), n=405	0.235
GLU (mg/dL)	153(122-194) ^a , n=396	154 (125-195.75) ^a , n=356	170 (136.5-226) ^b , n=405	<0.001
LAC (mmol/L)	2.5(1.6-4.5), n=312	2.7(1.5-4.4), n=286	2.3(1.4-4.2), n=325	0.324
BIL (mg/dL)	1.1(0.5-3.1), n=262	1.2(0.6-2.4), n=255	1 (0.5-2.5), n=284	0.528

Abbreviations: BMI: Body mass index; HGB: hemoglobin; WBC: white blood cell count; PLT: platelet count; ALB: albumin; CRE: creatinine; BUN: urea nitrogen; GLU: glucose; LAC: lactate; BIL: bilirubin; Na: sodium; Cl: chlorine; K: potassium. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

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Table 5. Result of the Cox proportional hazard regression analysis

Exposure	Non-adjusted HR, <i>p</i> Value	Adjusted HR, <i>p</i> Value
<i>Model 1</i>		
BMI	0.98(0.97-0.99), <0.0001	0.98(0.97,0.99), 0.0001
BMI		
<25, kg/m ²	1.00(Reference)	1.00(Reference)
25-30, kg/m ²	0.78(0.64,0.96), 0.0158	0.78(0.64,0.95), 0.0148
>30, kg/m ²	0.68(0.56,0.83), 0.0001	0.68(0.56,0.83), 0.0002
<i>Model 2</i>		
BMI	0.98(0.97,0.99), <0.0001	0.97(0.96,0.99), 0.0008
BMI		
<25, kg/m ²	1.00(Reference)	1.00(Reference)
25-30, kg/m ²	0.78(0.64,0.96), 0.0158	0.79(0.61,1.02), 0.0729
>30, kg/m ²	0.68(0.56,0.83), 0.0001	0.66(0.51,0.86), 0.0021
<i>Model 3</i>		
BMI	0.98(0.97,0.99), <0.0001	0.97(0.96,0.99), 0.0009
BMI		
<25, kg/m ²	1.00(Reference)	1.00(Reference)
25-30, kg/m ²	0.78(0.64-0.96), 0.0158	0.72(0.56,0.94), 0.0152
>30, kg/m ²	0.68(0.56.0.83), 0.0001	0.66(0.50,0.86), 0.0022
<i>Model 4</i>		
BMI	0.98(0.97,0.99), <0.0001	0.96(0.95,0.98), <0.0001
BMI		
<25, kg/m ²	1.00(Reference)	1.00(Reference)
25-30, kg/m ²	0.78(0.64,0.96), 0.0158	0.54(0.40,0.73), <0.0001
>30, kg/m ²	0.68(0.56,0.83), 0.0001	0.48(0.36,0.65), <0.0001

Model 1: Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity
Model 2: Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity; HGB; GLU; ALB.
Model 3: Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity; HGB; GLU; ALB; Charlson comorbidity index.
Model 4: Adjusted for Charlson comorbidity index.
Abbreviations: BMI: Body mass index; SOFA: sepsis-related organ failure assessment; ICU: intensive care unit; WBC: white blood cell counting.

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Legends for the figures

Figure 1. Flowchart of study cohort selection.

Figure 2. Kaplan–Meier curve for 90-days survival stratified by BMI.

Abbreviations: BMI: Body mass index; Fig. 2 represents 90-days Kaplan–Meier curves stratified by BMI in three groups, $P < 0.001$ by log-rank test.

Figure 3. 90-days Kaplan–Meier curve of patients without (A) and with (B) sepsis stratified by BMI. Abbreviations: BMI: Body mass index; Fig. 3(A) and 3(B) represents 90-days Kaplan–Meier curves of patients without and with sepsis respectively. In log rank test $P < 0.001$, $P < 0.05$, respective.

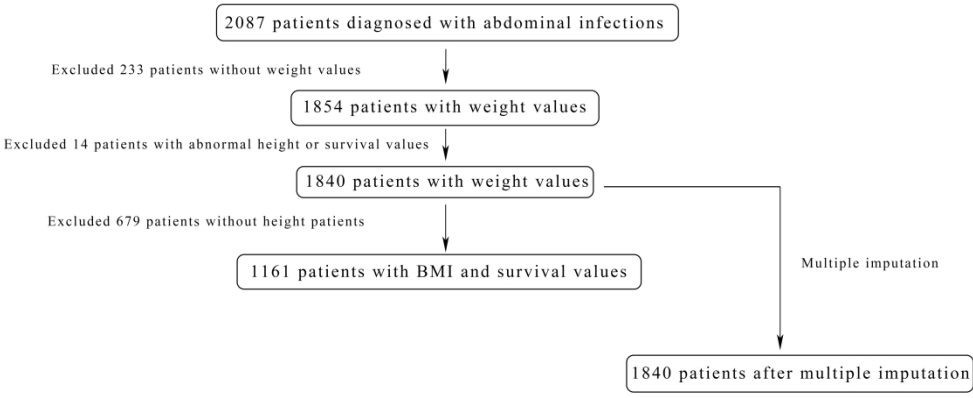


Figure 1. Flowchart of study cohort selection.

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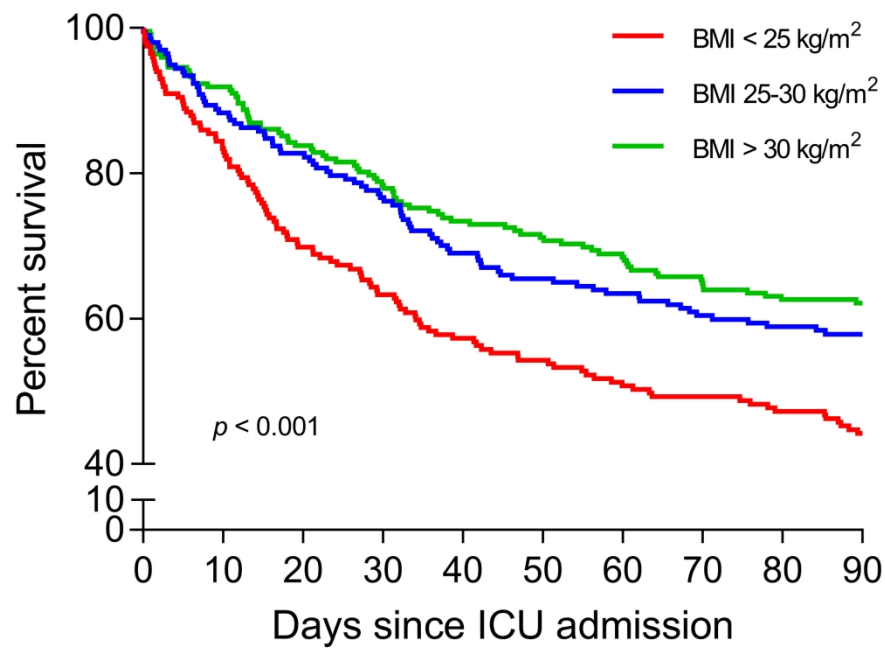


Figure 2. Kaplan-Meier curve for 90-days survival stratified by BMI. Abbreviations: BMI: Body mass index; Fig. 2 represents 90-days Kaplan-Meier curves stratified by BMI in three groups, $P < 0.001$ by log-rank test.

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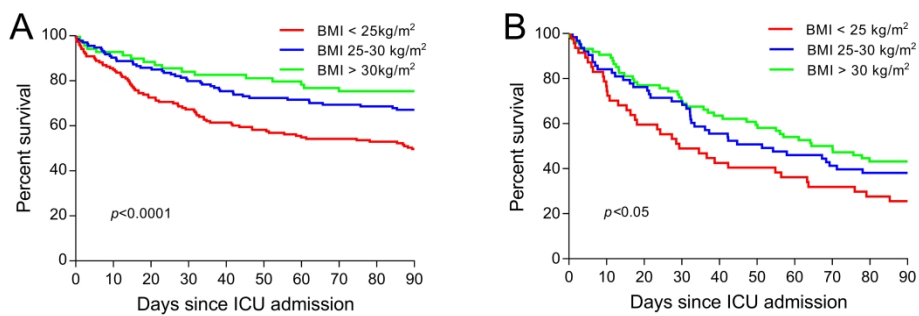


Figure 3. 90-days Kaplan–Meier curve of patients without (A) and with(B) sepsis stratified by BMI. Abbreviations: BMI: Body mass index; Fig. 3(A) and 3(B) represents 90-days Kaplan–Meier curves of patients without and with sepsis respectively. In log rank test $P<0.001$, $P<0.05$, respective.

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Supplementary material:

Table S1. ICD-9 codes, diagnostics and number of specific diagnoses by BMI category

ICD-9	diagnostics	n, (%)				<i>p</i> value
		BMI <25	BMI 25-30	BMI >30	TOTAL	
53110	Acute gastric ulcer with perforation, without mention of obstruction	3(0.75)	2(0.56)	2(0.49)	7(0.60)	NS
53111	Acute gastric ulcer with perforation, with obstruction	1(0.25)	0	0	1(0.08)	NS
53120	Acute gastric ulcer with hemorrhage and perforation, without mention of obstruction	1(0.25)	0	0	1(0.08)	NS
53150	Chronic or unspecified gastric ulcer with perforation, without mention of obstruction	3(0.75)	0	2(0.49)	5(0.42)	NS
53160	Chronic or unspecified gastric ulcer with hemorrhage and perforation, without mention of obstruction	0	1(0.28)	1(0.24)	2(0.17)	NS
53210	Acute duodenal ulcer with perforation, without mention of obstruction	2(0.5)	3(0.84)	3(0.73)	8(0.68)	NS
53220	Acute duodenal ulcer with hemorrhage and perforation, without mention of obstruction	0(0)	4(1.12)	2(0.49)	6(0.51)	NS
53250	Chronic or unspecified duodenal ulcer with perforation,	4(1)	2(0.56)	4(1.98)	10(0.85)	NS

	without mention of obstruction						
53251	Chronic unspecified duodenal ulcer with perforation, with obstruction	or 0	1(0.28)	0	1(0.08)	NS	
53260	Chronic unspecified duodenal ulcer with hemorrhage and perforation, without mention of obstruction	or 1(0.25)	4(1.12)	0	5(0.42)	NS	
53450	Chronic unspecified gastrojejunal ulcer with perforation, without mention of obstruction	or 0	1(0.28)	1(0.24)	2(0.17)	NS	
53641	Infection of gastrostomy	7(1.75)	4(1.12)	6(1.47)	17(1.46)	NS	
5400	Acute appendicitis with generalized peritonitis	7(1.75)	4(1.12)	3(0.73)	14(1.20)	NS	
5401	Acute appendicitis with peritoneal abscess	4(1)	3(0.84)	5(1.23)	12(1.03)	NS	
5511	Umbilical hernia with gangrene	0	1(0.28)	0	1(0.08)	NS	
55120	Ventral hernia, unspecified, with gangrene	0	1(0.28)	0	1(0.08)	NS	
55129	Other ventral hernia with gangrene	1(0.25)	0	0	1(0.08)	NS	
5513	Diaphragmatic hernia with gangrene	1(0.25)	0	1(0.24)	2(0.17)	NS	
5518	Hernia of other specified sites, with gangrene	1(0.25)	0	0	1(0.08)	NS	
56081	Intestinal peritoneal	or 48a(12)	25a, b(7.00)	22b(5.42)	95(8.16)	NS	

	adhesions with					
	obstruction					
	(postoperative)					
	(postinfection)					
56722	Peritoneal abscess	23(5.75)	25(7.00)	20(4.92)	68(5.84)	NS
56729	Other suppurative peritonitis	18(4.5)	21(5.88)	19(4.67)	58(4.98)	NS
56738	Other retroperitoneal abscess	2(0.5)	1(0.28)	5(1.23)	8(0.68)	NS
56789	Other specified peritonitis	4(1)	5(1.40)	4(0.98)	13(1.11)	NS
5679	Unspecified peritonitis	10(2.5)	11(3.08)	8(1.97)	29(2.49)	NS
5680	Peritoneal adhesions (postoperative) (postinfection)	42(10.5)	44(12.3)	50(12.31)	136(11.6)	NS
56961	Infection of colostomy or enterostomy	2(0.5)	1(0.28)	4(0.98)	7(0.60)	NS
56981	Fistula of intestine, excluding rectum and anus	22(5.5)	12(3.36)	18(4.43)	52(4.47)	NS
56983	Perforation of intestine	47(11.75)	33(9.24)	45(11.0)	125(10.7)	NS
5754	Perforation of gallbladder	5(1.25)	2(0.56)	6(1.47)	13(1.11)	NS
5763	Perforation of bile duct	0	1(0.28)	1(0.24)	2(0.17)	NS
5764	Fistula of bile duct	4(1)	1(0.28)	0	5(0.42)	NS
5770	Acute pancreatitis	137a(34.25)	144a, b(40.3)	174b(42.86)	455(39.1)	0.037
53121	Acute gastric ulcer with hemorrhage and perforation, with obstruction	0	0	0	0	NS
53151	Chronic or unspecified gastric ulcer with perforation, with obstruction	0	0	0	0	NS
53161	Chronic or unspecified gastric	0	0	0	0	NS

	ulcer	with						
	hemorrhage	and						
	perforation,	with						
	obstruction							
53211	Acute duodenal	0	0	0	0	0	NS	
	ulcer	with						
	perforation,	with						
	obstruction							
53221	Acute duodenal	0	0	0	0	0	NS	
	ulcer	with						
	hemorrhage	and						
	perforation,	with						
	obstruction							
53261	Chronic or	0	0	0	0	0	NS	
	unspecified							
	duodenal ulcer							
	with hemorrhage							
	and perforation,							
	with obstruction							
53310	Acute peptic ulcer	0	0	0	0	0	NS	
	of unspecified site							
	with perforation,							
	without mention of							
	obstruction							
53311	Acute peptic ulcer	0	0	0	0	0	NS	
	of unspecified site							
	with perforation,							
	with obstruction							
53320	Acute peptic ulcer	0	0	0	0	0	NS	
	of unspecified site							
	with hemorrhage							
	and perforation,							
	without mention of							
	obstruction							
53321	Acute peptic ulcer	0	0	0	0	0	NS	
	of unspecified site							
	with hemorrhage							
	and perforation,							
	with obstruction							
53350	Chronic or	0	0	0	0	0	NS	
	unspecified peptic							
	ulcer of unspecified							
	site with							
	perforation,							

		without mention of						
		obstruction						
53351	Chronic	or	0	0	0	0	NS	
	unspecified	peptic						
	ulcer of unspecified							
	site	with						
	perforation,	with						
	obstruction							
53360	Chronic	or	0	0	0	0	NS	
	unspecified	peptic						
	ulcer of unspecified							
	site	with						
	hemorrhage	and						
	perforation,							
	without mention of							
	obstruction							
53361	Chronic	or	0	0	0	0	NS	
	unspecified	peptic						
	ulcer of unspecified							
	site	with						
	hemorrhage	and						
	perforation,	with						
	obstruction							
53410	Acute gastrojejunal		0	0	0	0	NS	
	ulcer	with						
	perforation,							
	without mention of							
	obstruction							
53411	Acute gastrojejunal		0	0	0	0	NS	
	ulcer	with						
	perforation,	with						
	obstruction							
53420	Acute gastrojejunal		0	0	0	0	NS	
	ulcer	with						
	hemorrhage	and						
	perforation,							
	without mention of							
	obstruction							
53421	Acute gastrojejunal		0	0	0	0	NS	
	ulcer	with						
	hemorrhage	and						
	perforation,	with						
	obstruction							
53430	Acute gastrojejunal		0	0	0	0	NS	

	ulcer	without						
	mention	of						
	hemorrhage	or						
	perforation,							
	without mention of							
	obstruction							
53451	Chronic	or	0	0	0	0	NS	
	unspecified							
	gastrojejunal ulcer							
	with perforation,							
	with obstruction							
53460	Chronic	or	0	0	0	0	NS	
	unspecified							
	gastrojejunal ulcer							
	with hemorrhage							
	and perforation,							
	without mention of							
	obstruction							
53461	Chronic	or	0	0	0	0	NS	
	unspecified							
	gastrojejunal ulcer							
	with hemorrhage							
	and perforation,							
	with obstruction							
53901	Infection due to	0	0	0	0	NS		
	gastric band							
	procedure							
53981	Infection due to	0	0	0	0	NS		
	other bariatric							
	procedure							
55121	Incisional ventral	0	0	0	0	NS		
	hernia, with							
	gangrene							
5519	Hernia of	0	0	0	0	NS		
	unspecified site,							
	with gangrene							
56739	Other	0	0	0	0	NS		
	retroperitoneal							
	infections							
5755	Fistula of	0	0	0	0	NS		
	gallbladder							

Abbreviations: BMI: Body mass index; The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

TableS2. Univariate analysis of baseline characteristics by BMI category after adjustment of confounding factors

	BMI<25 kg/m ² (n=357)	BMI 25-30 kg/m ² (n=357)	BMI>30 kg/m ² (n=357)	<i>p</i> value
Age, n(%)				0.137
<45	51(14.29)	47(13.17)	43(12.04)	
45-64	116(32.49) ^a	120(33.61) ^{a,b}	150(42.02) ^b	
65-89	161(45.10)	171(47.90)	157(43.98)	
>90	29(8.12) ^a	19(5.32) ^a	7(1.96) ^b	
Female, n (%)	167(46.78)	141(39.50)	162(45.38)	0.115
Ethnicity, n (%)				0.199
White	264(73.95)	254(71.15)	268(75.07)	
Black	37(10.36)	36(10.08)	34(9.52)	
Hispanic or latino	10(2.80)	14(3.92)	8(2.24)	
Asian	6(1.68)	11(3.08)	1(0.28)	
Other	40(11.20)	42(11.76)	46(12.89)	
Marital status, n (%)				0.303
Married	167(46.78)	196(54.90)	183(51.26)	
Single/divorced/separated/unkn				
own	142(39.78)	121(33.89)	128(35.85)	
Widowed	48(11.20)	40(11.20)	46(12.89)	
Admission type, n (%)				0.036
Elective	33(9.24) ^a	50(14.01) ^{a,b}	55(15.41) ^b	
Emergency/urgent	324(90.76) ^a	307(85.99) ^{a,b}	302(84.59) ^b	
Insurance type, n (%)				0.550
Medicare/Medicaid	237(66.39)	236(66.11)	224(62.75)	
Private	108(30.25)	109(30.53)	125(35.01)	
Other	12(3.36)	12(3.36)	8(2.24)	
SOFA	5(3-8) ^a	5(3-7) ^{a,b}	5(3-9) ^b	0.014

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SAPS II	40(30-50)	39(29-50)	39(29.5-50)	0.794
SIRS	3(3-4)	3(3-4)	3(3-4)	0.805
qSOFA	2(1-2)	2(1-2)	2(1-2)	0.122
OASIS	34(27-40)	33(28-41)	34(27-41)	0.943
Charlson comorbidity index	1(0-3)	2(0-3)	1(0-3)	0.817

Abbreviations: BMI: Body mass index; SOFA: sepsis-related organ failure assessment; SAPSII: Simplified Acute Physiology Score II; SIRS: systemic inflammatory response syndrome; OASIS: Oxford Acute Severity of Illness Score. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification. Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

Table S3. Univariate analysis of clinical outcome by BMI category after adjustment of confounding factors

	BMI<25 kg/m ² (n=357)	BMI25-30kg/m ² (n=357)	BMI>30 kg/m ² (n=357)	<i>p</i>
Mortality,n(%)				
Hospital mortality	69(19.33)	65(18.21)	51(14.29)	0.174
30-day mortality	65(18.21)	47(13.17)	45(12.61)	0.066
90-day mortality	99(27.73)	83(23.25)	76(21.29)	0.119
Length of stay ,day(IQR)				
Hospital LOS	14.98(8.53-28.53)	15.39(7.85-27.03)	16.16(9.12-29.87)	0.16
Living patients(n=886)	15.07(8.85-27.82)	14.33(7.91-24.88)	16.58(9.63-29.93)	0.082
Dead patients(n=185)	14.16(5.28-29.69)	17.98(7.08-33.25)	13.39(5.95-29.82)	0.992
ICU LOS	3.13(1.83-7.81) ^a	3.60(1.90-8.91) ^a	4.97(2.21-13.45) ^b	<0.001
Living patients(n=957)	3.10(1.78-6.61) ^a	3.25(1.82-7.74) ^a	4.93(2.21-13.29) ^b	<0.001
Dead patients(n=185)	5.91(2.21-13.96)	11.71(3.74-31.11)	6.86(2.08-15.09)	0.096

Abbreviations: BMI: Body mass index; LOS: length of stay. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification. Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

71 **Table S4. Univariate analysis of requirement of organ support therapy by BMI category after**
72 **adjustment of confounding factors**

	BMI<25kg/m ² (n=357)	BMI25–30kg/m ² (n=357)	BMI>30 kg/m ² (n=357)	<i>p</i>
Ventilation , n(%)	188(52.66)	203(56.86)	219(61.34)	0.064
Dialysis, n (%)	21(5.9)	30(8.4)	28(7.8)	0.4
Vasoactive agent, n(%)	123(34.45)	123(34.45)	129(36.13)	0.863

73 Abbreviations: BMI: Body mass index; The letter a and b were used to indicate the
74 difference between groups and if there is statistical difference between the two
75 subgroups, different letters shall be used for identification. Adjusted for age, gender,
76 admission type, insurance type, marital status, ethnicity.

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Table S5. Univariate analysis of laboratory examination by BMI category

	BMI<25kg/m ²	BMI25-30kg/m ²	BMI>30kg/m ²	<i>p</i>
HGB	9.50(8.30-10.70),n=354	9.60(8.4-10.80),n=355	9.70(8.6-11.2),n=356	0.053
WBC	10(6.1-14.53),n=354	9.7(6.5-13.8),n=355	10.7(6.83-14.58),n=356	0.145
PLT	184.5(114.5-269.5)n=354	182(124-252)n=355	187(123.5-269.5)n=357	0.732
CRE	1.1(0.8-1.8) ^a ,n=354	1.2(0.9-2.2) ^b ,n=355	1.4(0.9-2.3) ^b ,n=357	<0.001
BUN	25(16-39),n=354	25(16-41),n=355	26(16-44.5),n=357	0.57
ALB	2.6(2.2-3.1),n=208	2.7(2.2-3.2),n=215	2.7(2.3-3.1),n=201	0.597
Cl	108(105-113) ^{a,b} ,n=354	109(105-112) ^a ,n=356	108(104-112) ^b ,n=357	0.021
K	3.6(3.2-4.0),n=354	3.7(3.3-4.0),n=356	3.7(3.4-4.1),n=357	0.124
Na	135(132-139) ^a ,n=354	136(133-139) ^{a,b} ,n=356	137(134-139) ^b ,n=357	0.042
GLU	152(122.75-194) ^a ,n=354	154(125-195.75) ^a ,n=356	168(136.5-224) ^b ,n=357	0.001
LAC	2.6(1.6-4.6),n=279	2.7(1.5-4.425),n=286	2.4(1.4-4.2),n=287	0.329
BIL	1(0.5-2.85)	1.2(0.6-2.425)	1.1(0.6-2.5)	0.397

Abbreviations: BMI: Body mass index; HGB: hemoglobin; WBC: white blood cell count; PLT: platelet count; ALB: albumin; CRE: creatinine; BUN: urea nitrogen; GLU: glucose; LAC: lactate; BIL: bilirubin; Na: sodium; Cl: chlorine; K: potassium. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification. Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

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Table S6. The results of subgroup analysis of multi-factor regression analysis		
Exposure	Acute pancreatitis HR, <i>p</i> Value	Other diagnostics HR, <i>p</i> Value
Non-adjusted		
BMI	0.98 (0.96, 1.00), 0.0612	0.98 (0.96, 0.99), 0.0009
BMI		
<25 kg/m ²	1.0(Reference)	1.0(Reference)
25-30 kg/m ²	0.66 (0.46, 0.93), 0.0188	0.89 (0.70, 1.13), 0.3328
>30 kg/m ²	0.67 (0.49, 0.94), 0.0184	0.72 (0.57, 0.92), 0.0086
Adjust		
BMI	0.98 (0.95, 1.00), 0.0821	0.97 (0.95, 0.99), 0.0047
BMI		
<25 kg/m ²	1.0(Reference)	1.0(Reference)
25-30 kg/m ²	0.65 (0.42, 1.01), 0.0534	0.81 (0.57, 1.15), 0.2391
>30 kg/m ²	0.70 (0.46, 1.08), 0.1065	0.61 (0.42, 0.89), 0.0103

Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity; HGB; GLU; ALB; Charlson comorbidity index.

Table S7. The results of multi-factor regression analysis after multiple imputation

Exposure	MI.ITER= 0 HR, <i>p</i> value	MI.ITER= 1 HR, <i>p</i> value	MI.ITER= 2 HR, <i>p</i> value	MI.ITER= 3 HR, <i>p</i> value	MI.ITER= 4 HR, <i>p</i> value	MI.ITER= 5 HR, <i>p</i> value
Non-adjusted						
BMI	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001
BMI <25 kg/m ²	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)
25-30 kg/m ²	0.78 (0.64, 0.96) 0.0158	0.75 (0.64, 0.88) 0.0005	0.85 (0.73, 1.01) 0.0589	0.81 (0.69, 0.95) 0.0110	0.82 (0.69, 0.96) 0.0159	0.79 (0.67, 0.93) 0.0049
>30 kg/m ²	0.68 (0.56, 0.83) 0.0001	0.68 (0.58, 0.80) <0.0001	0.68 (0.58, 0.80) <0.0001	0.66 (0.56, 0.78) <0.0001	0.71 (0.61, 0.84) <0.0001	0.68 (0.57, 0.80) <0.0001
Adjusted						
BMI	0.98 (0.96, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001
BMI <25 kg/m ²	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)
25-30 kg/m ²	0.74 (0.61, 0.91) 0.0042	0.74 (0.63, 0.88) 0.0004	0.82 (0.69, 0.97) 0.0192	0.79 (0.67, 0.94) 0.0069	0.80 (0.68, 0.95) 0.0088	0.77 (0.65, 0.91) 0.0019
>30 kg/m ²	0.65 (0.53, 0.79) <0.0001	0.65 (0.55, 0.77) <0.0001	0.65 (0.55, 0.77) <0.0001	0.63 (0.53, 0.74) <0.0001	0.68 (0.58, 0.81) <0.0001	0.66 (0.56, 0.79) <0.0001

Adjusted for gender; admission age; SOFA; admission type; insurance; marital status;
ethnicity; HGB; GLU; ALB; Charlson comorbidity index.

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Table S8. Subgroup analysis of multi-factor regression analysis after multiple imputation						
Exposure	MI.ITER=0 HR, <i>p</i> value	MI.ITER= 1 HR, <i>p</i> value	MI.ITER= 2 HR, <i>p</i> value	MI.ITER= 3 HR, <i>p</i> value	MI.ITER= 4 HR, <i>p</i> value	MI.ITER= 5 HR, <i>p</i> value
Acute pancreatitis						
Non-adjusted						
BMI	0.98 (0.96, 1.00) 0.0612	0.98 (0.97, 1.00) 0.0348	0.98 (0.96, 1.00) 0.0288	0.98 (0.97, 1.00) 0.0491	0.99 (0.97, 1.00) 0.0863	0.99 (0.97, 1.01) 0.1758
Adjust						
BMI	0.99 (0.97, 1.01) 0.3791	0.99 (0.97, 1.01) 0.1755	0.99 (0.97, 1.01) 0.1986	0.99 (0.97, 1.01) 0.2298	0.99 (0.97, 1.01) 0.2988	1.00 (0.98, 1.02) 0.8201
Other patients						
Non-adjusted						
BMI	0.98 (0.96, 0.99) 0.0009	0.97 (0.96, 0.99) <0.0001	0.98 (0.96, 0.99) <0.0001	0.97 (0.96, 0.98) <0.0001	0.98 (0.96, 0.99) <0.0001	0.97 (0.96, 0.99) <0.0001
Adjust						
BMI	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001
192	Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity; HGB; GLU; ALB; Charlson comorbidity index.					
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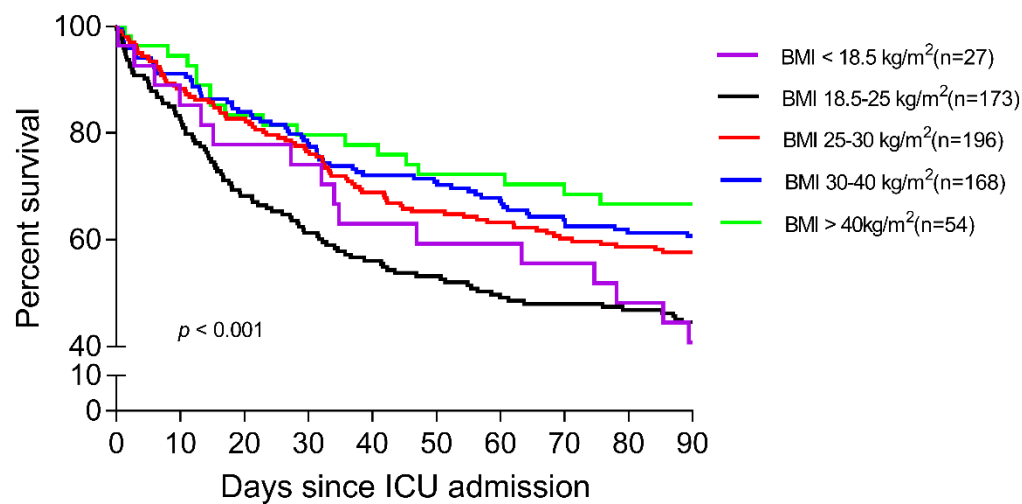


Figure S1. Kaplan–Meier curve for 90-days survival stratified by BMI.

Abbreviations: BMI: Body mass index; Fig.S1 represents 90-days Kaplan–Meier curves, $P < 0.001$ by log-rank test.

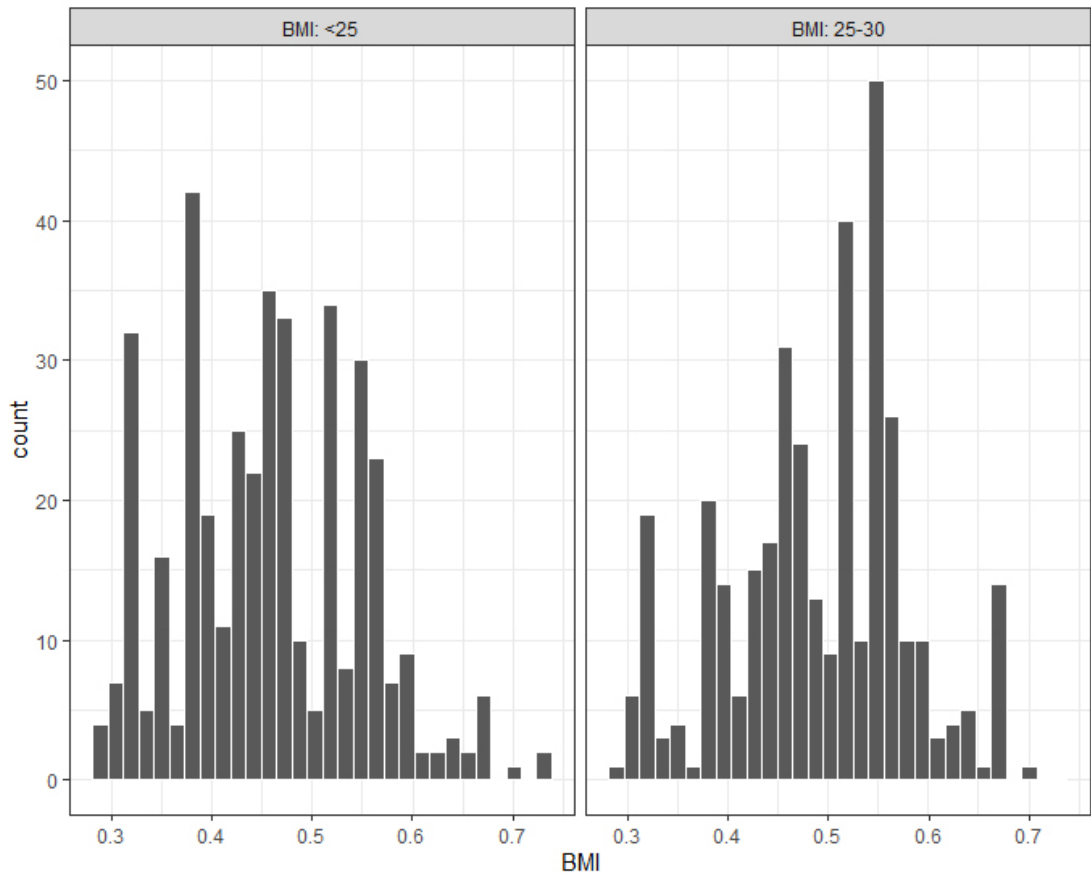


Figure S2. Propensity score counting of normal and overweight patients.

Abbreviations: BMI: Body mass index;

Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

Distribution of Propensity Scores

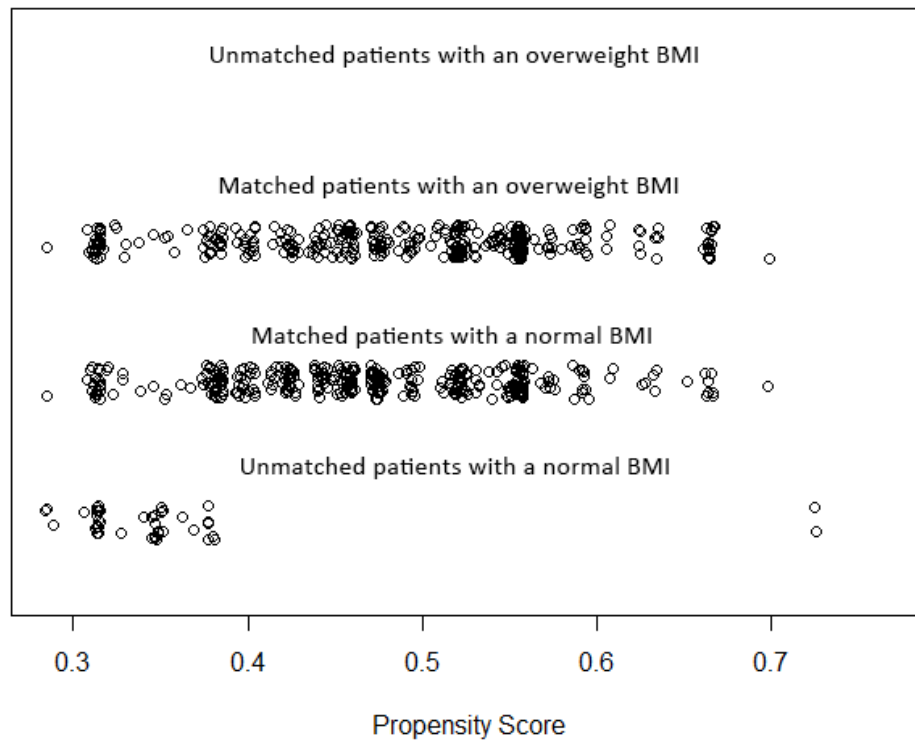


Figure S3. Distribution of propensity scores between normal and overweight patients. Abbreviations: BMI: Body mass index; Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

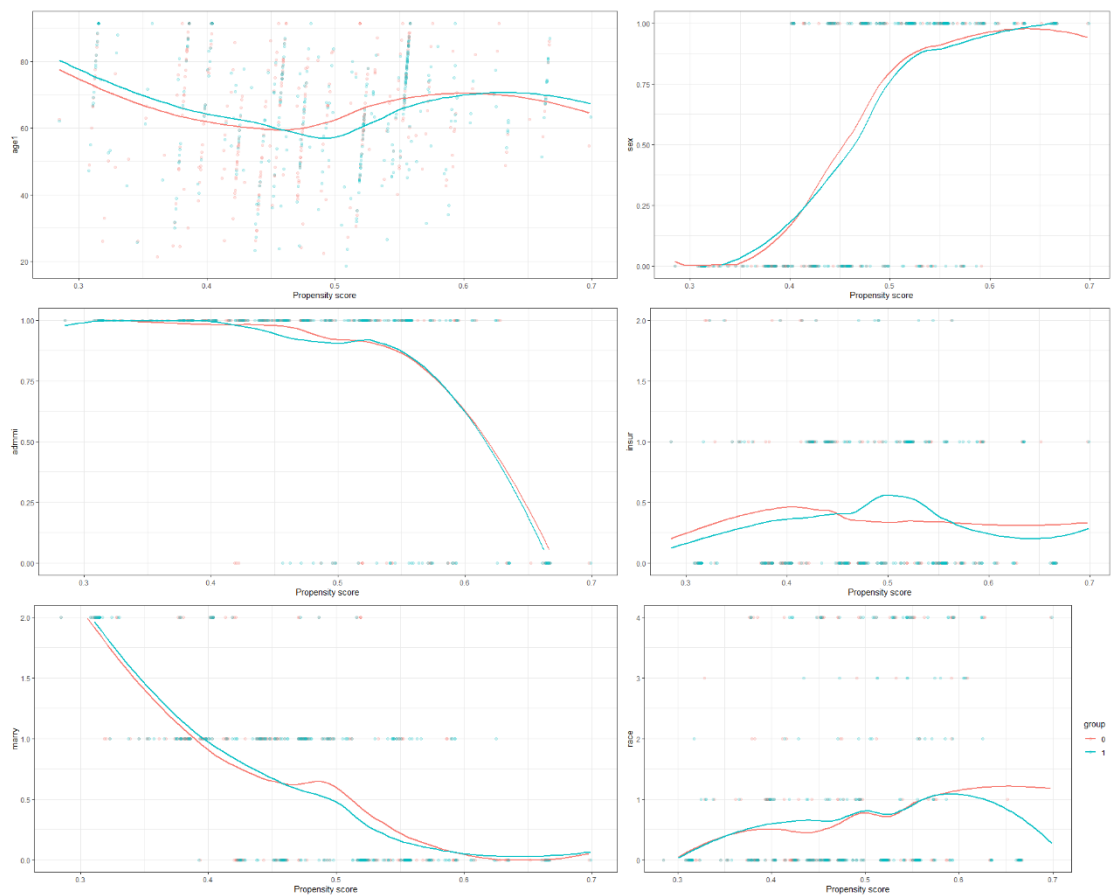


Figure S4. Trend of baseline characteristics after adjustment for confounding factors. Abbreviations: BMI: Body mass index; age1: Admission age of patients; sex: gender of patients; admmi: Admission type of patients; insur: Insurance type of patients; marry: Marital status of patients; race: Ethnicity of patients; group 0: patients with an overweight BMI; group 1: patients with a normal BMI; Adjusted for age , gender ,admission type, insurance type ,marital status , ethnicity.

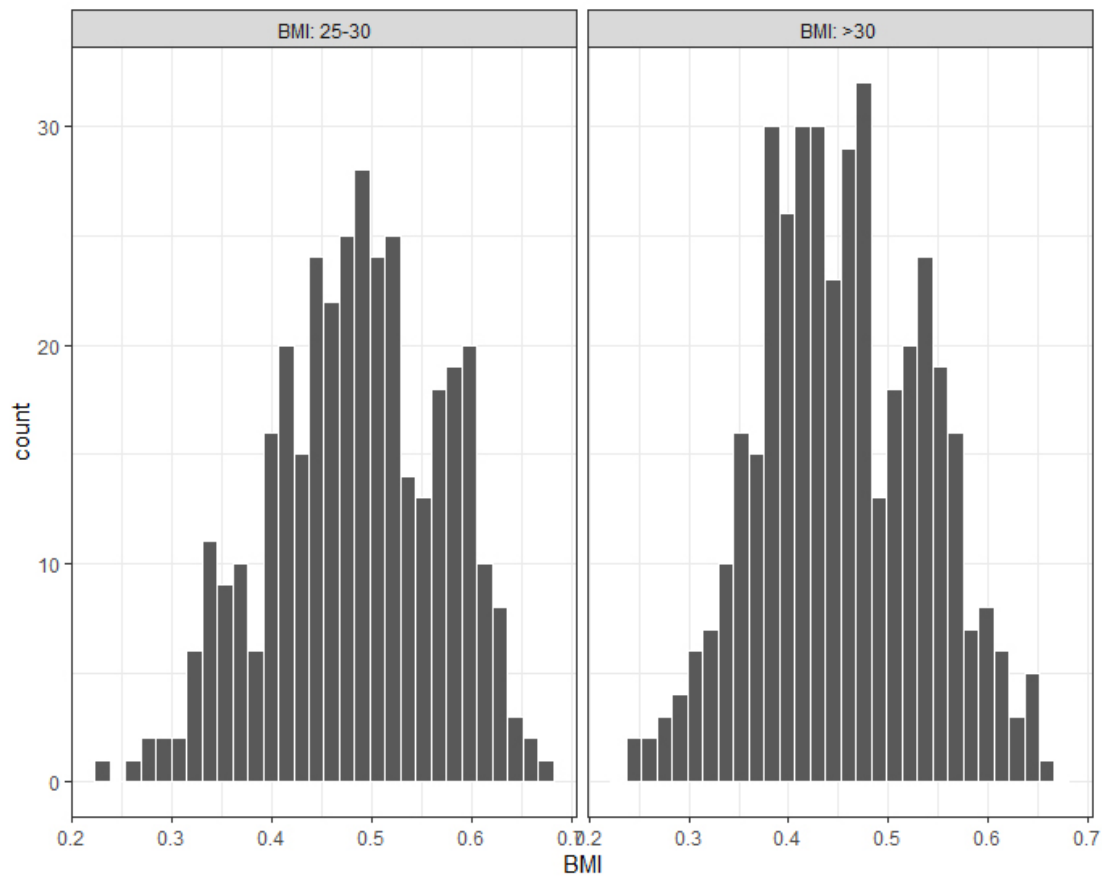


Figure S5. Propensity score counting of obese and overweight patients.

Abbreviations: BMI: Body mass index;

Adjusted for age , gender ,admission type, insurance type ,marital status , ethnicity.

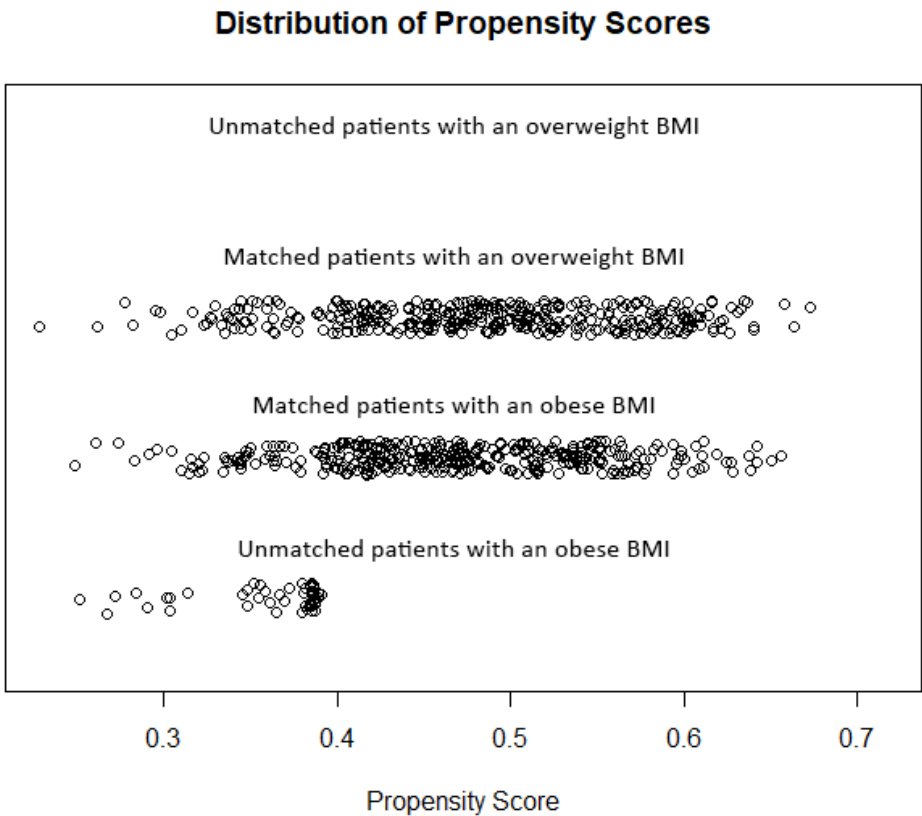


Figure S6. Distribution of propensity scores between obese and overweight patients. Abbreviations: BMI: Body mass index; Adjusted for age , gender ,admission type, insurance type ,marital status , ethnicity.

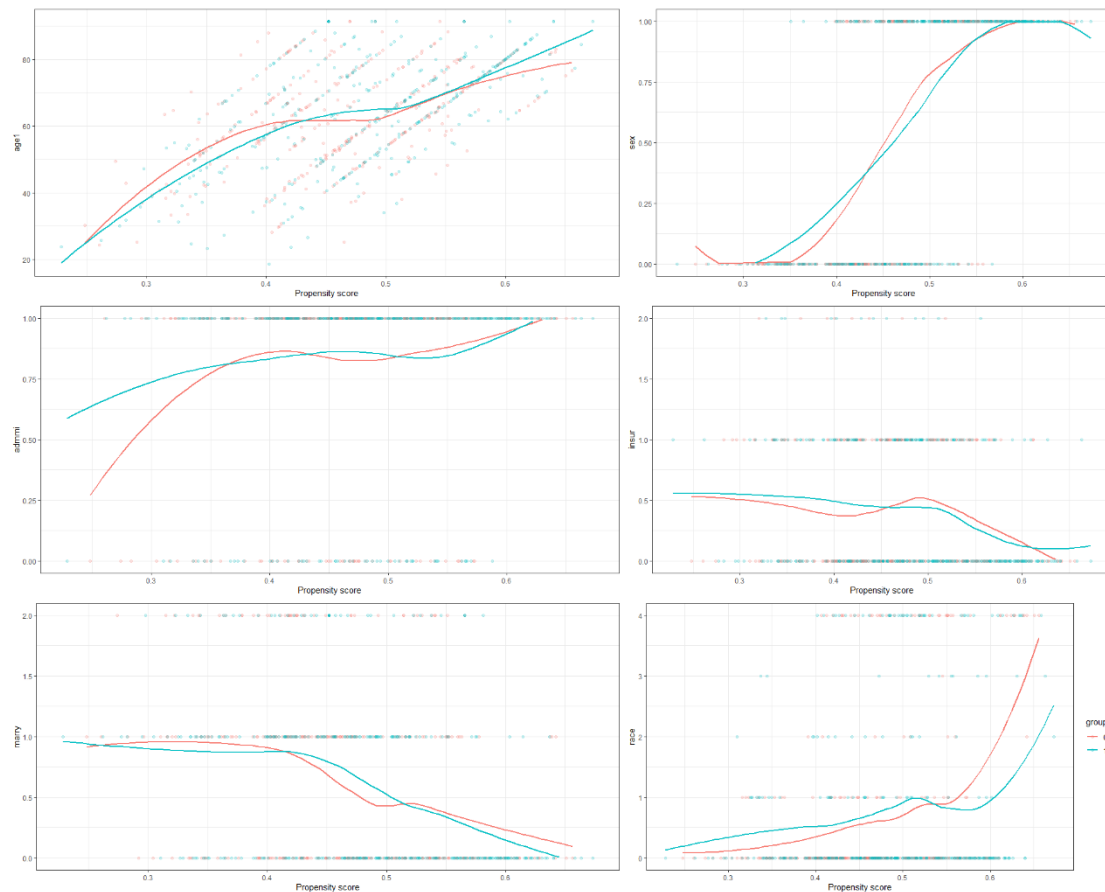


Figure S7. Trend of baseline characteristics after adjustment for confounding factors. Abbreviations: BMI: Body mass index; age1: Admission age of patients; sex: gender of patients; admmi: Admission type of patients; insur: Insurance type of patients; marry: Marital status of patients; race: Ethnicity of patients; group 0: patients with an overweight BMI; group 1: patients with a obese BMI; Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

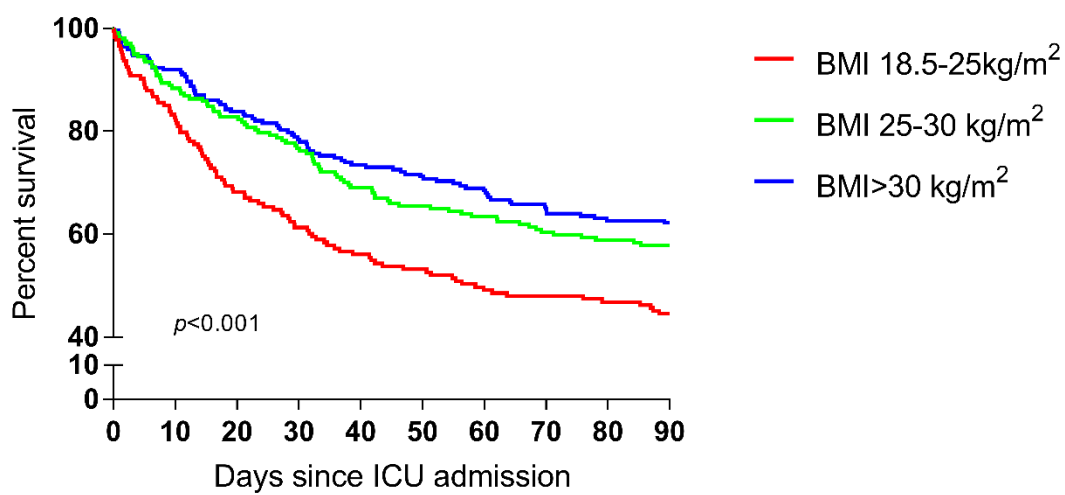


Figure S8. Kaplan–Meier curve for 90-days survival stratified by BMI.
Abbreviations: BMI: Body mass index; Fig.S8 represents 90-days Kaplan–Meier curves, P<0.001 by log-rank test.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2	Design: Retrospective study.
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2	IAI patients with an overweight or obese BMI might have lower 90-day mortality than patients with a normal BMI.
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	IAs are common surgical emergencies and have been reported as major contributors to non-trauma deaths in emergency departments worldwide and as a common complication of abdominal surgery
Objectives	3	State specific objectives, including any prespecified hypotheses	4	The aim of this study was to determine the relationship between BMI and the prognosis of patients with IAs by using the Medical Information Mart for Intensive Care (MIMIC-III) database
Methods				
Study design	4	Present key elements of study design early in the paper	6	The primary endings were the 90- days mortality after ICU admission.

Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	The database maintained by the Laboratory for Computational Physiology at the Massachusetts Institute of Technology (MIT). In MIMIC database, all diagnostics correspond to International Classification of Diseases (ICD-9) codes.
Participants	6	<p>(a) <i>Cohort study</i>—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</p> <p><i>Case-control study</i>—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</p> <p><i>Cross-sectional study</i>—Give the eligibility criteria, and the sources and methods of selection of participants</p> <p>(b) <i>Cohort study</i>—For matched studies, give matching criteria and number of exposed and unexposed</p> <p><i>Case-control study</i>—For matched studies, give matching criteria and the number of controls per case</p>	5	For patients who had multiple ICU admissions, only the first admission record was kept. The exclusion criterion included: (1) age under 18 years old (2) the weight data was missing.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6	Finally, all patients are divided into three groups: normal BMI group ($BMI < 25kg/m^2$), overweight BMI group(25-30 kg/m^2) and obese BMI group ($BMI > 30kg/m^2$). There is not a specific diagnosis of IAI in ICD-9 coding, so we include all the possible diagnosis related to IAIs in ICD-9 into our study cohort, and all ICD-9 codes, diagnostics

				and numbers of specific diagnoses are listed in Table S1.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6	Data extraction and management
Bias	9	Describe any efforts to address potential sources of bias	7	We used propensity score match to adjusting for confounding factors, including age, gender, admission type, ethnicity, marital status and insurance type.
Study size	10	Explain how the study size was arrived at	8	Finally, after excluded 679 patients without height patients, a total of 1161 patients were finally included in the study

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7	If none of the above requirements were met or the data were not continuous variables, then the data are described as the median and interquartile range, and the Wilcoxon rank-sum test was used for comparisons.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7	We used propensity score match to adjusting for confounding factors, including age, gender, admission type, ethnicity, marital status and insurance type.
		(b) Describe any methods used to examine subgroups and interactions	7	We tested the collinearity of the variables included in the statistical analysis, and found that VIF of all variables was less than 3, hence there was no statistical collinearity in the included variables.
		(c) Explain how missing data were addressed	7	We used multiple imputation (MI), based on 5 replications and a chained equation approach method in the R MI procedure, to account for missing data on height
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy		
		(e) Describe any sensitivity analyses	10	However, in the multi-factor regression analysis of subgroup analysis of acute pancreatitis and other patients, when BMI was

			employed as a continuous variable, the adjusted HR value were 0.98(0.95,1.00) and 0.97(0.95,0.99) for acute pancreatitis patients and other patients, respectively
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	The MIMIC-III database includes 2087 patients diagnosed with intra-abdominal infection according to the criteria we mentioned above. Among these patients, 233 lacked weight data and were excluded from the study, and 14 patients with abnormal data records were excluded (e.g., height value> 300 meter, survival time < 0 day). Multiple imputation was used to account for missing data on height in the rest of 1840 patients. Finally, after excluded 679 patients without height patients, a total of 1161 patients were finally included in the study
		(b) Give reasons for non-participation at each stage	The MIMIC-III database includes 2087 patients diagnosed with intra-abdominal infection according to the criteria we mentioned above. Among these patients, 233 lacked weight data and were excluded from the study, and 14 patients with abnormal data records were

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				excluded (e.g., height value> 300 meter, survival time < 0 day). Multiple imputation was used to account for missing data on height in the rest of 1840 patients. Finally, after excluded 679 patients without height patients, a total of 1161 patients were finally included in the study
		(c) Consider use of a flow diagram	8	Figure1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8	Table 1 shows the baseline characteristics of patients grouped by BMI.
		(b) Indicate number of participants with missing data for each variable of interest	8	Finally, after excluded 679 patients without height patients, a total of 1161 patients were finally included in the study (Figure 1).
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	9	The K–M curve for 90- day survival by BMI is shown in Figure 2.
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	9	The mortality of patients with BMI < 25 kg/m ² was significantly higher than that of patients with an obese BMI at 30 days after entering the ICU (18.55% vs. 11.85%, P=0.016, respectively),
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10	When BMI was employed as a continuous variable, the adjusted HR value in the four

		models were separately 0.98 (0.97, 0.99), 0.97 (0.96, 0.99), 0.97 (0.96, 0.99), and 0.96(0.95, 0.98).
(b) Report category boundaries when continuous variables were categorized	9	In different subgroups, patients with a BMI > 25 kg/m ² had significantly better survival than those with a BMI < 25 kg/m ²
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10	BMI was employed as a continuous variable or a classification variable, the adjusted HR value in the models showed that BMI were protective factor of the 90-day mortality in patients with IAs

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10	However, in the multi-factor regression analysis of subgroup analysis of acute pancreatitis and other patients
Discussion				
Key results	18	Summarise key results with reference to study objectives	10	In this retrospective study, we used the MIMIC-III database to study the relationship between BMI and the short-term mortality of patients with abdominal infection.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14	This study still has several limitations.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14	IAI patients with an overweight and obese BMI have lower 90-day mortality than patients with a normal BMI.
Generalisability	21	Discuss the generalisability (external validity) of the study results	12	This is a phenomenon called the obesity paradox, which means that overweight and obese patients are recognized as they often have more basic diseases, such as hypertension, cardiovascular disease and diabetes.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15	Funding None.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Association between body-mass index and short-term mortality in patients with intra-abdominal infections: a retrospective, single-centre cohort study using the Medical Information Mart for Intensive Care database

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31 **Abstract**

32 **Objectives:** This study aimed to determine the relationship between the body mass
33 index (BMI) and short-term mortality of patients with intra-abdominal infection (IAI)
34 using the Medical Information Mart for Intensive Care (MIMIC-III) database.

35 **Design:** Retrospective cohort study.

36 **Setting:** Adult intensive care units (ICUs) at a tertiary hospital in the USA .

37 **Participants:** Adult IAI ICU patients from 2001 to 2012 in the MIMIC-III database.

38 **Interventions:** In univariate analysis, we compared the differences in the
39 characteristics of patients in each BMI group. Cox regression models were used to
40 evaluate the relationships between BMI and short-term prognosis.

41 **Primary and secondary outcome measures:** 90-day survival.

42 **Results:** In total, 1161 patients with IAI were included. There were 399 (34.4%)
43 patients with a normal BMI ($< 25 \text{ kg/m}^2$), 357(30.8%) overweight patients (25-30
44 kg/m^2), and 405(34.9%) obese patients ($> 30 \text{ kg/m}^2$) who tended to be younger (p
45 <0.001) and had higher Sequential Organ Failure Assessment (SOFA) scores ($p <0.05$).
46 The mortality of obese patients at 90 days was lower than that of patients with a normal
47 BMI (20.74% vs. 23.25%, $p <0.05$), but their length of stay (LOS) in the ICU was
48 higher (4.9 days vs. 3.6 days, $p <0.001$); however, their rate of mechanical ventilation
49 utilisation was higher (61.48% vs. 56.86%, $p <0.05$). In the Cox regression model, we
50 also confirmed that BMI was a protective factor in patients with IAIs, and the adjusted
51 mortality rate of patients with a higher BMI was 0.97- times lower than that of patients
52 with a lower BMI ($p <0.001$, hazard ratio [HR] =0.97, 95% CI 0.96-0.99).

53 **Conclusions:** IAI patients with an overweight or obese status might have lower 90-day
54 mortality than patients with a normal BMI.

55 **Strengths and limitations of this study**

- 56 • To our knowledge, this is the first study to evaluate the association between
57 BMI and the short-term mortality of patients with abdominal infection.
- 58 • Multiple imputation was used to handle the missing values.
- 59 • This study is essentially a retrospective single-centre study, which makes it
60 difficult to completely exclude the influence of residual confounding factors.

- A considerable number of patients' data are missing, especially various laboratory test data, which may cause selection bias.
- Given the observational nature of this study, we can't determine causality between the BMI and mortality.

Key word: Intra-abdominal infection; BMI; MIMIC-III; Big data; Mortality; ICU;

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911. INTRODUCTION

92 Intra-abdominal infections (IAIs) are common surgical emergencies and have been
93 reported as major contributors to non-trauma deaths in emergency departments
94 worldwide and a common complication of abdominal surgery ¹. IAIs are the second
95 most common cause of sepsis, and the second most common infectious disease among
96 inpatients. The death rate of IAIs can reach 20%, indicating a commonly poor prognosis
97 in patients ^{2 3}. IAIs can be divided into uncomplicated and complicated types.
98 Uncomplicated IAIs affect a single organ, and complicated IAIs describe an extension
99 of the infection into the peritoneal space. The resultant physiologic response may
100 develop into a systemic inflammatory response syndrome (SIRS)⁴.

101 The body mass index(BMI), calculated as the weight divided by the square of the height,
102 is used by most health organizations, including the World Health Organization (WHO),
103 as a screening tool for diagnosing obesity⁵. Overweight and obesity are uniformly
104 associated with a substantially increased risk of death⁶. In patients not admitted to the
105 intensive care unit (ICU), such as endometrial and breast cancer patients, BMI can be
106 used as a prognostic indicator ^{7 8}. Similarly, in ICU patients, such as liver transplant
107 patients, morbid obesity has an impact on patient survival and post-transplant
108 complications⁹. Furthermore, at least a quarter of patients in U.S. ICUs have a BMI
109 indicating overweight, obesity or morbid obesity status ¹⁰. As mentioned above, patients
110 with IAIs also tend to develop severe conditions and were admitted in the ICU. Previous
111 studies have shown that obesity plays a protective role in some diseases (such as chronic
112 kidney disease, AIDS), which is a special phenomenon called the obesity paradox ¹¹
113 ¹².However, in ICU patients with IAIs, whether BMI is a risk factor or a protective
114 factor, considering the obesity paradox , still needs further study.

115 This study was aimed to determine the relationship between BMI and the 90-day
116 mortality of patients with IAIs using the Medical Information Mart for Intensive Care
117 (MIMIC-III) database¹³.The MIMIC-III database is a large, single-centre database
118 comprising information related to patients admitted to critical care units at a large
119 tertiary care hospital. Data included vital signs, medications, laboratory measurements,
120 diagnostic codes, hospital length of stay, survival data, etc. The data cover 53,423

distinct hospital admissions for adult patients admitted to critical care units between 2001 and 2012, and many studies have been conducted to explore the clinical features of ICU patients using the database¹⁴⁻¹⁶.

MATERIALS AND METHODS

2.1. Database

In this article, we did a retrospective cohort study using a publicly available critical care medicine database, MIMIC-III. This database contains unidentified medical information from 53,423 patients admitted to the critical care units of the Beth Israel Deaconess Medical Center in Boston, Massachusetts, from 2001 to 2012. The database maintained by the Laboratory for Computational Physiology at the Massachusetts Institute of Technology (MIT). In MIMIC database, all diagnostics correspond to International Classification of Diseases (ICD-9) codes. The use of MIMIC-III database was under the approval from the review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center¹⁷. The database is freely available, in that any researcher who accepts the data-use agreement and has completed the “protecting human subjects” training can apply for permission to access the data. We did not need patient consent or ethics approval, as all of the data were de-identified. All authors completed the “protecting human subjects” training.

2.2. Study population

There is no specific IAI diagnosis in ICD-9 coding; therefore, we included all the possible diagnoses related to IAIs in ICD-9 into our study cohort, and all ICD-9 codes, diagnostics and numbers of specific diagnoses are listed in Table S1. For patients who had multiple ICU admissions, only the first admission record was kept. The exclusion criteria were as follows: (1) those under 18 years old and (2) missing weight data. According to the BMI classification standard of the WHO, we divided the patients into five groups: underweight (BMI < 18.5 kg/m²), normal weight (BMI: 18.5 to <25 kg/m²), overweight (BMI: 25 to <30 kg/m²), obese (BMI 30 to <40 kg/m²), and morbidly obese (BMI > 40 kg/m²). However, in this grouping method, the number of patients in the underweight and morbidly obese subgroups was not sufficient (n = 27 and 54, respectively, as shown in Figure S1). Finally, all patients were divided into three groups:

normal BMI group ($\text{BMI} < 25\text{kg/m}^2$), overweight BMI group ($25\text{--}30\text{ kg/m}^2$) and obese BMI group ($\text{BMI} > 30\text{kg/m}^2$).

2.3. Data extraction and management

We used the structure query language (SQL) in PostgreSQL (version 9.5) to retrieve the data. The following data were extracted from the MIMIC-III database on the first day of ICU admission: age; sex; ethnicity; admission weight; admission height; admission diagnosis; admission type; Sequential Organ Failure Assessment (SOFA) score; Simplified Acute Physiology Score II (SAPSII); Charlson Comorbidity Index; use of vasopressors; renal replacement therapy (RRT); mechanical ventilation use; values of hemoglobin(HGB); white blood cell(WBC); platelet count(PLT); albumin(ALB); sodium(Na); chlorine(Cl) ; potassium(K); creatinine(CRE);blood urea nitrogen(BUN); glucose(GLU) ; lactate(LAC) , and bilirubin(BIL) levels in the first 24 h of ICU admission; length of stay(LOS) before ICU admission; length of stay (both ICU and hospital); intake and output. The SOFA score was calculated within the first 24 h after ICU admission. If a variable was measured more than once in the first 24 h, the value that indicated a worse prognosis was used. In addition, dates of birth for patients aged over 89 years were moved to obscure their true age and comply with HIPAA regulations: these patients appear in the database with ages of over 300 years, but the median age of these patients was 91.5 years, so we modified their age to 91.5 years.

2.4. Outcomes

The primary endings was the 90-day mortality after ICU admission.

2.5. Patient and public involvement

We did not need patient consent or ethics approval, as all data were de-identified. The use of MIMIC-III database was approved by the review boards of the MIT and Beth Israel Deaconess Medical Centre.

2.6. Statistical analysis

First, univariate analysis was used to compare all variables. If the data satisfied a normal distribution and the variance was homogeneous, the data were expressed as the mean \pm standard deviation, and Student's t-test was used for comparisons. If the variance was

not homogeneous, one-way ANOVA was used for the comparisons. If none of the above requirements were met or the data were not continuous variables, then the data were described as the median and interquartile range, and the Wilcoxon rank-sum test was used for comparisons. Categorical variables were presented as numbers and percentages and compared using Pearson's chi-square test or Fisher's exact test as appropriate. We used the log-rank test and 90-day Kaplan–Meier(K-M) curves to carry out the survival analysis, and determined whether BMI associated with 90-day mortality. In addition, we compared the 90-day survival curves between subgroups of patients with and without sepsis using log-rank test.

Propensity score matching (PSM) was performed to minimize the influence of confounding factors on selection bias. The propensity scores were elicited from matched patients in a 1:1 ratio with greedy matching algorithms without replacement. We adjusted for age, gender, admission type, ethnicity, marital status and insurance type.

We used multiple imputation (MI), based on five replications and a chained equation approach method in the R STUDIO MI procedure, to account for missing data on height and the missing laboratory test¹⁸. Multivariate analyses were adjusted for the possible variables that may affect the prognosis of patients to determine the relationship between BMI and 90- day mortality.

We tested the collinearity of the variables included in the statistical analysis, and found that the variance inflation factor (VIF) of all variables was < 3 ; hence, there was no statistical collinearity in the included variables.

Variables with $p < 0.10$ in univariate analysis were included in the Cox regression model as confounders to determine whether BMI was the independent risk factor of the 90-day survival rates. However, since SOFA scores included BIL and CRE level, PLT count, mechanical ventilation use, and vasoactive drug use, and Charlson comorbidity index includes comorbidity, to avoid instability of the model caused by collinearity among variables, we did not adjust these variables in the statistical analysis. SPSS (version 25.0; IBM, Armonk, NY) and EmpowerStats (version 2018-05-05, copyright 2009 X&Y Solutions, Inc) were used for data analysis; a two-tailed $p < 0.05$

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was considered statistically significant. R STUDIO was used for PSM to adjusting for confounding factors, and the PSM results was showed in Figures S2-S7.

RESULTS

3.1. Population and baseline characteristics

The MIMIC-III database includes 2,087 patients diagnosed with IAI according to the criteria mentioned above. Among these patients, 233 lacked weight data and were excluded from the study, and 14 patients with abnormal data records were excluded (e.g., height value> 300 m, survival time < 0 day). MI was used to account for missing data on height in the remaining 1840 patients. Finally, after excluding 679 patients without height measurements, a total of 1,161 patients were finally included in the study (Figure 1).

Table 1 shows the baseline characteristics of patients grouped according to their BMI. There were 399 patients with BMI < 25 kg/m², 357 patients with BMI 25-30 kg/m² and 405 patients with BMI > 30 kg/m², accounting for 34.37%, 30.75% and 34.88% of the patients, respectively. In the subgroup aged 45-64 years, the proportion of patients with an obese status was higher than that of patients with a normal and an overweight BMI (42.96% vs. 31.58% and, 42.96% vs. 33.61%, respectively, *p*<0.05), while in the subgroup of patients older than 90 years, the result was the opposite (1.73% vs. 8.02% and 1.73% vs.5.32, respectively, *p*<0.05). The proportion of females in the group of patients with an overweight status was lower than that in the other groups (*p*<0.001). There was no significant difference in ethnicity between the three groups (*p*=0.183). However, there were significant differences between the three groups in regard to marital status and admission type (*p*= 0.008 and 0.009, respectively). The group with BMI < 25 kg/m² had lower SOFA scores on the first day of admission than the obese group (*p*=0.039). However, there was no significant difference between the two groups with regard to SAPS II, SIRS, qSOFA score, OASIS score and Charlson Comorbidity Index (*p* > 0.05). Table S2 shows the baseline characteristics after adjusting for confounding factors. After adjusting for confounding factors listed above, SOFA scores remained significantly different between groups (*p* <0.05).

3.2. Univariate analysis of outcomes

241 The mortality rates at different times of admission and the LOS of patients in the
242 different BMI groups are shown in Table 2.

243 The mortality of patients with BMI < 25 kg/m² was significantly higher than that of
244 obese patients at 30 days after admission to the ICU (18.55% vs. 11.85%, respectively,
245 $p=0.016$), which was the same at 90 days after admission to the ICU (28.07% vs.
246 20.74%, respectively, $p=0.048$). In addition, the median LOS for patients with a BMI<
247 25, 25-30 and > 30kg/m² in the ICU was 3.13, 3.59 and 4.93 days,
248 respectively($p<0.001$), and the obese group spent significantly more time in the ICU
249 than the former two groups ($p<0.05$). However, in the subgroup analysis, only those
250 patients who did not die in the ICU showed significant differences, while those who
251 died did not ($p<0.001$ and $p=0.166$, respectively). After adjusting for confounding
252 factors, the LOS in the ICU of obese patients was still significantly longer than that of
253 the other two groups ($p<0.001$, Table S3). In subgroup analysis, the conclusion was the
254 same as above, which may be due to the bias caused by the number of deceased patients.
255 The K–M curve for the 90- day survival by BMI is shown in Figure 2. This shows that
256 the group with an overweight and obese BMI had a significant survival advantage.
257 ($p<0.001$ by log-rank test). After excluding patients with BMI < 18.5 kg/m², the K-M
258 curve was rebuilt (Figure S8), and the result did not change ($p<0.001$ by log-rank test).
259 The 90-day survival curve stratified according to the BMI in patients with and without
260 sepsis is shown in Figure 3. In different subgroups, patients with a BMI > 25 kg/m² had
261 significantly better survival than those with a BMI < 25 kg/m² ($p<0.001$ and $p<0.05$,
262 respectively, by log-rank test).

263 We also compared the use of mechanical ventilation, vasoactive drugs and dialysis
264 between the three groups as shown in Table 3. The proportion of patients with an obese
265 BMI who needed mechanical ventilation was higher than that in patients with a normal
266 BMI (61.48% vs. 52.38%, $p=0.034$). However, in regard to the use of vasoactive drugs
267 and dialysis, there was no significant difference between the three groups. After
268 adjusting for confounding factors, there was no significant difference in the use of
269 mechanical ventilation (Table S4).

270 The results of several laboratory tests stratified by BMI are shown in Table 4.

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Significant differences were observed in the HGB, WBC, Cl, CRE and GLU levels between the three groups ($p=0.048, 0.035, 0.007, 0.001$ and <0.001 , respectively). After adjusting for confounding factors, there was no significant difference in HGB levels among the groups, but there was a significant difference in Na levels ($p=0.042$, Table S5).

3.3. Cox proportional hazards analyses of 90- day mortality

We imported variables with p values < 0.10 in univariate analysis into Cox proportional hazards analyses after testing the collinearity of the variables. When BMI was employed as a continuous variable, the adjusted HR values in the four models were 0.98 (0.97, 0.99), 0.97 (0.96, 0.99), 0.97 (0.96, 0.99), and 0.96(0.95, 0.98). When BMI was applied as a classification variable, it was also associated with the 90-day mortality of patients with IAIs (Table 5). However, in the multi-factor regression analysis of the subgroup analysis of acute pancreatitis and other patients, when BMI was employed as a continuous variable, the adjusted HR values were 0.98(0.95,1.00) and 0.97(0.95,0.99) for acute pancreatitis patients and other patients, respectively (Table S6), while both before and after the adjustment, the HR values were almost the same, and the p value were close to 0.05,which may be due to the sample size($n=321$ and $n=355$,respectively after adjustment).

Considering the high proportion of missing height value in the patient group, we conducted MI with height values, and calculated the BMI with weight values and imputed height values. Whether BMI was employed as a continuous variable or a classification variable, the adjusted HR value in the models showed that BMI was a protective factor of the 90-day mortality in patients with IAIs (Table S7). The results in the Table S8 shows that in the imputed data, BMI was not a protective factor in patients with acute pancreatitis, but it was still a protective factor in other IAI patients. Excluding acute pancreatitis patients from the analysis did not affect the results.

2974. Discussion

In this retrospective study, we used the MIMIC-III database to study the relationship between BMI and the short-term mortality of patients with abdominal infection. By comparing the survival curve and 90-day mortality of the three groups, it was found

that the short-term prognosis of overweight (25-30 kg/m²) and obese (>30kg/m²) patients was significantly better than that in the normal group.

By comparing the baseline characteristics of the three groups of patients, a significant difference was observed in the overall age composition of the three groups and in the 45-64 and >90 age subgroups between the three groups, and this statistical difference between subgroups still exists after adjusting for confounding factors. Subsequently, in our study, overweight patients were more likely to be males. However, previous studies have shown that obese cohorts tend to be younger and have a higher female prevalence¹⁹. The possible cause of this discrepancy, as mentioned in previous studies, could be that male patients are more likely to develop abdominal infections such as appendicitis, and smoking is a probable cause for this increased risk^{20 21}.

Currently, studies on the association of obesity with patients outcomes are mainly focused on sepsis, and the results are ambiguous and contradictory²²⁻²⁴. In this study, we expanded the scope of this relationship to study the association between BMI and the short-term outcomes of patients with IAIs. Our finding shows that obese patients had a higher SOFA score at admission, indicating a worse degree of organ failure than that in patients with a lower BMI, and the incidence of sepsis events was higher in patients with a higher BMI. Previous studies have shown that people who were overweight or obese had higher susceptibility to developing postsurgical infections, and respiratory tract infections and tended to develop more severe infections, which is consistent with the results of our study; however, the short-term outcome of these patients was better^{25 26}. The same contradiction exists in our laboratory test results. According to a previous study, serum CRE was an independent risk factor for clinical failure, but in our cohort, obese patients had significantly higher CRE values, which should lead to a worse clinical outcome²⁷. Previous studies also showed that CRE minimums at baseline were considered a predictor of short-term mortality²⁸. However, some studies have reported that CRE can predict multiple organ failure²⁹. This may be related to the baseline characteristics of our study population, and CRE level no longer appears as an independent factor that associated with the prognosis after adjusting for the baseline characteristics. Among the laboratory tests included in our study, the HGB in the obese

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and overweight group was higher than that in the other group. Contrarily, a higher HGB value can provide more oxygen to tissues and reduce hypoxia, whereas obese patients may originally have a higher HGB value, they may therefore confer a survival advantage. After adjusted, there was no significant difference in HGB levels, but the median of HGB in the obese and overweight group still higher than that in the other group. Furthermore, it was found that patients without sepsis but with IAIs can also benefit from a higher BMI. This shows that BMI has a protective effect not only in patients with severe conditions, such as sepsis patients but also in patients with a milder condition. However, once sepsis occurs in patients with abdominal infection, the short-term prognosis will be significantly worse.

Our study also found that patients with a higher BMI had a higher probability of receiving mechanical ventilation, which was also reported in previous studies³⁰. This may be related to the impact of obesity on the respiratory system, obese patients tend to have higher respiratory rates and lower tidal volumes, and lung volumes tend to be decreased, especially the expiratory reserve volume³¹. BMI was associated with an increased risk of acute respiratory distress syndrome (ARDS) in a weight-dependent manner but was not associated with mortality³². As mentioned above, obese patients are also more likely to receive mechanical ventilation as well as the attention of medical staff³³. In summarize, patients with a higher BMI have a poor health foundation and are more likely to progress to critical illness, but there are also some indicators, such as HGB level that may prevent organ failure caused by critical illness in this process. In addition, they are more likely to receive advanced modes of mechanical ventilation, dialysis, liver function support and medical resources.

In the final Cox regression model, BMI remained a protective factor after adjusting for confounding variables. This is a phenomenon called the obesity paradox, which means that overweight and obese patients are recognised as they often have more basic diseases, such as hypertension, cardiovascular disease and diabetes. Their general health is also worse than that of patients with a normal BMI, and some studies have shown that BMI is associated with an incidence rate of more than 20 types of cancers, but BMI still shows protective effects and improves the prognosis of patients. The

reasons and underlying mechanisms have not been clarified³⁴. Some studies have suggested that patients with obesity-associated comorbidities, such as hypertension may require less vasoactive drugs and fluid resuscitation in the treatment process; severe IAs can lead to sepsis that requires fluid resuscitation, and a restrictive fluid strategy would reduce the burden of heart or lung injuries to protect organ function^{35 36}. Drugs that patients with cardiovascular disease take in the long term, such as aspirin, might play a protective role in IAs, antiplatelet drugs can inhibit coagulation and inflammatory reactions in models of sepsis, reducing damage to organ function; and clinical studies also suggest that aspirin may improve the prognosis of patients with sepsis³⁷.

The protective effect of diabetes may occur through an unidentified hormonal intermediary, or it may be caused by antidiabetic drugs such as rosiglitazone taken by diabetic patients, which increases the serum levels of adiponectin, thus resulting in a better prognosis^{38 39}. A recent study also indicated an association between metformin use prior to admission and lower mortality in septic adult patients with diabetes mellitus. Metformin may supply higher amounts of LAC, serving as an energetic carbon source, thus making energy available to ischaemic tissue^{40 41}. Second, in acute catabolic reactions caused by IAs, stored fuel and nutritional reserves might be critical in obese patients. In our study, the higher CRE values of overweight and obese patients also support this standpoint; however, in IAs, due to anorexia and acute gastrointestinal dysfunction, the energy supply is frequently insufficient⁴². Third, adipocytes can release adipokines and inflammatory factors such as Interleukin-10 and leptin, which can regulate the immune response and improve the prognosis of patients with an acute inflammatory response⁴³. A previous study indicated that lipopolysaccharides may be sequestered in adipose tissue via the very-low-density lipoprotein receptor, and this sequestration may contribute to improved sepsis survival; when BMI was greater than 25 kg/m², this effect was accentuated⁴⁴. In addition, the difference in nursing level may also be associated with the prognosis of obese patients. As mentioned earlier, obese patients often suffer from more basic diseases and complications, and they are more likely to receive the attention of nursing staff, receiving more active treatment³³. Finally,

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previous studies suggest that BMI is not the best indicator to accurately evaluate obesity, which leads to the obesity paradox^{45 46}. This study has several limitations. First, this was a retrospective single centre study. Similar to other observational studies, it is difficult to completely exclude the influence of residual confounding factors. Second, due to the characteristics of the database itself, a considerable number of patients' data were missing, especially various laboratory test data, which may cause selection bias; however, we did not introduce the missing indicators into the final Cox regression model. Third, in this study, we only obtained the baseline characteristic information of patients and some of their laboratory examination results within 24 h after admission, but did not specifically study their infection and treatment process (such as the use of antibiotics), and the disparate interventions in the two groups with regard to these factors may lead to deviations in our results. Next, given the observational nature of this study, we can't determine causality between the BMI and mortality. Finally, the total sample size of the database was very large, but the number of subgroups in our study was relatively small, which may also affect the reliability of our results.

5.CONCLUSION

IAI patients with an overweight and obese status have lower 90-day mortality than patients with a normal BMI. The protection of BMI exists not only in patients with severe conditions, such as sepsis patients, but also in patients with milder conditions.

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Authors' contributions

Li QL participated in the research design, data analysis and writing of the paper; **Tong YM** participated in the data collecting; **Li QL, Tong YM** contributed equally to this work. **Liu SN** participated in data analysis and revising of the paper; **Yang KB** participated in the data cleaning; **Liu C and Zhang JY** provided substantial advice in designing the study and assisting in the division of labor, writing and revising the paper.

Competing interests

The authors declare that they have no competing interests.

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Data Availability Statement

MIMIC-III, a freely accessible critical care database. Johnson AEW, Pollard TJ, Shen L, Lehman L, Feng M, Ghassemi M, Moody B, Szolovits P, Celi LA, and Mark RG. Scientific Data (2016). DOI: 10.1038/sdata.2016.35. Available from: <http://www.nature.com/articles/sdata201635> and <https://mimic.mit.edu/>

Ethics Statement

The use of MIMIC-III database was under the approval from the review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. The database is freely available, in that any researcher who accepts the data-use agreement and has completed the “protecting human subjects” training can apply for permission to access the data. We did not need patient consent or ethics approval, and permission to participate was also not appropriate, because our review was a retrospective study of data reuse, and the message of the patients was anonymous.

Patient consent for publication

Not required.

Consent for publication

Not applicable.

Reference

1. Sartelli M, Chichom-Mefire A, Labricciosa FM, et al. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections. *World J Emerg Surg* 2017;12:29. doi: 10.1186/s13017-017-0141-6 [published Online First: 2017/07/14]
2. Hecker A, Reichert M, Reuss CJ, et al. Intra-abdominal sepsis: new definitions and current clinical standards. *Langenbecks Arch Surg* 2019;404(3):257-71. doi: 10.1007/s00423-019-01752-7 [published Online First: 2019/01/28]
3. Eggimann P, Pittet D. Infection control in the ICU. *Chest* 2001;120(6):2059-93.

- 453 4. Shirah GR, O'Neill PJ. Intra-abdominal Infections. *Surg Clin North Am* 2014;94(6):1319-33. doi:
454 10.1016/j.suc.2014.08.005
- 455 5. Gonzalez MC, Correia MITD, Heymsfield SB. A requiem for BMI in the clinical setting. *Curr Opin Clin*
456 *Nutr Metab Care* 2017;20(5):314-21. doi: 10.1097/MCO.0000000000000395
- 457 6. Flegal KM, Ioannidis JPA, Doehner W. Flawed methods and inappropriate conclusions for health
458 policy on overweight and obesity: the Global BMI Mortality Collaboration meta-analysis. *J*
459 *Cachexia Sarcopenia Muscle* 2019;10(1) doi: 10.1002/jcsm.12378
- 460 7. Heetun A, Cutress RI, Copson ER. Early breast cancer: why does obesity affect prognosis? *Proc Nutr*
461 *Soc* 2018;77(4):369-81. doi: 10.1017/S0029665118000447
- 462 8. Secord AA, Hasselblad V, Von Gruenigen VE, et al. Body mass index and mortality in endometrial
463 cancer: A systematic review and meta-analysis. *Gynecol Oncol* 2016;140(1):184-90. doi:
464 10.1016/j.ygyno.2015.10.020
- 465 9. Barone M, Viggiani MT, Losurdo G, et al. Systematic review with meta-analysis: post-operative
466 complications and mortality risk in liver transplant candidates with obesity. *Aliment Pharmacol*
467 *Ther* 2017;46(3):236-45. doi: 10.1111/apt.14139
- 468 10. Wang Y, Beydoun MA. The obesity epidemic in the United States--gender, age, socioeconomic,
469 racial/ethnic, and geographic characteristics: a systematic review and meta-regression
470 analysis. *Epidemiol Rev* 2007;29:6-28. doi: 10.1093/epirev/mxm007 [published Online First:
471 2007/05/19]
- 472 11. Kalantar-Zadeh K, Abbott KC, Salahudeen AK, et al. Survival advantages of obesity in dialysis patients.
473 *Am J Clin Nutr* 2005;81(3):543-54 2005
- 474 12. Chlebowski RT, Grosvenor M, Lillington L, et al. Dietary Intake and Counseling, Weight Maintenance,
475 and the Course of HIV Infection. *Journal of the American Dietetic Association* 1995;95(4):428-
476 35. doi: 10.1016/s0002-8223(95)00115-8
- 477 13. Johnson AE, Pollard TJ, Shen L, et al. MIMIC-III, a freely accessible critical care database. *Sci Data*
478 2016;3:160035. doi: 10.1038/sdata.2016.35 [published Online First: 2016/05/25]
- 479 14. Han D, Zhang L, Zheng S, et al. Prognostic Value of Blood Urea Nitrogen/Creatinine Ratio for Septic
480 Shock: An Analysis of the MIMIC-III Clinical Database. *Biomed Res Int* 2021;2021:5595042. doi:
481 10.1155/2021/5595042
- 482 15. Guo Q, Li H, Ouyang H, et al. Heart Rate Fluctuation and Mortality in Critically Ill Myocardial
483 Infarction Patients: A Retrospective Cohort Study. *Front Cardiovasc Med* 2021;8:577742. doi:
484 10.3389/fcvm.2021.577742
- 485 16. Zhang W, Wang Y, Li W, et al. The Association Between the Baseline and the Change in Neutrophil-
486 to-Lymphocyte Ratio and Short-Term Mortality in Patients With Acute Respiratory Distress
487 Syndrome. *Front Med (Lausanne)* 2021;8:636869. doi: 10.3389/fmed.2021.636869
- 488 17. Johnson AEW, Pollard TJ, Shen L, et al. MIMIC-III, a freely accessible critical care database. *Scientific*
489 *data* 2016;3:160035. doi: 10.1038/sdata.2016.35
- 490 18. Park S-Y, Freedman ND, Haiman CA, et al. Association of Coffee Consumption With Total and Cause-
491 Specific Mortality Among Nonwhite Populations. *Ann Intern Med* 2017;167(4):228-35. doi:
492 10.7326/M16-2472
- 493 19. Li S, Hu X, Xu J, et al. Increased body mass index linked to greater short- and long-term survival in
494 sepsis patients: A retrospective analysis of a large clinical database. *Int J Infect Dis*
495 2019;87:109-16. doi: 10.1016/j.ijid.2019.07.018 [published Online First: 2019/07/30]
- 496 20. Ferris M, Quan S, Kaplan BS, et al. The Global Incidence of Appendicitis: A Systematic Review of

- Population-based Studies. *Ann Surg* 2017;266(2):237-41. doi: 10.1097/SLA.0000000000002188 [published Online First: 2017/03/14]
21. Montgomery SM, Pounder RE, Wakefield AJ. Smoking in adults and passive smoking in children are associated with acute appendicitis. *Lancet* 1999;353(9150):379.
22. Trivedi V, Bavishi C, Jean R. Impact of obesity on sepsis mortality: A systematic review. *J Crit Care* 2015;30(3):518-24. doi: 10.1016/j.jcrc.2014.12.007
23. Wang S, Liu X, Chen Q, et al. The role of increased body mass index in outcomes of sepsis: a systematic review and meta-analysis. *BMC Anesthesiol* 2017;17(1):118. doi: 10.1186/s12871-017-0405-4
24. Wang H, Shi Y, Bai Z-H, et al. Higher body mass index is not a protective risk factor for 28-days mortality in critically ill patients with acute kidney injury undergoing continuous renal replacement therapy. *Ren Fail* 2019;41(1):726-32. doi: 10.1080/0886022X.2019.1650767
25. Maccioni L, Weber S, Elgizouli M, et al. Obesity and risk of respiratory tract infections: results of an infection-diary based cohort study. *BMC Public Health* 2018;18(1):271. doi: 10.1186/s12889-018-5172-8
26. Dhurandhar NV, Bailey D, Thomas D. Interaction of obesity and infections. *Obes Rev* 2015;16(12):1017-29. doi: 10.1111/obr.12320
27. White BP, Wagner JL, Barber KE, et al. Risk Factors for Failure in Complicated Intraabdominal Infections. *South Med J* 2018;111(2):125-32. doi: 10.14423/SMJ.0000000000000770
28. Thongprayoon C, Cheungpasitporn W, Kittanamongkolchai W, et al. Optimum methodology for estimating baseline serum creatinine for the acute kidney injury classification. *Nephrology (Carlton)* 2015;20(12):881-86. doi: 10.1111/nep.12525
29. Dewar DC, Tarrant SM, King KL, et al. Changes in the epidemiology and prediction of multiple-organ failure after injury. *J Trauma Acute Care Surg* 2013;74(3):774-79. doi: 10.1097/TA.0b013e31827a6e69
30. Sakr Y, Alhussami I, Nanchal R, et al. Being Overweight Is Associated With Greater Survival in ICU Patients: Results From the Intensive Care Over Nations Audit. *Crit Care Med* 2015;43(12):2623-32. doi: 10.1097/CCM.0000000000001310 [published Online First: 2015/10/03]
31. Littleton SW. Impact of obesity on respiratory function. *Respirology* 2012;17(1):43-9. doi: 10.1111/j.1440-1843.2011.02096.x [published Online First: 2011/11/02]
32. Gong MN, Bajwa EK, Thompson BT, et al. Body mass index is associated with the development of acute respiratory distress syndrome. *Thorax* 2010;65(1):44-50. doi: 10.1136/thx.2009.117572
33. O'Brien JM, Philips GS, Ali NA, et al. The association between body mass index, processes of care, and outcomes from mechanical ventilation: a prospective cohort study. *Critical care medicine* 2012;40(5):1456-63. doi: 10.1097/CCM.0b013e31823e9a80
34. Bhaskaran K, Douglas I, Forbes H, et al. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *The Lancet* 2014;384(9945):755-65. doi: 10.1016/s0140-6736(14)60892-8
35. Wacharasint P, Boyd JH, Russell JA, et al. One size does not fit all in severe infection: obesity alters outcome, susceptibility, treatment, and inflammatory response. *Critical care (London, England)* 2013;17(3):R122. doi: 10.1186/cc12794
36. Stewart RM, Park PK, Hunt JP, et al. Less is more: improved outcomes in surgical patients with conservative fluid administration and central venous catheter monitoring. *J Am Coll Surg* 2009;208(5) doi: 10.1016/j.jamcollsurg.2009.01.026

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37. Wang Y, Ouyang Y, Liu B, et al. Platelet activation and antiplatelet therapy in sepsis: A narrative review. *Thromb Res* 2018;166:28-36. doi: 10.1016/j.thromres.2018.04.007

38. Kuperman EF, Showalter JW, Lehman EB, et al. The impact of obesity on sepsis mortality: a retrospective review. *BMC Infect Dis* 2013;13:377. doi: 10.1186/1471-2334-13-377

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* 2009;145(5):550-57. doi: 10.1016/j.surg.2009.01.010

40. Liang H, Ding X, Li L, et al. Association of preadmission metformin use and mortality in patients with sepsis and diabetes mellitus: a systematic review and meta-analysis of cohort studies. *Critical care (London, England)* 2019;23(1):50. doi: 10.1186/s13054-019-2346-4

41. Hui S, Ghergurovich JM, Morscher RJ, et al. Glucose feeds the TCA cycle via circulating lactate. *Nature* 2017;551(7678):115-18. doi: 10.1038/nature24057 [published Online First: 2017/10/19]

42. Niedziela J, Hudzik B, Niedziela N, et al. The obesity paradox in acute coronary syndrome: a meta-analysis. *Eur J Epidemiol* 2014;29(11):801-12. doi: 10.1007/s10654-014-9961-9

43. McLaughlin T, Deng A, Yee G, et al. Inflammation in subcutaneous adipose tissue: relationship to adipose cell size. *Diabetologia* 2010;53(2):369-77. doi: 10.1007/s00125-009-1496-3

44. Shimada T, Topchiy E, Leung AKK, et al. Very Low Density Lipoprotein Receptor Sequesters Lipopolysaccharide Into Adipose Tissue During Sepsis. *Critical care medicine* 2020;48(1):41-48. doi: 10.1097/CCM.0000000000004064

45. Xing Z, Tang L, Chen J, et al. Association of predicted lean body mass and fat mass with cardiovascular events in patients with type 2 diabetes mellitus. *CMAJ* 2019;191(38):E1042-E48. doi: 10.1503/cmaj.190124

46. Xing Z, Peng Z, Wang X, et al. Waist circumference is associated with major adverse cardiovascular events in male but not female patients with type-2 diabetes mellitus. *Cardiovasc Diabetol* 2020;19(1):39. doi: 10.1186/s12933-020-01007-6

Table1. Univariate analysis of baseline characteristics by BMI category

	BMI<25	BMI 25-30	BMI>30	P value
	kg/m ²	kg/m ²	kg/m ²	
	(n=399)	(n=357)	(n=405)	
Age, n (%)	66.56(50.16-80.25) ^a	66.79(52.43-77.63) ^b	62.97(51.94-72.92) ^b	<0.001
<45	64(16.04)	47(13.17)	60(14.81)	
45-64	126(31.58) ^a	120(33.61) ^a	174(42.96) ^b	
65-89	177(44.36)	171(47.90)	164(40.49)	
>90	32(8.02) ^a	19(5.32) ^a	7(1.73) ^b	
Female, n (%)	207(51.88) ^a	141(39.50) ^b	206(50.86) ^a	0.001
Ethnicity, n (%)				0.183
White	297(74.43)	255(71.43)	305(75.31)	
Black	40(10.03)	36(10.08)	38(9.38)	
Hispanic or latino	11(2.76)	14(3.92)	11(2.72)	
Asian	7(1.75)	11(3.08)	1(0.25)	
Other	44(11.03)	41(11.49)	50(12.35)	
Marital status, n (%)				0.008
Married	169(42.36) ^a	196(54.90) ^b	196(48.40) ^{a,b}	
Single/divorced/separated/unknown	161(40.35)	121(33.89)	156(38.52)	
n				
Widowed	69(17.29)	40(11.20)	53(13.09)	
Admission type, n (%)				0.009
Elective	35(8.77) ^a	50(14.01) ^{a,b}	64(15.80) ^b	
Emergency/urgent	364(91.23) ^a	307(86.00) ^{a,b}	341(84.20) ^b	
Insurance type, n (%)				0.604

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Medicare/Medicaid	261(65.41)	236(66.11)	250(61.73)	
Private	125(31.33)	109(30.53)	144(35.56)	
Other	13(3.26)	12(3.36)	11(2.72)	
SOFA	5(2-7) ^a	5(3-7) ^{a,b}	5(3-8) ^b	0.039
SAPS II	40(30-50)	39(29-50)	38(28-49)	0.473
SIRS	3(3-4)	3(3-4)	3(3-4)	0.786
qSOFA	2(1-2)	2(1-2)	2(1-2)	0.185
OASIS	34(27-40)	33(28-41)	34(27-41)	0.941
Charlson comorbidity index	1(0-3)	2(1-3)	1(0-3)	0.719

Abbreviations: BMI: Body mass index; SOFA: sepsis-related organ failure assessment; SAPSII: Simplified Acute Physiology Score II; SIRS: systemic inflammatory response syndrome; OASIS: Oxford Acute Severity of Illness Score. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

Table 2. Univariate analysis of mortality and length of stay by BMI category

	BMI <25 kg/m ² (n=399)	BMI 25–30 kg/m ² (n=357)	BMI >30 kg/m ² (n=405)	<i>p</i>
Mortality, n (%)				
Hospital mortality	78(19.55)	65(18.21)	57(14.07)	0.102
30-day mortality	74(18.55) ^a	46(12.89) ^{a,b}	48(11.85) ^b	0.016
90-day mortality	112(28.07) ^a	83(23.25) ^{a,b}	84(20.74) ^b	0.048
Length of stay, day(IQR)				
Hospital LOS	14.9(8.4-28.6)	15.4(7.9-27.0)	16.2(9.1-29.8)	0.137
Living patients(n=962)	15.0(8.7-28.6)	14.3(7.9-24.9)	16.4(9.3-29.8)	0.059
Dead patients(n=201)	13.9(5.4-29.3)	17.9(7.1-33.3)	13.7(6.2-30.7)	0.412
ICU LOS	3.1(1.8-7.8) ^a	3.6(1.9-8.9) ^a	4.9(2.2-13.6) ^b	<0.001
Living patients(n=1036)	3.1(1.7-6.7) ^a	3.3(1.8-7.7) ^a	4.7(2.2-13.2) ^b	<0.001
Dead patients(n=125)	7.2(2.2-14.1)	11.7(3.7-31.1)	8.8(2.2-17.7)	0.166

Abbreviations: BMI: Body mass index; LOS: length of stay. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

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Table 3. Univariate analysis of requirement of organ support therapy by BMI category

	BMI<25kg/m ² (n=399)	BMI25–30kg/m ² (n=357)	BMI>30 kg/m ² (n=405)	<i>p</i>
Ventilation , n(%)	209(52.38) ^a	203(56.86) ^{a,b}	249(61.48) ^b	0.034
Dialysis, n (%)	24(6.01)	30(8.40)	32(7.90)	0.409
Vasoactive agent, n (%)	138(34.59)	123(34.45)	143(35.31)	0.964

Abbreviations: BMI: Body mass index; The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

Table 4. Univariate analysis of laboratory examination by BMI category

	BMI<25kg/m ²	BMI25-30kg/m ²	BMI>30kg/m ²	<i>p</i>
HGB (g/dL)	9.5(8.3-10.7) ^a , n=396	9.60(8.4-10.8) ^{a,b} , n=355	9.7(8.5-11.2) ^b , n=403	0.048
WBC (K/uL)	10.1(6.2-14.9) ^{a,b} , n=396	9.7(6.5-13.8) ^a , n=355	10.9(7.1-15.2) ^b , n=404	0.035
PLT (K/uL)	184.5(112.3-268), n=396	182 (124-252), n=355	190(126-273.5), n=405	0.402
CRE (mg/dL)	1.1(0.8-1.8) ^a , n=396	1.2(0.9-2.2) ^b , n=355	1.3(0.9-2.2) ^b , n=405	0.001
BUN (mg/dL)	24(16-39), n=396	25(16-41), n=355	25(16-44), n=405	0.610
ALB (g/dL)	2.6(2.2-3.1), n=234	2.7(2.2-3.2), n=215	2.7(2.3-3.1), n=228	0.463
Cl (mEq/L)	109(105-113) ^a , n=396	109(105-112) ^a , n=356	108(104-111) ^b , n=405	0.007
K (mEq/L)	3.6(3.2-4.0), n=396	3.7(3.3-4.0), n=356	3.7(3.4-4.1), n=405	0.168
Na (mEq/L)	136(132-139), n=396	136(133-139), n=356	136(133.5-139), n=405	0.235
GLU (mg/dL)	153(122-194) ^a , n=396	154 (125-195.75) ^a , n=356	170 (136.5-226) ^b , n=405	<0.001
LAC (mmol/L)	2.5(1.6-4.5), n=312	2.7(1.5-4.4), n=286	2.3(1.4-4.2), n=325	0.324
BIL (mg/dL)	1.1(0.5-3.1), n=262	1.2(0.6-2.4), n=255	1 (0.5-2.5), n=284	0.528

Abbreviations: BMI: Body mass index; HGB: hemoglobin; WBC: white blood cell count; PLT: platelet count; ALB: albumin; CRE: creatinine; BUN: urea nitrogen; GLU: glucose; LAC: lactate; BIL: bilirubin; Na: sodium; Cl: chlorine; K: potassium. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

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Table 5. Result of the Cox proportional hazard regression analysis

Exposure	Non-adjusted HR, <i>p</i> Value	Adjusted HR, <i>p</i> Value
<i>Model 1</i>		
BMI	0.98(0.97-0.99), <0.0001	0.98(0.97,0.99), 0.0001
BMI		
<25, kg/m ²	1.00(Reference)	1.00(Reference)
25-30, kg/m ²	0.78(0.64,0.96), 0.0158	0.78(0.64,0.95), 0.0148
>30, kg/m ²	0.68(0.56,0.83), 0.0001	0.68(0.56,0.83), 0.0002
<i>Model 2</i>		
BMI	0.98(0.97,0.99), <0.0001	0.97(0.96,0.99), 0.0008
BMI		
<25, kg/m ²	1.00(Reference)	1.00(Reference)
25-30, kg/m ²	0.78(0.64,0.96), 0.0158	0.79(0.61,1.02), 0.0729
>30, kg/m ²	0.68(0.56,0.83), 0.0001	0.66(0.51,0.86), 0.0021
<i>Model 3</i>		
BMI	0.98(0.97,0.99), <0.0001	0.97(0.96,0.99), 0.0009
BMI		
<25, kg/m ²	1.00(Reference)	1.00(Reference)
25-30, kg/m ²	0.78(0.64-0.96), 0.0158	0.72(0.56,0.94), 0.0152
>30, kg/m ²	0.68(0.56.0.83), 0.0001	0.66(0.50,0.86), 0.0022
<i>Model 4</i>		
BMI	0.98(0.97,0.99), <0.0001	0.96(0.95,0.98), <0.0001
BMI		
<25, kg/m ²	1.00(Reference)	1.00(Reference)
25-30, kg/m ²	0.78(0.64,0.96), 0.0158	0.54(0.40,0.73), <0.0001
>30, kg/m ²	0.68(0.56,0.83), 0.0001	0.48(0.36,0.65), <0.0001

Model 1: Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity
Model 2: Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity; HGB; GLU; ALB.
Model 3: Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity; HGB; GLU; ALB; Charlson comorbidity index.
Model 4: Adjusted for Charlson comorbidity index.
Abbreviations: BMI: Body mass index; SOFA: sepsis-related organ failure assessment; ICU: intensive care unit; WBC: white blood cell counting.

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Legends for the figures

Figure 1. Flowchart of study cohort selection.

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Figure 2. Kaplan–Meier curve for 90-days survival stratified by BMI.

Abbreviations: BMI: Body mass index; Fig. 2 represents 90-days Kaplan–Meier curves stratified by BMI in three groups, $P < 0.001$ by log-rank test.

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Figure 3. 90-days Kaplan–Meier curve of patients without (A) and with(B) sepsis stratified by BMI. Abbreviations: BMI: Body mass index; Fig. 3(A) and 3(B) represents 90-days Kaplan–Meier curves of patients without and with sepsis respectively. In log rank test $P < 0.001$, $P < 0.05$, respective.

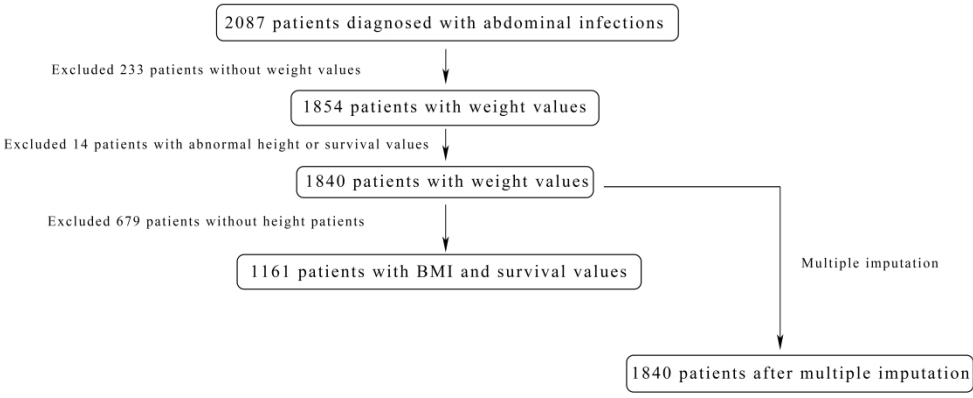


Figure 1. Flowchart of study cohort selection.

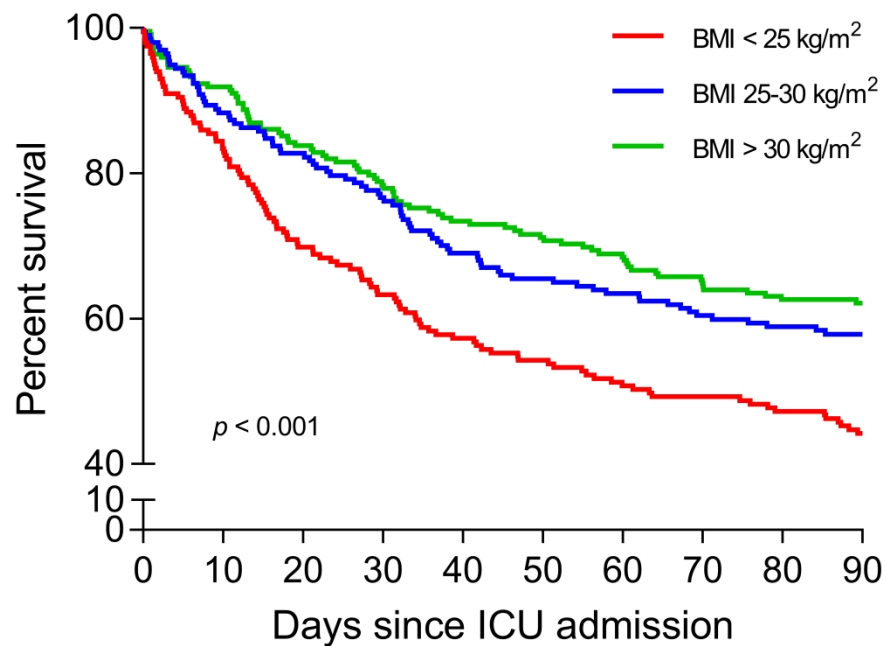


Figure 2. Kaplan-Meier curve for 90-days survival stratified by BMI. Abbreviations: BMI: Body mass index; Fig. 2 represents 90-days Kaplan-Meier curves stratified by BMI in three groups, $P < 0.001$ by log-rank test.

105x76mm (1200 x 1200 DPI)

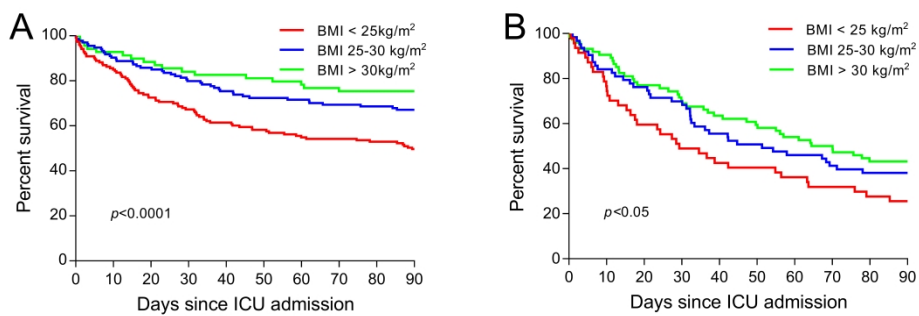


Figure 3. 90-days Kaplan–Meier curve of patients without (A) and with(B) sepsis stratified by BMI. Abbreviations: BMI: Body mass index; Fig. 3(A) and 3(B) represents 90-days Kaplan–Meier curves of patients without and with sepsis respectively. In log rank test P<0.001, P<0.05, respective.

195x71mm (1200 x 1200 DPI)

Supplementary material:

Table S1. ICD-9 codes, diagnostics and number of specific diagnoses by BMI category

ICD-9	diagnostics	n, (%)				<i>p</i> value
		BMI <25	BMI 25-30	BMI >30	TOTAL	
53110	Acute gastric ulcer with perforation, without mention of obstruction	3(0.75)	2(0.56)	2(0.49)	7(0.60)	NS
53111	Acute gastric ulcer with perforation, with obstruction	1(0.25)	0	0	1(0.08)	NS
53120	Acute gastric ulcer with hemorrhage and perforation, without mention of obstruction	1(0.25)	0	0	1(0.08)	NS
53150	Chronic or unspecified gastric ulcer with perforation, without mention of obstruction	3(0.75)	0	2(0.49)	5(0.42)	NS
53160	Chronic or unspecified gastric ulcer with hemorrhage and perforation, without mention of obstruction	0	1(0.28)	1(0.24)	2(0.17)	NS
53210	Acute duodenal ulcer with perforation, without mention of obstruction	2(0.5)	3(0.84)	3(0.73)	8(0.68)	NS
53220	Acute duodenal ulcer with hemorrhage and perforation, without mention of obstruction	0(0)	4(1.12)	2(0.49)	6(0.51)	NS
53250	Chronic or unspecified duodenal ulcer with perforation,	4(1)	2(0.56)	4(1.98)	10(0.85)	NS

	without mention of obstruction						
53251	Chronic unspecified duodenal ulcer with perforation, with obstruction	or 0	1(0.28)	0	1(0.08)	NS	
53260	Chronic unspecified duodenal ulcer with hemorrhage and perforation, without mention of obstruction	or 1(0.25)	4(1.12)	0	5(0.42)	NS	
53450	Chronic unspecified gastrojejunal ulcer with perforation, without mention of obstruction	or 0	1(0.28)	1(0.24)	2(0.17)	NS	
53641	Infection of gastrostomy	7(1.75)	4(1.12)	6(1.47)	17(1.46)	NS	
5400	Acute appendicitis with generalized peritonitis	7(1.75)	4(1.12)	3(0.73)	14(1.20)	NS	
5401	Acute appendicitis with peritoneal abscess	4(1)	3(0.84)	5(1.23)	12(1.03)	NS	
5511	Umbilical hernia with gangrene	0	1(0.28)	0	1(0.08)	NS	
55120	Ventral hernia, unspecified, with gangrene	0	1(0.28)	0	1(0.08)	NS	
55129	Other ventral hernia with gangrene	1(0.25)	0	0	1(0.08)	NS	
5513	Diaphragmatic hernia with gangrene	1(0.25)	0	1(0.24)	2(0.17)	NS	
5518	Hernia of other specified sites, with gangrene	1(0.25)	0	0	1(0.08)	NS	
56081	Intestinal peritoneal	or 48a(12)	25a, b(7.00)	22b(5.42)	95(8.16)	NS	

	adhesions with					
	obstruction					
	(postoperative)					
	(postinfection)					
56722	Peritoneal abscess	23(5.75)	25(7.00)	20(4.92)	68(5.84)	NS
56729	Other suppurative peritonitis	18(4.5)	21(5.88)	19(4.67)	58(4.98)	NS
56738	Other retroperitoneal abscess	2(0.5)	1(0.28)	5(1.23)	8(0.68)	NS
56789	Other specified peritonitis	4(1)	5(1.40)	4(0.98)	13(1.11)	NS
5679	Unspecified peritonitis	10(2.5)	11(3.08)	8(1.97)	29(2.49)	NS
5680	Peritoneal adhesions (postoperative) (postinfection)	42(10.5)	44(12.3)	50(12.31)	136(11.6)	NS
56961	Infection of colostomy or enterostomy	2(0.5)	1(0.28)	4(0.98)	7(0.60)	NS
56981	Fistula of intestine, excluding rectum and anus	22(5.5)	12(3.36)	18(4.43)	52(4.47)	NS
56983	Perforation of intestine	47(11.75)	33(9.24)	45(11.0)	125(10.7)	NS
5754	Perforation of gallbladder	5(1.25)	2(0.56)	6(1.47)	13(1.11)	NS
5763	Perforation of bile duct	0	1(0.28)	1(0.24)	2(0.17)	NS
5764	Fistula of bile duct	4(1)	1(0.28)	0	5(0.42)	NS
5770	Acute pancreatitis	137a(34.25)	144a, b(40.3)	174b(42.86)	455(39.1)	0.037
53121	Acute gastric ulcer with hemorrhage and perforation, with obstruction	0	0	0	0	NS
53151	Chronic or unspecified gastric ulcer with perforation, with obstruction	0	0	0	0	NS
53161	Chronic or unspecified gastric	0	0	0	0	NS

	ulcer	with						
	hemorrhage	and						
	perforation,	with						
	obstruction							
53211	Acute duodenal	0	0	0	0	0	NS	
	ulcer	with						
	perforation,	with						
	obstruction							
53221	Acute duodenal	0	0	0	0	0	NS	
	ulcer	with						
	hemorrhage	and						
	perforation,	with						
	obstruction							
53261	Chronic or	0	0	0	0	0	NS	
	unspecified							
	duodenal ulcer							
	with hemorrhage							
	and perforation,							
	with obstruction							
53310	Acute peptic ulcer	0	0	0	0	0	NS	
	of unspecified site							
	with perforation,							
	without mention of							
	obstruction							
53311	Acute peptic ulcer	0	0	0	0	0	NS	
	of unspecified site							
	with perforation,							
	with obstruction							
53320	Acute peptic ulcer	0	0	0	0	0	NS	
	of unspecified site							
	with hemorrhage							
	and perforation,							
	without mention of							
	obstruction							
53321	Acute peptic ulcer	0	0	0	0	0	NS	
	of unspecified site							
	with hemorrhage							
	and perforation,							
	with obstruction							
53350	Chronic or	0	0	0	0	0	NS	
	unspecified peptic							
	ulcer of unspecified							
	site with							
	perforation,							

		without mention of						
		obstruction						
53351	Chronic	or	0	0	0	0	NS	
	unspecified	peptic						
	ulcer of unspecified							
	site	with						
	perforation,	with						
	obstruction							
53360	Chronic	or	0	0	0	0	NS	
	unspecified	peptic						
	ulcer of unspecified							
	site	with						
	hemorrhage	and						
	perforation,							
	without mention of							
	obstruction							
53361	Chronic	or	0	0	0	0	NS	
	unspecified	peptic						
	ulcer of unspecified							
	site	with						
	hemorrhage	and						
	perforation,	with						
	obstruction							
53410	Acute gastrojejunal		0	0	0	0	NS	
	ulcer	with						
	perforation,							
	without mention of							
	obstruction							
53411	Acute gastrojejunal		0	0	0	0	NS	
	ulcer	with						
	perforation,	with						
	obstruction							
53420	Acute gastrojejunal		0	0	0	0	NS	
	ulcer	with						
	hemorrhage	and						
	perforation,							
	without mention of							
	obstruction							
53421	Acute gastrojejunal		0	0	0	0	NS	
	ulcer	with						
	hemorrhage	and						
	perforation,	with						
	obstruction							
53430	Acute gastrojejunal		0	0	0	0	NS	

	ulcer	without						
	mention	of						
	hemorrhage	or						
	perforation,							
	without mention of							
	obstruction							
53451	Chronic	or	0	0	0	0	NS	
	unspecified							
	gastrojejunal ulcer							
	with perforation,							
	with obstruction							
53460	Chronic	or	0	0	0	0	NS	
	unspecified							
	gastrojejunal ulcer							
	with hemorrhage							
	and perforation,							
	without mention of							
	obstruction							
53461	Chronic	or	0	0	0	0	NS	
	unspecified							
	gastrojejunal ulcer							
	with hemorrhage							
	and perforation,							
	with obstruction							
53901	Infection due to	0	0	0	0	NS		
	gastric band							
	procedure							
53981	Infection due to	0	0	0	0	NS		
	other bariatric							
	procedure							
55121	Incisional ventral	0	0	0	0	NS		
	hernia, with							
	gangrene							
5519	Hernia of	0	0	0	0	NS		
	unspecified site,							
	with gangrene							
56739	Other	0	0	0	0	NS		
	retroperitoneal							
	infections							
5755	Fistula of	0	0	0	0	NS		
	gallbladder							

Abbreviations: BMI: Body mass index; The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification.

TableS2. Univariate analysis of baseline characteristics by BMI category after adjustment of confounding factors

	BMI<25 kg/m ² (n=357)	BMI 25-30 kg/m ² (n=357)	BMI>30 kg/m ² (n=357)	<i>p</i> value
Age, n(%)				0.137
<45	51(14.29)	47(13.17)	43(12.04)	
45-64	116(32.49) ^a	120(33.61) ^{a,b}	150(42.02) ^b	
65-89	161(45.10)	171(47.90)	157(43.98)	
>90	29(8.12) ^a	19(5.32) ^a	7(1.96) ^b	
Female, n (%)	167(46.78)	141(39.50)	162(45.38)	0.115
Ethnicity, n (%)				0.199
White	264(73.95)	254(71.15)	268(75.07)	
Black	37(10.36)	36(10.08)	34(9.52)	
Hispanic or latino	10(2.80)	14(3.92)	8(2.24)	
Asian	6(1.68)	11(3.08)	1(0.28)	
Other	40(11.20)	42(11.76)	46(12.89)	
Marital status, n (%)				0.303
Married	167(46.78)	196(54.90)	183(51.26)	
Single/divorced/separated/unkn				
own	142(39.78)	121(33.89)	128(35.85)	
Widowed	48(11.20)	40(11.20)	46(12.89)	
Admission type, n (%)				0.036
Elective	33(9.24) ^a	50(14.01) ^{a,b}	55(15.41) ^b	
Emergency/urgent	324(90.76) ^a	307(85.99) ^{a,b}	302(84.59) ^b	
Insurance type, n (%)				0.550
Medicare/Medicaid	237(66.39)	236(66.11)	224(62.75)	
Private	108(30.25)	109(30.53)	125(35.01)	
Other	12(3.36)	12(3.36)	8(2.24)	
SOFA	5(3-8) ^a	5(3-7) ^{a,b}	5(3-9) ^b	0.014

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SAPS II	40(30-50)	39(29-50)	39(29.5-50)	0.794
SIRS	3(3-4)	3(3-4)	3(3-4)	0.805
qSOFA	2(1-2)	2(1-2)	2(1-2)	0.122
OASIS	34(27-40)	33(28-41)	34(27-41)	0.943
Charlson comorbidity index	1(0-3)	2(0-3)	1(0-3)	0.817

Abbreviations: BMI: Body mass index; SOFA: sepsis-related organ failure assessment; SAPSII: Simplified Acute Physiology Score II; SIRS: systemic inflammatory response syndrome; OASIS: Oxford Acute Severity of Illness Score. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification. Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

Table S3. Univariate analysis of clinical outcome by BMI category after adjustment of confounding factors

	BMI<25 kg/m ² (n=357)	BMI25-30kg/m ² (n=357)	BMI>30 kg/m ² (n=357)	<i>p</i>
Mortality,n(%)				
Hospital mortality	69(19.33)	65(18.21)	51(14.29)	0.174
30-day mortality	65(18.21)	47(13.17)	45(12.61)	0.066
90-day mortality	99(27.73)	83(23.25)	76(21.29)	0.119
Length of stay ,day(IQR)				
Hospital LOS	14.98(8.53-28.53)	15.39(7.85-27.03)	16.16(9.12-29.87)	0.16
Living patients(n=886)	15.07(8.85-27.82)	14.33(7.91-24.88)	16.58(9.63-29.93)	0.082
Dead patients(n=185)	14.16(5.28-29.69)	17.98(7.08-33.25)	13.39(5.95-29.82)	0.992
ICU LOS	3.13(1.83-7.81) ^a	3.60(1.90-8.91) ^a	4.97(2.21-13.45) ^b	<0.001
Living patients(n=957)	3.10(1.78-6.61) ^a	3.25(1.82-7.74) ^a	4.93(2.21-13.29) ^b	<0.001
Dead patients(n=185)	5.91(2.21-13.96)	11.71(3.74-31.11)	6.86(2.08-15.09)	0.096

Abbreviations: BMI: Body mass index; LOS: length of stay. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification. Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

71 **Table S4. Univariate analysis of requirement of organ support therapy by BMI category after**
72 **adjustment of confounding factors**

	BMI<25kg/m ² (n=357)	BMI25–30kg/m ² (n=357)	BMI>30 kg/m ² (n=357)	<i>p</i>
Ventilation , n(%)	188(52.66)	203(56.86)	219(61.34)	0.064
Dialysis, n (%)	21(5.9)	30(8.4)	28(7.8)	0.4
Vasoactive agent, n(%)	123(34.45)	123(34.45)	129(36.13)	0.863

73 Abbreviations: BMI: Body mass index; The letter a and b were used to indicate the
74 difference between groups and if there is statistical difference between the two
75 subgroups, different letters shall be used for identification. Adjusted for age, gender,
76 admission type, insurance type, marital status, ethnicity.

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Table S5. Univariate analysis of laboratory examination by BMI category

	BMI<25kg/m ²	BMI25-30kg/m ²	BMI>30kg/m ²	<i>p</i>
HGB	9.50(8.30-10.70),n=354	9.60(8.4-10.80),n=355	9.70(8.6-11.2),n=356	0.053
WBC	10(6.1-14.53),n=354	9.7(6.5-13.8),n=355	10.7(6.83-14.58),n=356	0.145
PLT	184.5(114.5-269.5)n=354	182(124-252)n=355	187(123.5-269.5)n=357	0.732
CRE	1.1(0.8-1.8) ^a ,n=354	1.2(0.9-2.2) ^b ,n=355	1.4(0.9-2.3) ^b ,n=357	<0.001
BUN	25(16-39),n=354	25(16-41),n=355	26(16-44.5),n=357	0.57
ALB	2.6(2.2-3.1),n=208	2.7(2.2-3.2),n=215	2.7(2.3-3.1),n=201	0.597
Cl	108(105-113) ^{a,b} ,n=354	109(105-112) ^a ,n=356	108(104-112) ^b ,n=357	0.021
K	3.6(3.2-4.0),n=354	3.7(3.3-4.0),n=356	3.7(3.4-4.1),n=357	0.124
Na	135(132-139) ^a ,n=354	136(133-139) ^{a,b} ,n=356	137(134-139) ^b ,n=357	0.042
GLU	152(122.75-194) ^a ,n=354	154(125-195.75) ^a ,n=356	168(136.5-224) ^b ,n=357	0.001
LAC	2.6(1.6-4.6),n=279	2.7(1.5-4.425),n=286	2.4(1.4-4.2),n=287	0.329
BIL	1(0.5-2.85)	1.2(0.6-2.425)	1.1(0.6-2.5)	0.397

Abbreviations: BMI: Body mass index; HGB: hemoglobin; WBC: white blood cell count; PLT: platelet count; ALB: albumin; CRE: creatinine; BUN: urea nitrogen; GLU: glucose; LAC: lactate; BIL: bilirubin; Na: sodium; Cl: chlorine; K: potassium. The letter a and b were used to indicate the difference between groups and if there is statistical difference between the two subgroups, different letters shall be used for identification. Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

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Table S6. The results of subgroup analysis of multi-factor regression analysis		
Exposure	Acute pancreatitis HR, <i>p</i> Value	Other diagnostics HR, <i>p</i> Value
Non-adjusted		
BMI	0.98 (0.96, 1.00), 0.0612	0.98 (0.96, 0.99), 0.0009
BMI		
<25 kg/m ²	1.0(Reference)	1.0(Reference)
25-30 kg/m ²	0.66 (0.46, 0.93), 0.0188	0.89 (0.70, 1.13), 0.3328
>30 kg/m ²	0.67 (0.49, 0.94), 0.0184	0.72 (0.57, 0.92), 0.0086
Adjust		
BMI	0.98 (0.95, 1.00), 0.0821	0.97 (0.95, 0.99), 0.0047
BMI		
<25 kg/m ²	1.0(Reference)	1.0(Reference)
25-30 kg/m ²	0.65 (0.42, 1.01), 0.0534	0.81 (0.57, 1.15), 0.2391
>30 kg/m ²	0.70 (0.46, 1.08), 0.1065	0.61 (0.42, 0.89), 0.0103

Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity; HGB; GLU; ALB; Charlson comorbidity index.

Table S7. The results of multi-factor regression analysis after multiple imputation

Exposure	MI.ITER= 0 HR, <i>p</i> value	MI.ITER= 1 HR, <i>p</i> value	MI.ITER= 2 HR, <i>p</i> value	MI.ITER= 3 HR, <i>p</i> value	MI.ITER= 4 HR, <i>p</i> value	MI.ITER= 5 HR, <i>p</i> value
Non-adjusted						
BMI	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001
BMI <25 kg/m ²	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)
25-30 kg/m ²	0.78 (0.64, 0.96) 0.0158	0.75 (0.64, 0.88) 0.0005	0.85 (0.73, 1.01) 0.0589	0.81 (0.69, 0.95) 0.0110	0.82 (0.69, 0.96) 0.0159	0.79 (0.67, 0.93) 0.0049
>30 kg/m ²	0.68 (0.56, 0.83) 0.0001	0.68 (0.58, 0.80) <0.0001	0.68 (0.58, 0.80) <0.0001	0.66 (0.56, 0.78) <0.0001	0.71 (0.61, 0.84) <0.0001	0.68 (0.57, 0.80) <0.0001
Adjusted						
BMI	0.98 (0.96, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001	0.98 (0.97, 0.99) <0.0001
BMI <25 kg/m ²	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)	1.0(Reference)
25-30 kg/m ²	0.74 (0.61, 0.91) 0.0042	0.74 (0.63, 0.88) 0.0004	0.82 (0.69, 0.97) 0.0192	0.79 (0.67, 0.94) 0.0069	0.80 (0.68, 0.95) 0.0088	0.77 (0.65, 0.91) 0.0019
>30 kg/m ²	0.65 (0.53, 0.79) <0.0001	0.65 (0.55, 0.77) <0.0001	0.65 (0.55, 0.77) <0.0001	0.63 (0.53, 0.74) <0.0001	0.68 (0.58, 0.81) <0.0001	0.66 (0.56, 0.79) <0.0001

Adjusted for gender; admission age; SOFA; admission type; insurance; marital status;
ethnicity; HGB; GLU; ALB; Charlson comorbidity index.

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Table S8. Subgroup analysis of multi-factor regression analysis after multiple imputation						
Exposure	MI.ITER=0 HR, <i>p</i> value	MI.ITER= 1 HR, <i>p</i> value	MI.ITER= 2 HR, <i>p</i> value	MI.ITER= 3 HR, <i>p</i> value	MI.ITER= 4 HR, <i>p</i> value	MI.ITER= 5 HR, <i>p</i> value
Acute pancreatitis						
Non-adjusted						
BMI	0.98 (0.96, 1.00) 0.0612	0.98 (0.97, 1.00) 0.0348	0.98 (0.96, 1.00) 0.0288	0.98 (0.97, 1.00) 0.0491	0.99 (0.97, 1.00) 0.0863	0.99 (0.97, 1.01) 0.1758
Adjust						
BMI	0.99 (0.97, 1.01) 0.3791	0.99 (0.97, 1.01) 0.1755	0.99 (0.97, 1.01) 0.1986	0.99 (0.97, 1.01) 0.2298	0.99 (0.97, 1.01) 0.2988	1.00 (0.98, 1.02) 0.8201
Other patients						
Non-adjusted						
BMI	0.98 (0.96, 0.99) 0.0009	0.97 (0.96, 0.99) <0.0001	0.98 (0.96, 0.99) <0.0001	0.97 (0.96, 0.98) <0.0001	0.98 (0.96, 0.99) <0.0001	0.97 (0.96, 0.99) <0.0001
Adjust						
BMI	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001	0.97 (0.96, 0.98) <0.0001
192	Adjusted for gender; admission age; SOFA; admission type; insurance; marital status; ethnicity; HGB; GLU; ALB; Charlson comorbidity index.					
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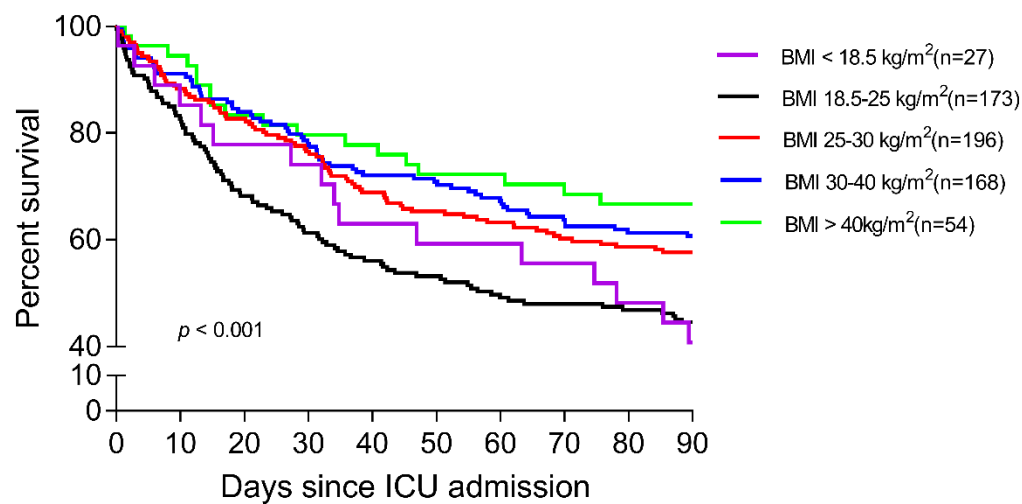


Figure S1. Kaplan–Meier curve for 90-days survival stratified by BMI.

Abbreviations: BMI: Body mass index; Fig.S1 represents 90-days Kaplan–Meier curves, $P < 0.001$ by log-rank test.

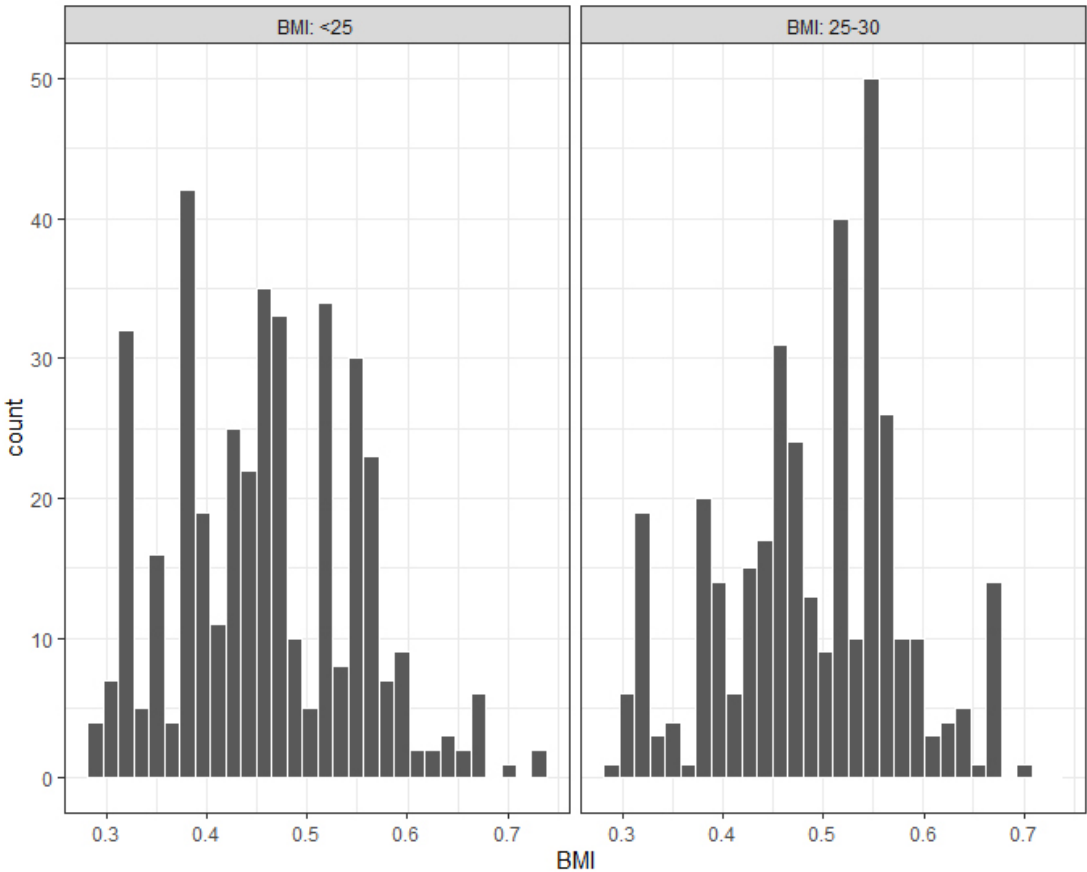


Figure S2. Propensity score counting of normal and overweight patients.

Abbreviations: BMI: Body mass index;

Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

Distribution of Propensity Scores

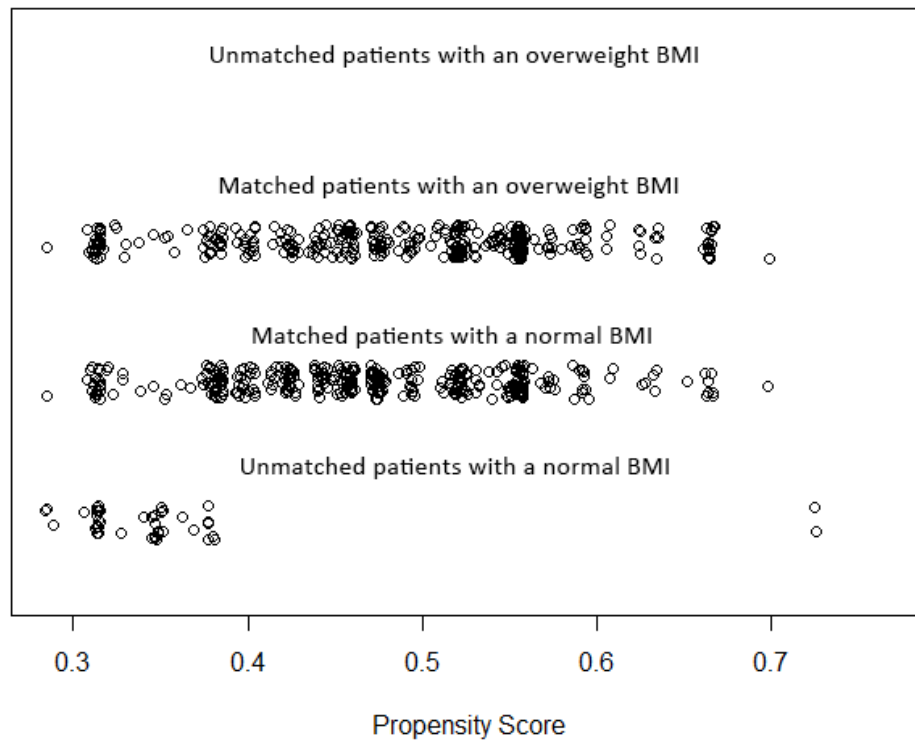


Figure S3. Distribution of propensity scores between normal and overweight patients. Abbreviations: BMI: Body mass index; Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

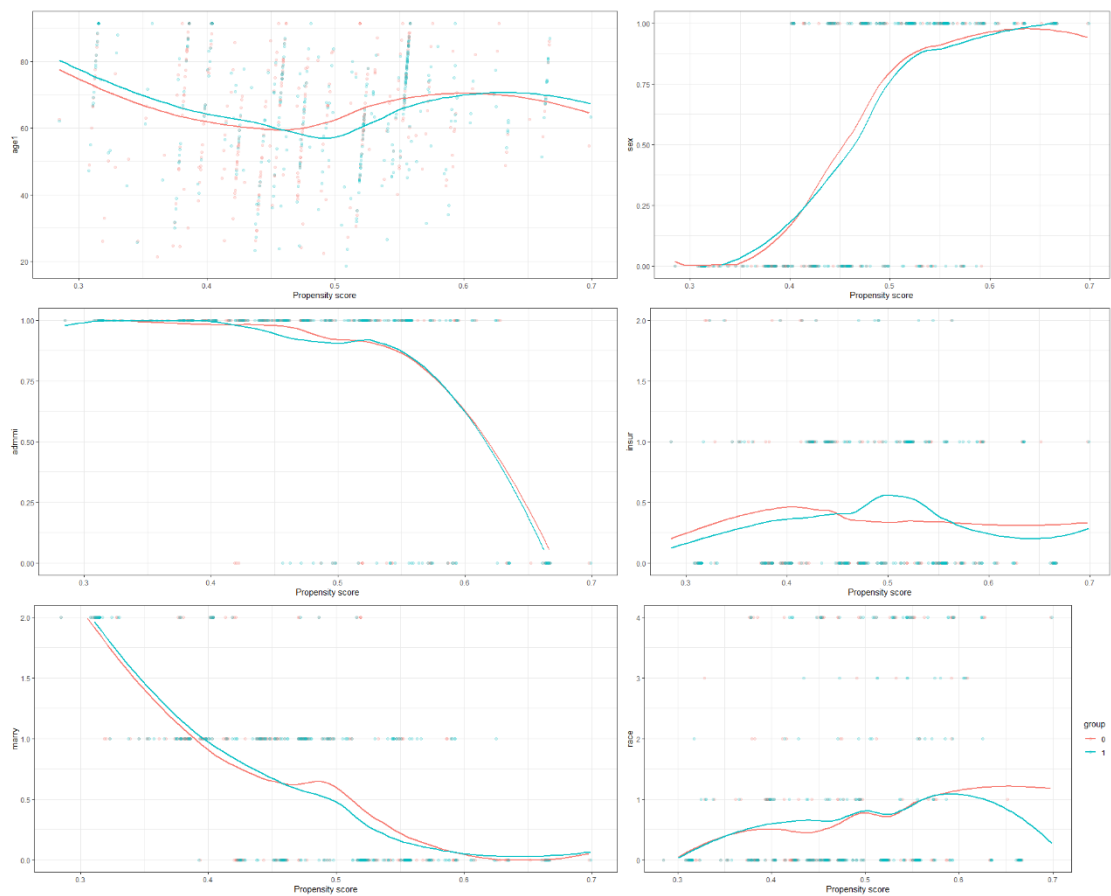


Figure S4. Trend of baseline characteristics after adjustment for confounding factors. Abbreviations: BMI: Body mass index; age1: Admission age of patients; sex: gender of patients; admmi: Admission type of patients; insur: Insurance type of patients; marry: Marital status of patients; race: Ethnicity of patients; group 0: patients with an overweight BMI; group 1: patients with a normal BMI; Adjusted for age , gender ,admission type, insurance type ,marital status , ethnicity.

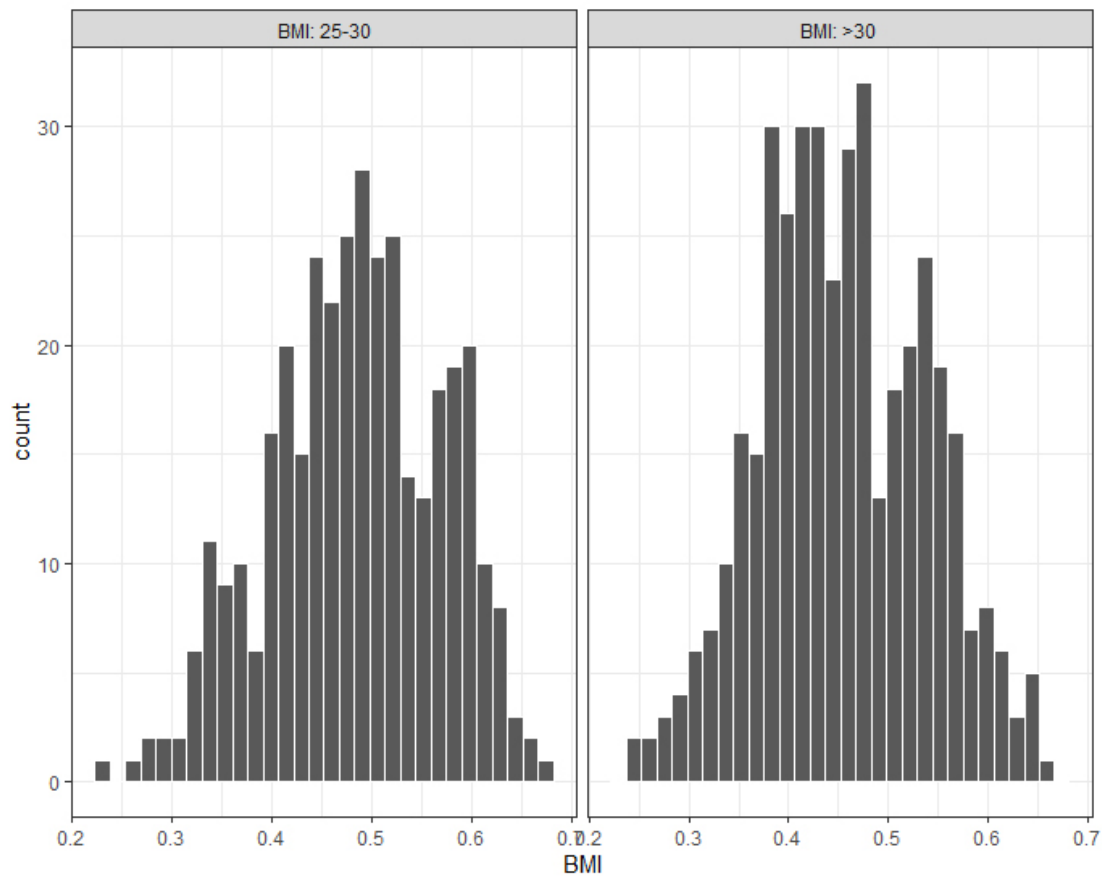


Figure S5. Propensity score counting of obese and overweight patients.

Abbreviations: BMI: Body mass index;

Adjusted for age , gender ,admission type, insurance type ,marital status , ethnicity.

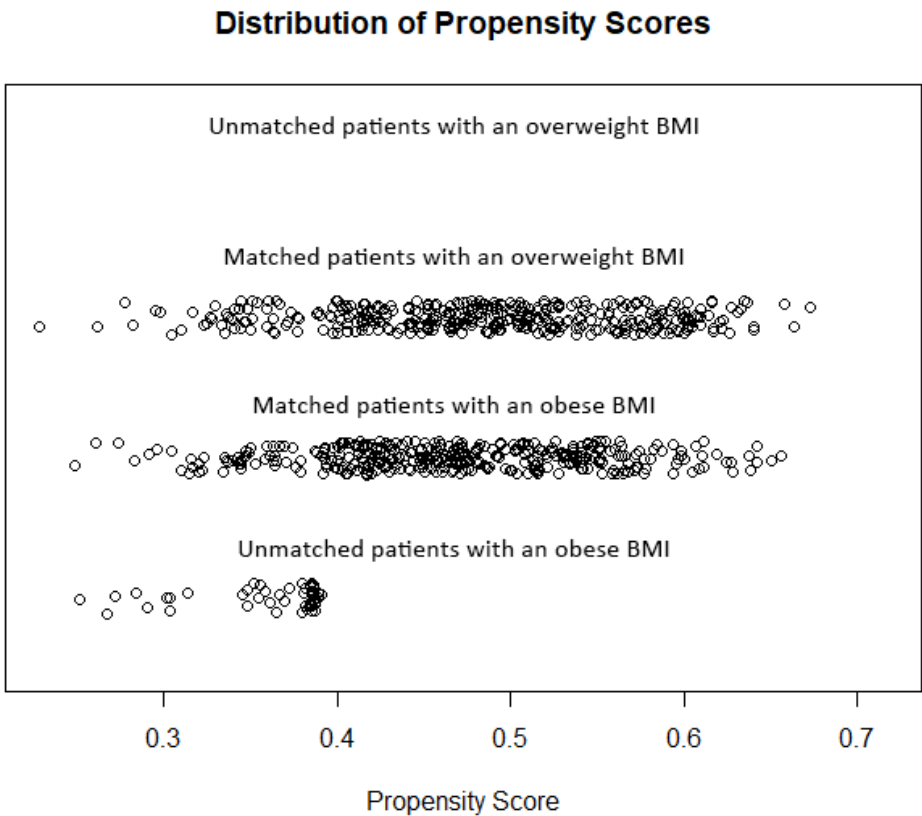


Figure S6. Distribution of propensity scores between obese and overweight patients. Abbreviations: BMI: Body mass index; Adjusted for age , gender ,admission type, insurance type ,marital status , ethnicity.

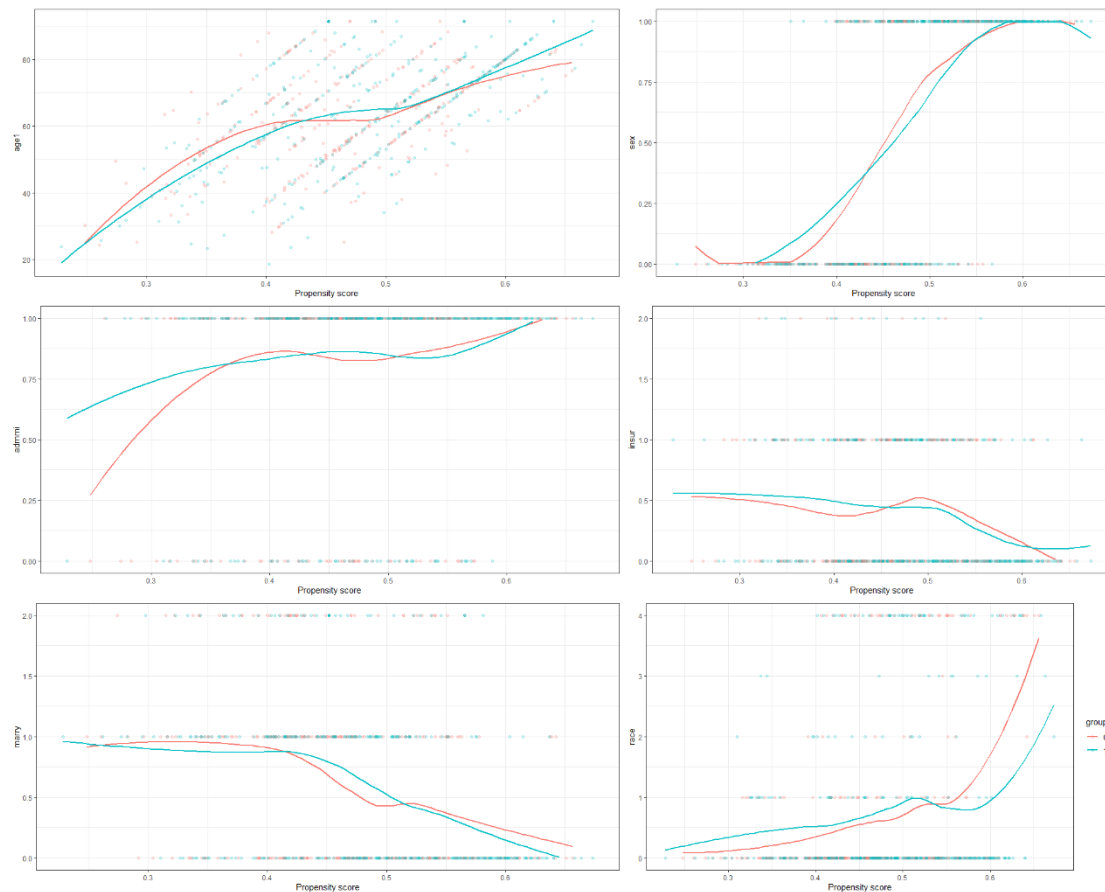


Figure S7. Trend of baseline characteristics after adjustment for confounding factors. Abbreviations: BMI: Body mass index; age1: Admission age of patients; sex: gender of patients; admmi: Admission type of patients; insur: Insurance type of patients; marry: Marital status of patients; race: Ethnicity of patients; group 0: patients with an overweight BMI; group 1: patients with a obese BMI; Adjusted for age, gender, admission type, insurance type, marital status, ethnicity.

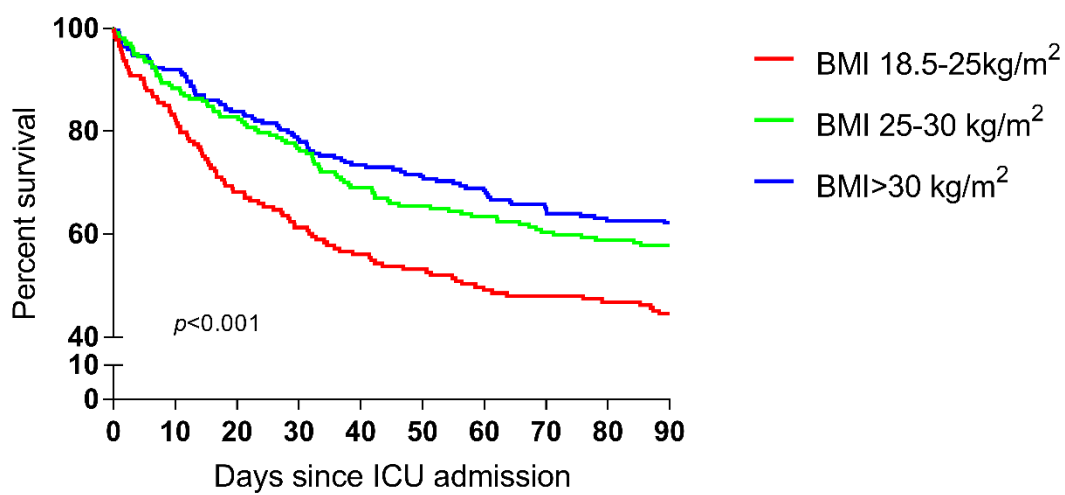


Figure S8. Kaplan–Meier curve for 90-days survival stratified by BMI.

Abbreviations: BMI: Body mass index; Fig.S8 represents 90-days Kaplan–Meier curves, $P < 0.001$ by log-rank test.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2	Design: Retrospective study.
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2	IAI patients with an overweight or obese BMI might have lower 90-day mortality than patients with a normal BMI.
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	IAs are common surgical emergencies and have been reported as major contributors to non-trauma deaths in emergency departments worldwide and as a common complication of abdominal surgery
Objectives	3	State specific objectives, including any prespecified hypotheses	4	The aim of this study was to determine the relationship between BMI and the prognosis of patients with IAs by using the Medical Information Mart for Intensive Care (MIMIC-III) database
Methods				
Study design	4	Present key elements of study design early in the paper	6	The primary endings were the 90- days mortality after ICU admission.

Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	The database maintained by the Laboratory for Computational Physiology at the Massachusetts Institute of Technology (MIT). In MIMIC database, all diagnostics correspond to International Classification of Diseases (ICD-9) codes.
Participants	6	<p>(a) <i>Cohort study</i>—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</p> <p><i>Case-control study</i>—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</p> <p><i>Cross-sectional study</i>—Give the eligibility criteria, and the sources and methods of selection of participants</p> <p>(b) <i>Cohort study</i>—For matched studies, give matching criteria and number of exposed and unexposed</p> <p><i>Case-control study</i>—For matched studies, give matching criteria and the number of controls per case</p>	5	For patients who had multiple ICU admissions, only the first admission record was kept. The exclusion criterion included: (1) age under 18 years old (2) the weight data was missing.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6	Finally, all patients are divided into three groups: normal BMI group (BMI < 25kg/m ²), overweight BMI group(25-30 kg/m ²) and obese BMI group (BMI > 30kg/m ²). There is not a specific diagnosis of IAI in ICD-9 coding, so we include all the possible diagnosis related to IAIs in ICD-9 into our study cohort, and all ICD-9 codes, diagnostics

				and numbers of specific diagnoses are listed in Table S1.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6	Data extraction and management
Bias	9	Describe any efforts to address potential sources of bias	7	We used propensity score match to adjusting for confounding factors, including age, gender, admission type, ethnicity, marital status and insurance type.
Study size	10	Explain how the study size was arrived at	8	Finally, after excluded 679 patients without height patients, a total of 1161 patients were finally included in the study

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7	If none of the above requirements were met or the data were not continuous variables, then the data are described as the median and interquartile range, and the Wilcoxon rank-sum test was used for comparisons.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7	We used propensity score match to adjusting for confounding factors, including age, gender, admission type, ethnicity, marital status and insurance type.
		(b) Describe any methods used to examine subgroups and interactions	7	We tested the collinearity of the variables included in the statistical analysis, and found that VIF of all variables was less than 3, hence there was no statistical collinearity in the included variables.
		(c) Explain how missing data were addressed	7	We used multiple imputation (MI), based on 5 replications and a chained equation approach method in the R MI procedure, to account for missing data on height
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy		
		(e) Describe any sensitivity analyses	10	However, in the multi-factor regression analysis of subgroup analysis of acute pancreatitis and other patients, when BMI was

			employed as a continuous variable, the adjusted HR value were 0.98(0.95,1.00) and 0.97(0.95,0.99) for acute pancreatitis patients and other patients, respectively
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	The MIMIC-III database includes 2087 patients diagnosed with intra-abdominal infection according to the criteria we mentioned above. Among these patients, 233 lacked weight data and were excluded from the study, and 14 patients with abnormal data records were excluded (e.g., height value > 300 meter, survival time < 0 day). Multiple imputation was used to account for missing data on height in the rest of 1840 patients. Finally, after excluded 679 patients without height patients, a total of 1161 patients were finally included in the study
		(b) Give reasons for non-participation at each stage	The MIMIC-III database includes 2087 patients diagnosed with intra-abdominal infection according to the criteria we mentioned above. Among these patients, 233 lacked weight data and were excluded from the study, and 14 patients with abnormal data records were

				excluded (e.g., height value> 300 meter, survival time < 0 day). Multiple imputation was used to account for missing data on height in the rest of 1840 patients. Finally, after excluded 679 patients without height patients, a total of 1161 patients were finally included in the study
		(c) Consider use of a flow diagram	8	Figure1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8	Table 1 shows the baseline characteristics of patients grouped by BMI.
		(b) Indicate number of participants with missing data for each variable of interest	8	Finally, after excluded 679 patients without height patients, a total of 1161 patients were finally included in the study (Figure 1).
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	9	The K–M curve for 90- day survival by BMI is shown in Figure 2.
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	9	The mortality of patients with BMI < 25 kg/m ² was significantly higher than that of patients with an obese BMI at 30 days after entering the ICU (18.55% vs. 11.85%, P=0.016, respectively),
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10	When BMI was employed as a continuous variable, the adjusted HR value in the four

		models were separately 0.98 (0.97, 0.99), 0.97 (0.96, 0.99), 0.97 (0.96, 0.99), and 0.96(0.95, 0.98).
(b) Report category boundaries when continuous variables were categorized	9	In different subgroups, patients with a BMI > 25 kg/m ² had significantly better survival than those with a BMI < 25 kg/m ²
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10	BMI was employed as a continuous variable or a classification variable, the adjusted HR value in the models showed that BMI were protective factor of the 90-day mortality in patients with IAI

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10	However, in the multi-factor regression analysis of subgroup analysis of acute pancreatitis and other patients
Discussion				
Key results	18	Summarise key results with reference to study objectives	10	In this retrospective study, we used the MIMIC-III database to study the relationship between BMI and the short-term mortality of patients with abdominal infection.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14	This study still has several limitations.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14	IAI patients with an overweight and obese BMI have lower 90-day mortality than patients with a normal BMI.
Generalisability	21	Discuss the generalisability (external validity) of the study results	12	This is a phenomenon called the obesity paradox, which means that overweight and obese patients are recognized as they often have more basic diseases, such as hypertension, cardiovascular disease and diabetes.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15	Funding None.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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