Role of gender in the survival outcome of acute phase of major trauma: A nationwide, population-based study

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Abstract

Background: Animal models of trauma have shown that females have better posttraumatic survival; however, results of previous studies on the influence of gender on major trauma patients have been controversial. This study aimed to evaluate the association between gender and survival in major trauma patients.

Methods: We retrospectively analyzed patients registered in Taiwan's National Health Insurance Research Database between 2008 and 2012 with the diagnosis codes 800-939 and 950-957 (International Classification of Diseases, ninth revision, clinical modification). Data on gender, age, catastrophic illness, and new injury severity score (NISS) ≥16 were collected for comparing patients' mortality after trauma. Propensity score matching (PSM) was performed to eliminate dissimilarities in age, comorbidities, NISS, and primary traumatic regions between the genders.

Results: Among 10 012 major trauma patients included in the study cohort, 28.8% (n = 2880) were women. The PSM patient group consisted of 50% (2876 of 5752) women. Women had a higher 30-day (15.4% of women vs 13.8% of men; $p < 0.05$) and hospital (16.1% of women vs 14.5% of men; $p < 0.05$) mortality and lower incidence rates of acute respiratory dysfunction (62.5% of women vs 65.9% of men; $p < 0.005$) and acute hepatic dysfunction (0.8% of women vs 2.1% of men; $p < 0.001$). However, the analysis of PSM patient groups showed lower mortality rates in women with moderate trauma (NISS 16–24) in the acute phase within three days (1.4% of women vs 2.7% of men, $p = 0.03$). Analysis of patients with an NISS of 16–24 who died within three days showed a higher NISS in women than in men (19.7 ± 2.3 vs 18.0 ±1.9, respectively, $p < 0.05$).

Conclusion: There is no gender difference in 30-day or hospital mortality among major trauma patients. However, women admitted for moderate major trauma had higher survival within three days of major trauma.

Keywords: Acute phase; Gender; Major trauma; Mortality; Propensity score matching

1. INTRODUCTION

Trauma is among the top 10 causes of global mortality and has contributed to more than five million annual deaths both worldwide and in our country over the past few decades.[1,2] Despite continuous advances in prehospital and emergency department resuscitation damage control surgery and traumatic management in the last decade, brain injury, hemorrhage, sepsis, and multiple organ dysfunction syndrome (MODS) remain the major causes of mortality in trauma patients.[3–5] Reducing and improving treatment of posttrauma morbidities allows better in-hospital outcomes in trauma patients.

Animal models of trauma have shown that females have better posttraumatic survival and lower morbidity of MODS and sepsis, which are attributed to the effect of their hormones.[6–9] However, gender-related differences in posttraumatic outcomes remain unclear when compared with the well-established gender-related advantages in mortality and incidence of complications in animal models. First, some studies failed to show the priority of survival or lower incidence of morbidities in female patients with major trauma,[10–14] although Haider and others reported lower mortality[15–20] and incidence of sepsis or MODS[14,21–26] in women than in men among patients with multiple major trauma. Second, Wutzlern et al[27] and similar studies have reported that preexisting comorbidities increase hospital mortality rates in trauma patients. However, few studies have analyzed gender-based disparities in hospital mortality and morbidities in patients with major trauma after adjusting for differences in preexisting comorbidities.[27–33] More analyses based on large databases with preexisting comorbidities are critical for clarifying gender-related differences in outcomes in major trauma patients.

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Therefore, this retrospective analysis of data from the National Health Insurance Research Database (NHIRD) evaluated the association between gender and clinical outcomes in patients with major trauma.

2. METHODS

2.1. Data sources

The NHIRD is a nationwide population-based database derived from the National Health Insurance Program, which was implemented in March 1995 and covers almost all residents in Taiwan. The database contains all medical services claims data on outpatient, emergency, and inpatient care and is maintained by Taiwan's Health and Welfare Data Science Center of the Ministry of Health and Welfare.

2.2. Patients

Patients with a registered emergency department visit for trauma (with recorded ambulatory care expenditures on the visits file of the NHIRD) and those who were admitted to the hospital with an admission date within three days of the emergency department visit (with inpatient expenditures on the admissions file of the NHIRD with International Classification of Diseases, ninth revision, clinical modification [ICD-9-CM] main diagnosis codes

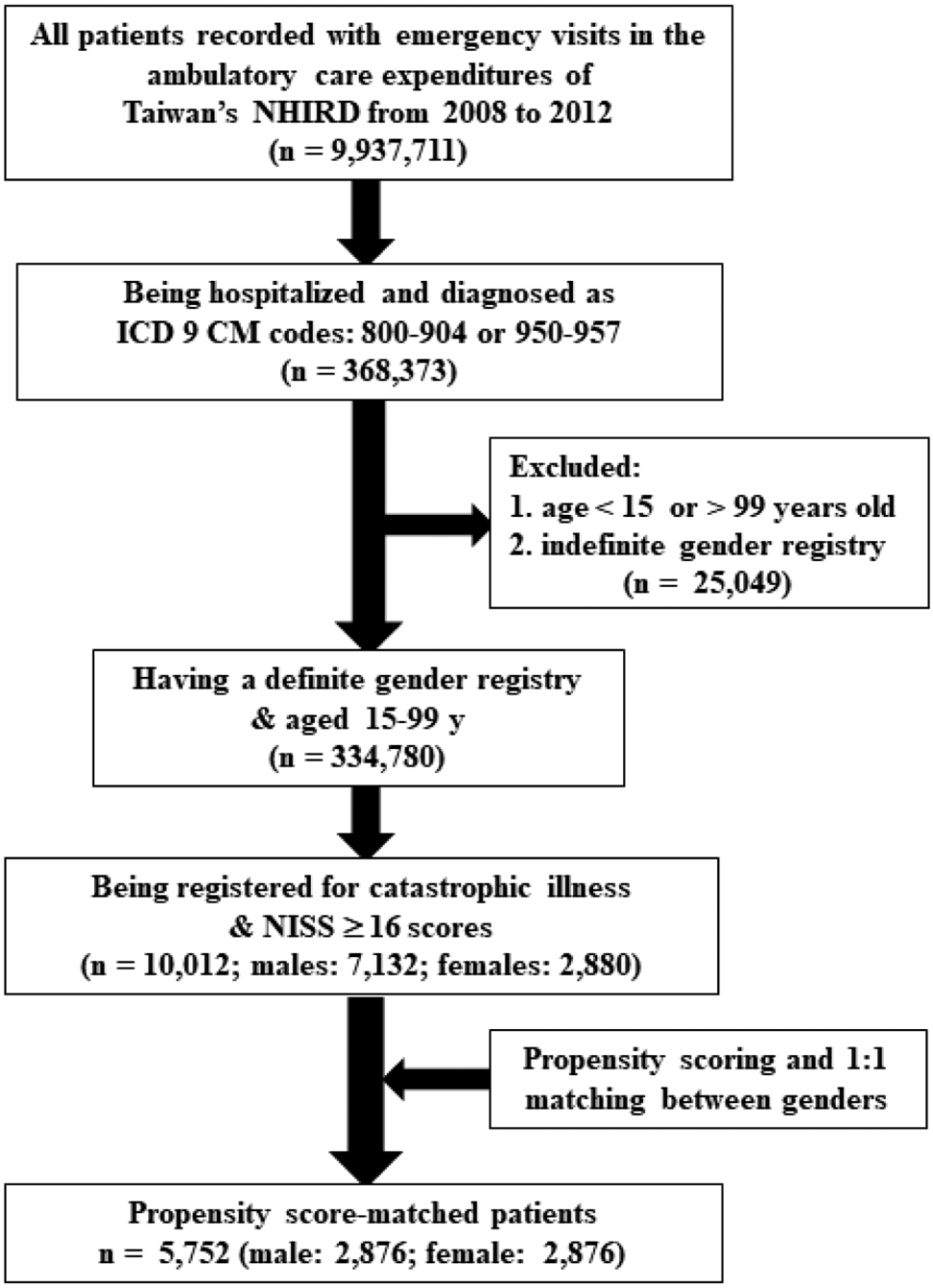

Fig. 1. Processing flow of the study cohort. The enrolled cases are trauma patients with a registry for catastrophic illness, new injury severity score (NISS) ≥ 16, and matched propensity scores with age, traumatic region, NISS, and comorbidities. NHIRD = National Health Insurance Research Database

of 800-939 and 950-957 between January 2008 and December 2012) were included for this study (Figure 1). Patients younger than 15 years or older than 99 years of age or lacking data on gender in the NHIRD registry during the event were excluded. Patients with severe injuries were defined as those with the ICD-9-CM code 959.99, with major trauma rated 16 or above on the severity scale (ie, injury severity score) in the registry for catastrophic illness patient file of the NHIRD and had a new injury severity score (NISS) above 15 at admission. Propensity score matching (PSM) was performed to avoid selection biases before examining the effect of gender on the outcome (Figure 1). The Ethics Committee of Cathay General Hospital reviewed and approval this study (IRB: CGH-LP103001).

2.3. Variables

Data on the number of patients with injuries to different body regions, preinjury comorbidities, complications, medical intervention including blood transfusion volume, mechanical ventilation days, hemodialysis, and hemodialysis days were collected for outcome analysis.

Preinjury comorbidities including cerebrovascular accident (ICD-9-CM code 430-436), congestive heart failure (404.03,404.13,404.11, 404.91, 404.93, or 428), liver dysfunction or liver cirrhosis (571, 571.2, 571.5, 571.6, 070.32, V02.61, 070.54, V02.62, or 070.52), diabetes mellitus (250), chronic kidney failure (250.40, 250.42, 585, 586, 404.02, 404.03, 404.11, 404.12, 404.13, 404.91, 404.92, 404.93, 582, 581, 587, 588, 403.1, or 403.91), chronic lung disease (490, 492, 494, 496, or 493), and malignancy (140-208) were included if the outpatient diagnosis was recorded more than twice on the ambulatory care expenditures in the visits file or on the registry for catastrophic illness patient file before the injury.

The complications included pneumonia, organ dysfunction, and sepsis.[34,35] The ICD-9-CM codes for the definition of complications are summarized in Table 1.

2.4. Main outcome measures

The primary outcomes were differences in in-hospital and 30-day mortality rates following major trauma between the matched gender groups. In-hospital mortality was determined according to the reasons for discharge in the inpatient expenditures on the admission file as death or critical ill discharge. The 30-day mortality rate was obtained from the National Register of Deaths.

2.5. Statistical analysis

Continuous variables were examined using unpaired Student's *t* tests. Categorical variables were examined using χ^2 tests and presented as percentages. Multiple logistic regression analysis was used to identify independent variables.

SAS System for Windows, version 9.3 (SAS Institute Inc., Cary, NC) was used for all data computing and statistical analyses. Stata module, the ICD Programs for Injury Categorization (ICDPIC) software version 3.0, and Stat version 12 were used to calculate the NISS of all participants. A result was considered statistically significant at $p < 0.05$.

PSM was used to balance age, comorbidities, and primary traumatic regions between the genders. We first estimated the propensity scores of every participant using logistic regression; thereafter, we used a one-to-one optimal matching algorithm to create new groups of different genders that resembled the varieties described above. The propensity score of a participant in the female group was matched first to one participant in the male group on eight decimal digits. If there was no match in the male group, an attempt was made to match seven decimal digits, and so on until a matching failed for four decimal digits.

3. RESULTS

3.1. Characteristics of patients

Between January 2008 and December 2012, a total of 9 937 711 patients were registered in the ambulatory care expenditures of Taiwan's NHIRD, of which 10 012 major traumatic patients met the study criteria (Fig. 1).

The study cohort consisted of 71.2% (n = 7132) male and 28.8% (n = 2880) female patients (Table 2). Mean patient age was 50.0 years, and mean NISS was 27.5; head injuries were the most common (up to 71.9%) primary diagnosis overall. The most common comorbidity was diabetes mellitus, which occurred in 10.1% (n = 1009) of all patients. A total of 68.87% (n = 6895) of all patients experienced organ dysfunction during the hospital course, with acute respiratory dysfunction being the most frequent, occurring in 64.9% (n = 6500) of all patients. Organ failure involving more than one organ was identified in 38.4% (n = 2647) of all patients with organ dysfunction. Sepsis occurred in 17.0% (n = 1700) of all patients. The mean hospital and intensive care unit (ICU) lengths of stay (LOS) were

Table 1.

ICD-9-CM codes for definition of complications

Complications	ICD-9-CM codes
All acute respiratory dysfunction	
Acute respiratory failure	96.70, 96.71., 96.72, 518.5, 518.81
Ventilator day: more than 3 days	93.90, 93.91, 57001B, 57023B
Acute respiratory dysfunction	Patients of all acute respiratory dysfunction other than postoperative respiratory failure
Postoperative respiratory dysfunction	Patients of all acute respiratory dysfunction with any one of 96020C, 96021C, 96022C
Acute renal dysfunction	39.95, 584, 580 or any one of 58001C, 58014C, 58018
Acute hepatic dysfunction	570, 572.2, 572.4, 573.4, 573.3
Cardiovascular dysfunction	
Shock	785.5, 458, 785,50, 785.59, 958.4, 785.51, 785.52, 404.03
Heart failure	404.13, 404.11, 404.91, 404.93, 428
Pneumonia	481–486
Sepsis	
Septicemia	038
Sepsis	995.91
Severe sepsis	995.92 or any ICD-9-CM Codes for a bacterial or fungal infection with any acute organ dysfunction defined as above

ICD-9-CM = international classification of disease 9th revision, clinical modification.

Table 2.

Demographic characteristics of all included patients

Variable	All	Males	Females	*p*
Case number	10 012	7132	2880	…
Age	50 ± 20	49 ± 20	53 ± 21	<0.001
NISS	27.5 ± 9.2	27.6 ± 9.2	27.4 ± 9.2	0.432
Trauma regions				
Head	7197 (71.9)	5082 (71.3)	2115 (73.4)	<0.05
Spine	552 (5.5)	455 (6.4)	97 (3.4)	<0.001
Thorax	994 (9.9)	726 (10.2)	268 (9.3)	0.186
Abdomen	648 (6.5)	456 (6.4)	192 (6.7)	0.615
Pelvis	112 (1.1)	67 (0.9)	45 (1.5)	<0.05
Upper extremity	117 (1.2)	72 (1.0)	45 (1.6)	<0.05
Lower extremity	392 (3.9)	274 (3.8)	118 (4.1)	0.551
Comorbidities				
Chronic neurological disease	428 (4.3)	303 (4.3)	125 (4.3)	0.837
Congestive heart failure	517 (5.3)	360 (5.1)	157 (5.5)	0.409
Chronic liver disease	472 (4.7)	362 (5.1)	110 (3.8)	<0.05
Diabetes mellitus	1009 (10.1)	667 (9.4)	342 (11.9)	<0.001
Chronic kidney disease	300 (3.0)	181 (2.5)	119 (4.1)	<0.001
Chronic lung disease	329 (3.3)	248 (3.5)	81 (2.8)	0.091
Malignancy	495 (4.9)	337 (4.7)	158 (5.5)	0.112
Complications				
Acute respiratory dysfunction (all)	6500 (64.9)	4701 (65.9)	1799 (62.5)	<0.05
Postoperative respiratory dysfunction	5399 (53.9)	3910 (54.8)	1489 (51.7)	<0.05
Acute respiratory dysfunction	1101 (11.0)	791 (11.1)	310 (10.8)	0.636
Acute renal dysfunction	205 (2.1)	120 (1.7)	85 (3.0)	<0.001
Acute hepatic dysfunction	174 (1.7)	151 (2.1)	23 (0.8)	<0.001
Acute cardiovascular dysfunction	2770 (27.7)	1972 (27.7)	798 (27.7)	0.953
Single organ dysfunction	6895 (68.9)	4977 (69.8)	1918 (66.6)	<0.05
Multiple organ dysfunction syndrome	2647 (26.4)	1897 (26.6)	750 (26.0)	0.567
Sepsis	1700 (17.0)	1267 (17.7)	433 (15.0)	<0.05
Thirty-day mortality	1429 (14.3)	986 (13.8)	443 (15.4)	<0.05
Hospital mortality	1497 (15.0)	1034 (14.5)	463 (16.1)	<0.05
Blood transfusion				
Packed RBC (U)	6.3 ± 9.4	6.4 ± 9.8	6.2 ± 8.3	0.264
Packed RBC (U) ≥5	4269 (42.6)	2989 (41.9)	1280 (44.4)	<0.05
Platelet phoresis, U	0.6 ± 1.8	0.6 ± 1.9	0.6 ± 1.7	0.950
Frozen plasma, U	4.7 ± 11.9	4.9 ±12.1	4.3 ± 11.3	<0.05
Ventilator days	10.5 ± 26.5	10.8 ± 28.6	9.8 ± 20.4	0.058
RRT, d	6.4 ± 8.5	6.3 ± 8.3	6.7 ± 8.9	0.120
IRRT, d	6.4 ± 8.8	6.0 ± 8.5	7.1 ± 9.1	0.436
CRRT, d	3.7 ± 3.6	4.0 ± 3.9	2.5 ± 1.9	<0.05
ICU LOS, d	10.2 ± 10.3	10.4 ± 10.6	9.8 ± 9.5	<0.05
Hospital LOS, d	27.7 ± 25.1	28.1 ± 25.7	26.6 ± 23.5	<0.05

Data are presents as n (%) or mean ± SD.

CRRT = continuous renal replacement therapy; ICU = intensive care unit; IRRT = intermittent renal replacement therapy; LOS = length of stay; NISS = new injury severity score; RRT = renal replacement therapy.

27.7 ± 25.1 and 10.2 ± 10.3 days, respectively. A total of 15.0% (n = 1497) of the patients died during hospitalization; 95.5% (n = 1429) died within 30 days.

We observed significant gender-based differences in age (male, 48.8 ± 19.9 years vs female, 53.1 ± 20.5 years, $p < 0.001$), distribution of primary traumatic body regions (head, 71.3%; spine, 6.4%; pelvis, 0.9%; and upper extremity, 1.0% in male vs head, 73.4%; spine, 3.4%; pelvis, 1.6%; and upper extremity, 1.6% in female patients; $p < 0.05$), and preexisting comorbidities (chronic liver disease, 5.1%; diabetes mellitus, 9.4%; and chronic kidney disease, 2.5% in male vs. chronic liver disease, 3.8%; diabetes mellitus, 11.9%; and chronic kidney disease, 4.1% in female patients; $p < 0.05$).

We observed significant differences in 30-day and hospital mortality rates between the genders. Female patients had higher 30-day (15.4% of female vs 13.8% of male patients; $p < 0.05$) and hospital (16.1% of female vs. 14.510% of male patients; $p < 0.05$) mortality rates than male patients.

The prevalence of complications including acute respiratory dysfunction (all) (65.9% of male vs 62.5% of female patients; $p < 0.05$), acute hepatic dysfunction (2.1% of male vs 0.8% of female patients; $p < 0.001$), any organ failure (69.8% of male vs 10.5% of female patients; $p < 0.05$), pneumonia (14.1% of male vs 10.5% of female patients; $p < 0.001$), and sepsis (17.7% of male vs 15.0% of female patients; $p = 0.001$) was higher in male than in female patients, while the prevalence of acute renal dysfunction (1.7% of male vs 3.0% of female patients; $p < 0.001$) was higher in male patients.

Among medical interventions, male patients received more frozen plasma transfusion units (average 4.9 ± 12.1 vs 4.3 ± 11.3 U, $p < 0.05$), had a higher probability of receiving more

than five units of packed red blood cell (PRBC) during transfusion, had longer durations of continuous renal replace therapy (4.0 ± 3.9 vs 2.5 ± 1.9 days; $p < 0.05$) and longer ICU (10.4 ± 10.6 vs 9.8 ± 9.5 days; $p < 0.05$) and hospital (28.1 ± 25.7 vs 26.6 ± 23.5 days; $p < 0.05$) LOS.

3.2. Characteristics of propensity matching patients

The PSM cohort included 5742 patients (Fig. 1), comprising 2786 female (99.9% of prematched female patients) and 2786 male (39.1% of prematched male patients) patients (Table 3). Dissimilarities in age, primary traumatic body regions, NISS, and comorbidities besides chronic liver disease were corrected in matching. No differences in 30-day or in-hospital mortality, the incidence of MODS, or therapeutic management (including blood transfusion, ventilator days, and renal replacement therapy) were observed between the genders. However, we observed differences in the incidence of sepsis, ICU LOS, and hospital LOS.

3.3. Mortality difference between genders in the acute phase of trauma and associated factor analysis

We divided the patients according to NISS (16–24 and >24) to further analyze mortality and observed a significant gender difference in three-day mortality for NISS 16–24 (men, 2.7% vs women, 1.4%; $p < 0.05$; Fig. 2A). However, there was neither significant difference between male and female patients in the 7-, 14-, 30-day, or hospital mortality in these patients with a NISS 16–24 nor for 3-, 7-, 14-, 30-day, or hospital mortality in patients with a NISS > 24 (Fig. 2A and B). Additional analysis of mortality-related covariates in patients with a NISS of 16–24 who died before day 4 showed no significant difference between the genders except that women had higher NISS than men (19.8 ± 2.3 vs 18.0 ± 1.9, $p < 0.05$; Table 4).

Table 3.

Demographic characteristics of propensity score-matched patient groups*

Variable	All	Males	Females	*p*
N	5752	2876	2876	…
Age	53.0 ± 20.5	52.9 ± 20.5	53.1 ± 20.5	0.742
NISS	27.4 ±9.1	27.4 ± 9.0	27.4 ± 9.2	0.806
Trauma regions				
Head	4259 (74.0)	2146 (74.6)	2113 (73.5)	0.321
Spine	210 (3.7)	113 (3.9)	97 (3.4)	0.261
Thorax	521 (9.1)	254 (8.8)	267 (9.3)	0.550
Abdomen	373 (6.4)	182 (6.3)	191 (6.6)	0.630
Pelvis	92 (1.6)	47 (1.6)	45 (1.6)	0.834
Upper extremity	88 (1.5)	43 (1.5)	45 (1.6)	0.830
Lower extremity	209 (3.6)	91 (3.2)	118 (4.1)	0.057
Comorbidities				
Chronic neurological disease	241 (4.2)	116 (4.0)	125 (4.4)	0.554
Congestive heart failure	300 (5.2)	143 (5.0)	157 (5.5)	0.406
Chronic liver disease	188 (3.3)	78 (2.7)	110 (3.8)	<0.05
Diabetes mellitus	686 (11.9)	345 (12.0)	341 (11.9)	0.871
Chronic kidney disease	240 (4.2)	122 (4.2)	118 (4.1)	0.792
Chronic lung disease	146 (2.5)	66 (2.3)	80 (2.8)	0.241
Malignancy	304 (5.3)	146 (5.1)	158 (5.5)	0.479
Complications				
Acute respiratory dysfunction	744 (12.9)	376 (13.1)	368 (12.8)	0.753
Acute renal dysfunction	156 (2.7)	72 (2.5)	84 (2.9)	0.330
Acute hepatic dysfunction	65 (1.1)	42 (1.5)	23 (0.8)	<0.05
Acute cardiovascular dysfunction	1680 (29.2)	833 (29.0)	847 (29.5)	0.685
Single organ dysfunction	2457 (42.7)	1257 (43.7)	1200 (41.7)	0.129
Multiple organ dysfunction syndrome	1585 (27.6)	805 (28.0)	780 (27.1)	0.461
Sepsis	998 (17.4)	554 (19.3)	444 (15.4)	<0.001
30-day mortality	862 (15.0)	417 (14.5)	445 (15.5)	0.301
Hospital mortality	903 (15.7)	440 (15.3)	463 (16.1)	0.405
Blood transfusion				
Packed RBC, U	6.29 ± 9.3	6.41 ± 10.2	6.19 ± 8.3	0.372
Packed RBC, U ≥5	2486 (43.2)	1209 (42.0)	1277 (44.4)	0.070
Platelet phoresis, U	0.6 ± 1.8	0.6 ± 1.8	0.6 ± 1.7	0.661
Frozen plasma, U	4.5 ± 11.7	4.7 ± 12.0	4.3 ± 11.3	0.235
Ventilator days	14.3 ± 35.5	15.2 ± 44.3	13.3 ± 22.8	0.086
Ventilator-free days	18.7 ± 21.2	19.4 ± 22.7	18.1 ±19.5	<0.05
RRT, d	6.7 ± 9.1	6.7 ± 9.2	6.7 ± 9.0	0.988
IRRT, d	7.0 ± 9.4	6.8 ± 9.7	7.2 ± 9.2	0.823
CRRT, d	3.0 ± 2.8	3.2 ± 3.1	2.4 ± 1.9	0.363
ICU LOS, d	10.3 ± 10.6	10.8 ± 11.5	9.8 ± 9.5	<0.001
Hospital LOS, d	27.9 ± 26.1	29.3 ± 28.4	26.6 ± 23.4	<0.001

Data are presented as n (%) or mean ± SD.

CRRT = continuous renal replacement therapy; ICU = intensive care unit; IRRT = intermittent renal replacement therapy; LOS = length of stay; NISS = new injury severity score; RRT = renal replacement therapy.

*Propensity score matching for eliminating dissimilarity in age, comorbidities, and primary traumatic regions between different genders.

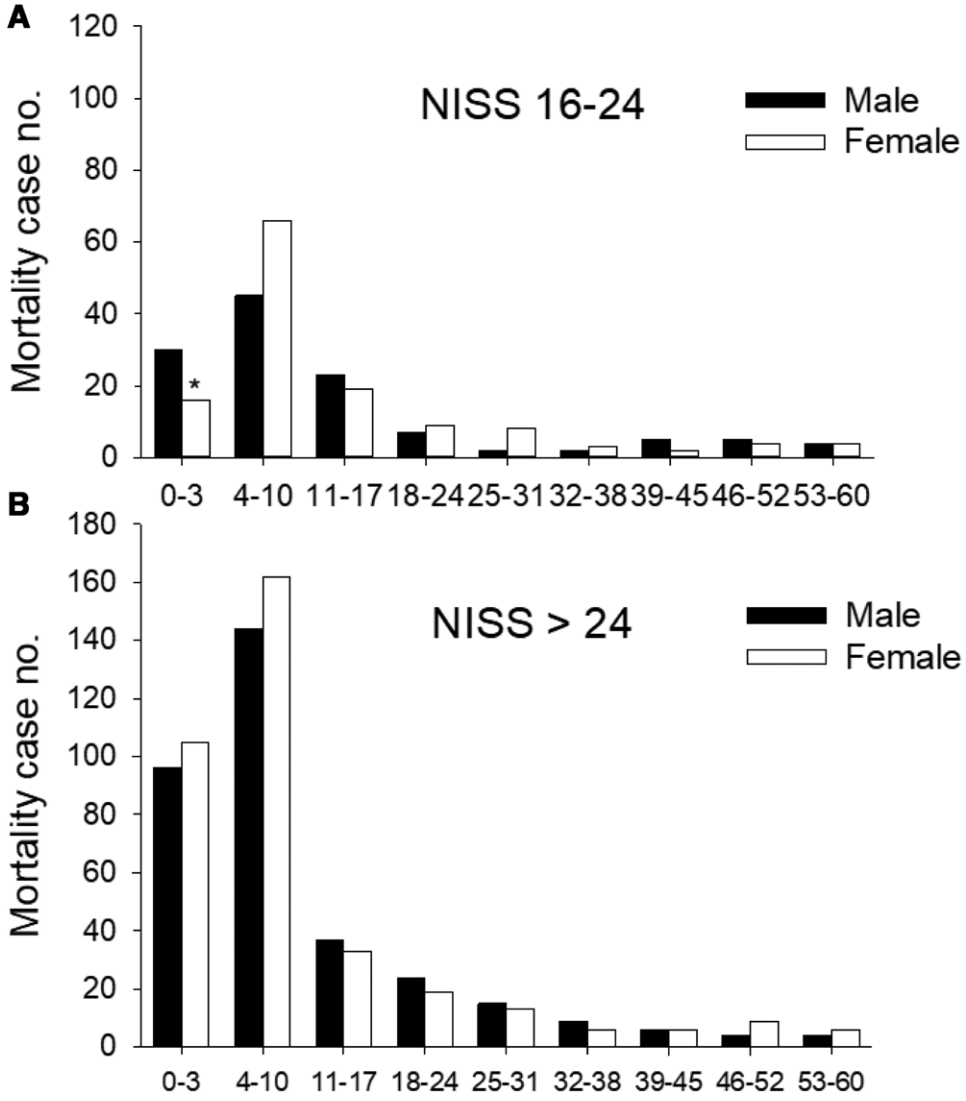

Fig. 2. Mortality case numbers of male and female patients during the first 60 days after trauma. A, Mortality case numbers with new injury severity score (NISS) 16 to 24 during the first 60 days after trauma. B, Mortality case numbers with NISS > 24 during the first 60 days after trauma. *$p < 0.05$ compared to male group of the same time period. ICD-9-CM = international classification of disease 9th revision, clinical modification.

4. DISCUSSION

Previous studies have reported lower 30-day and in-hospital mortality rates in post–major trauma hospitalized women and women of pre-menopause age than in men.[15–20] However, other studies did not report this difference.[10–13] Among studies reporting lower mortality rates in hospitalized female patients with major trauma, some did not assess the significance of the variables of post-grouping (age, injured body region, or injury severity)[15,16,19,24] and others did not adjust for preexisting comorbidities in their patient cohort.[15,16,18,20] Preexisting comorbidities including congestive heart failure, chronic obstructive pulmonary disease, asthma, hepatitis and liver cirrhosis, malignancy, and chronic kidney disease are associated with clinical outcomes of patients with major trauma.[27–32]

We initially divided our participants by age into pre-menopause (15–54 years)[36,37] and post-menopause (≥55 years) groups and observed no significant difference between gender subgroups in 30-day mortality (n = 473, 11.1% in male and n = 166, 12.4% in female patients; $p < 0.05$ in the pre-menopause group; n = 513, 17.9% in male and n = 277, 18.0% in female patients in the post-menopause group) or in-hospital mortality (n = 480, 11.3% in male and n = 168, 12.5% in female patients in the pre-menopause group; n = 554, 19.3% in male and n = 295, 19.2% in female patients in the post-menopause group). This finding is consistent with that reported by Harnod et al.[33] However, we observed a significant difference between the genders in mortality rates (30-day and in-hospital) after classifying all patients according to gender (n = 986, 13.8% in male and n = 443, 15.4% in female patients, $p < 0.05$ for 30-day mortality; n = 1034, 14.5% in male and n = 463, 16.1 % in female patients, $p < 0.05$ for in-hospital mortality). To reduce the confounding effect of the covariates listed above, we conducted PSM between these two groups, after which the difference in 30-day and in-hospital mortality was not statistically significant. This finding indicates that male gender is not an independent adverse prognostic factor for long-term survival in hospitalized patients with major trauma and is consistent with results previously reported.[13,20,26,33,36]

Table 4.

Differences in characteristics between genders in patients with new injury severity scores 16–24 and mortality during the first 3 days of hospitalization

Variable	Total	Males	Females	*p*
N	46	30	16	…
Age		54.6 ± 22.1	52.9 ± 17.8	0.790
NISS		18.0 ±1.9	19.8 ± 2.3	<0.05
Trauma region				
Head	39 (84.8)	25 (83.3)	14 (87.5)	0.708
Spine	0	0	0	…
Thorax	0	0	0	…
Abdomen	6 (13.0)	5 (16.7)	1 (6.3)	0.318
Pelvis	1 (2.2)	0	1 (6.3)	0.166
Upper extremity	0	0	0	…
Lower extremity	0	0	0	…
Comorbidities				
Chronic neurological disease	1 (2.2)	1 (3.3)	0	0.460
Congestive heart failure	2 (4.4)	1 (3.3)	1 (6.25)	0.644
Chronic liver disease	4 (8.7)	4 (13.3)	0	0.126
Diabetes mellitus	6 (13.0)	3 (10.0)	3 (18.8)	0.401
Chronic kidney disease	0	0	0	…
Chronic lung disease	3 (6.5)	2 (6.7)	1 (6.3)	0.957
Malignancy	5 (10.9)	3 (10.0)	2 (12.5)	0.795
Sepsis	21 (45.7)	15 (50.0)	6 (37.5)	0.418
Single organ dysfunction	46 (100.0)	30 (100.0)	16 (100.0)	>0.99
Acute respiratory dysfunction	21 (45.7)	15 (50.0)	6 (37.5)	0.418
Acute renal dysfunction	1 (2.2)	1 (3.3)	0 (0.0)	0.460
Acute hepatic dysfunction	2 (4.4)	2 (6.7)	0 (0.0)	0.291
Acute cardiovascular dysfunction	36 (78.3)	23 (76.7)	13 (81.3)	0.720
Multiple organ dysfunction syndrome	25 (54.4)	19 (63.3)	6 (37.5)	0.094
Packed RBC transfusion, U	…	8.53 ± 12.3	4.38 ± 4.3	0.102
Frozen plasma transfusion, U	…	4.73 ± 7.7	2.19 ± 3.7	0.138
Postoperative respiratory dysfunction	11 (23.9)	8 (26.7)	3 (18.8)	0.549
ICU LOS, d	…	1.93 ± 0.9	1.94 ± 0.9	0.988
Hospital LOS, d	…	1.93 ± 0.9	1.75 ± 0.8	0.497
Ventilator days	…	2.73 ± 1.4	2.75 ± 1.3	0.969

Data are presented as mean ± SD or n (%).

ICU = intensive care unit; LOS = length of stay; NISS = new injury severity score; RBC = red blood cell.

Further analysis of the survival rate of NISS subgroups revealed a lower mortality rate within the acute phase (before day 4) of major trauma in female patients admitted with moderate to major trauma (NISS 16–24; odds ratio = 0.51, $p < 0.05$). Comparison of the differences in covariates including age, NISS, injured body region, preexisting comorbidities, the incidence of postinjury MODS and sepsis, and treatment between the two groups showed a statistically significant difference in NISS; however, no other covariate was significantly different. Our finding that a significantly higher NISS in the PSM female group showed lower mortality than that in the PSM male group during the acute phase of major trauma suggests increased survival in hospitalized women with major trauma and a NISS of 16–24 during the acute period.

Oberholze et al,[38] Frink et al,[23] Trentzsch et al,[17,21] and Mörs et al[14] reported a lower incidence of sepsis in post–major trauma hospitalized female patients than in male patients. We also observed significant difference between the two groups in both demographic (n = 1267, 17.7% in males and n = 433, 15.0% in females, $p = 0.001$) and post-PSM (n = 554, 19.3% in males and n = 444, 15.4% in females, $p = 0.001$) data. This finding indicated a lower incidence of sepsis in hospitalized female patients with major trauma (odds ratio = 0.76, $p = 0.001$) within the acute phase of major trauma. Furthermore, we analyzed the incidence of sepsis between patients with a NISS of 16–24 at admission and death before hospitalization day 4 and all patients in the PSM groups throughout the hospital course and observed a significant difference (n = 21, 45.7% for NISS 16–24 and death before hospital day 4 and n = 998, 17.4% for all patients in the PSM group, $p < 0.001$). This finding indicated a higher incidence of sepsis in hospitalized patients within the acute phase of major trauma. This finding is in agreement with those of prior studies reporting changes in systemic interleukin (IL)-6 levels in patients with trauma. IL-6 is a proinflammatory cytokine that plays a central role in the postinjury inflammatory response, the increase of which is correlated to the trauma severity[38–40] and the development of sepsis[40,41] in the acute phase of trauma.

We observed no statistically significant differences in the incidence of MODS between the two groups in either the demographic (n = 1897, 26.6% in men and n = 750, 26.0% in women, $p = 0.57$) or the post-PSM (n = 805, 28.0% in men and n = 780, 27.1% in women, $p = 0.46$) data. The difference between genders remained nonsignificant even after the incidence of MODS across two age groups was surveyed (n = 1008, 23.7% in men and n = 294, 21.9% in women, $p = 0.19$ in the pre-menopause group and n = 889, 31.0% in men and n = 456, 29.6%, $p = 0.35$ in the post-menopause group). This finding is in agreement with that reported by Mörs et al.[14]

Our findings are discordant with those of several previous studies. These differences may be due to variability in injury severity in the enrolled cohorts.[17,26] While other studies had cohorts comprising patients with injury severities comparable

to those in our study, they did not adjust for preexisting chronic medical conditions to address potential confounding.[21,23,42]

The findings of the current study showed a lower number of ventilator-free days in women than in men (18.1 ± 19.5 vs 19.4±22.7 days, $p < 0.05$ in PSM groups), as well as lower LOS in the ICU (9.8 ± 9.5 vs 10.8 ± 11.5 days, $p < 0.001$, PSM groups) and hospital (26.6 ± 23.4 vs 29.3 ± 28.4 days, $p < 0.001$, PSM groups).

As a retrospective cohort study, our results were limited by the disadvantage inherent to its design. First, the NHIRD is a claims database, and validity of the data (technical or intentional errors for easier national health insurance reimbursement)[43] could have introduced bias despite the PSM to improve the validity. Second, the NHIRD does not contain detailed records of prior diseases and medical information on patients; thus, our analysis of risk factors for outcome in major trauma patients could be incomplete, despite our identification of these diseases by outpatient diagnosis, which was recorded on the ambulatory care expenditures in the visit file or the registry for patients with catastrophic illness before the injury. Finally, the classification of the trauma severity by NISS is not the same as by injury severity score, which may result in a lack of generalizability in outcomes between admitted patients with major trauma in the Taiwanese NHIRD and other countries.

In conclusion, there was no gender-based difference in long-term mortality in hospitalized patients with major trauma; however, women who were admitted for moderate major trauma had a survival advantage in the acute phase of major trauma. Moreover, hospitalized women with major trauma had a lower incidence of sepsis and shorter ICU and hospital LOS than men.

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