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Clinical Features and Direct Medical Cost of Splenic Injury in China

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Abstract

Objectives: This study evaluated the clinical features and direct medical cost of splenic injury during 2000-2013 in China.

Design Population-based observational study.

Methods: We used ‘The No. 1 Military Medical Project’ information system to conduct a retrospective study. Patients admitted from 2000 to 2013 were identified. Demographic data, management manner, clinical data, and direct medical cost (DMC) were collected. We performed a generalized linear method (GLM) using gamma distribution to assess the drivers of direct medical costs.

Results: we admitted 8083 patients with splenic injury who met the study criteria. Over the 14-year study period, 2782 (34.4%) patients were treated with NOM (non-operative management), 5301 (65.6%) with OM (operative management). From 2000 to 2013, the rate of NOM increased from 34.7% to 55.9%, while OM decreased from 65.3% to 44.1%. Mean per-patient DMC in both of NOM and OM increased from 2000 to 2013. In GLM analysis, male, old age, LOS, severe splenic injury grade, OM, ICU, blood transfusion, and tertiary hospitals were associated with higher DMC, while female and NOM was associated with lower DMC.

Conclusions：The management of splenic injury in China was influenced by Chinese health care policy and health care environment. Although NOM is now recognized as the standard of care in hemodynamically stable patients, the rate of patients of splenic injury underwent NOM in China was lower than any other countries. Medications were identified as the main DMC drivers. Specific policies should be made to relieve the

high medical cost burdens and build a harmonious medical environment.

Keywords: Splenic injury, Clinical features, Direct medical cost, Non-operative, Operative, China, Healthcare system reform

Strengths and limitations of this study

We provided the most comprehensive description of clinical features of splenic injury and its related direct medical cost in China.

This study is useful for government and health administration services to reform the health care policies to contain trauma-related medical costs, and it provides useful evidences for management of splenic trauma in China.

This research cannot tell what type of NOM was adopted in patients due to lack of related code in CTDB.

The categories of DMC cannot be extracted from 2010 to 2013 in CTDB.

Patients' comorbidities and concomitant injury were not included in CTDB.

The insurance types were not recorded in this database, we cannot estimate patients-related medical care utilization or provide comprehensive cost analysis of patients with splenic injury

Introduction

The spleen is an organ found in all vertebrates. Similar in structure to a large lymph node, its function is to alternatively get rid of immune complexes, circulating pathogens and senescent, dysfunctional, or infected red blood cell [1, 2]. Trauma is a leading cause of death, with approximately 5 million deaths reported each year globally. According to reports, splenic injuries take up to 16% to 23.8% of trauma, with a mortality rate of 9.3%, mainly in response to associated injuries and treatment [3]. Recently, management paradigms for splenic injury are always controversial. Although non operative management (NOM) has been recognized as a standard of producer in hemodynamically stable patients (an estimated success rate exceeding 80-90%) [3, 4], some literature contends old age, high grade of splenic trauma, the sign of a large hemoperitoneum, contrast extravasation on admission, high ISS value, low systolic blood pressure on admission, transfusion of more than one packed cells, and the presence of brain injury associated trauma may increase the probability of failure of NOM [5, 6].

At present most of the study on splenic injuries focused on the comparison of the medical technical and clinical outcomes of operative versus non operative management [4, 7]. The direct medical cost is a factor that cannot be neglected on evaluating if treatment strategies are proper from a health care economy point of view. There are only a few of reports on the cost of management of splenic injuries in multicenter studies [8-10]. Moreover, there is no data on the cost of management of splenic injuries in China, and the studies on the characteristic of splenic injuries in Chinese hospitals

were rarely reported.

The issues of medical cost in China are notably complicate due to its changing public medical insurance policy features [11]. Therefore, it is necessary to understand the association of structure of medical cost with different modality of strategies, which may provide some useful data and evidences for health care workers and health care policy makers, to a certain extent.

Materials and Methods

Data source

Data for this study was obtained from 'The No. 1 Military Medical Project' information system, which is part of the Chinese Trauma Databank (CTDB). It was built and maintained by the Information Center of the Medica department under the Ministry of General Logistics of the Chinese People's Liberation Army (PLA), possessing a lot of user group in China and covering more than 200 military hospitals and 90 public hospitals. The database collects large amounts of trauma care data aiming to help the research, prevention, and treatment of trauma.

All patients whose hospital information was included in the CTDB. Data handling in this system-based studies is performed without revealing the identity of any participants and therefore obtaining ethical approval is not required.

Study Design

This was a retrospective study using the data from the No. 1 Military Medical Project information system to identify inpatients with splenic injury (ICD9-CM 865.00-865.19) in 8 hospitals (6 tertiary and 2 secondary hospitals) between January 2000 and

December 2013. Patients who underwent splenectomy, splenorrhaphy and partial splenectomy were all defined as the operative management group, while the others were identified as NOM group.

Basic demographic data, direct medical cost, total length of hospital stay (LOS), injury pattern, trauma mechanism, transfusion, mortality, New Injury Severity Score (NISS) [12] and splenic injury grade [13] were collected. Exclusion criteria included patients who were dead on arrival at hospital and those patients for whom complete data are unavailable.

Estimation of costs

In our study, we extracted the direct medical cost (DMC) of each patient from the database, which includes medications, laboratory tests, imaging, surgery, transfusion, hospitalization (medical consumables, diagnostic procedures, material, etc.), and other costs (room costs, nursing care cost, etc.). However, there were only records of total direct medical costs in 2010-2013, the expenses category was missing during that period in CTDB.

Direct medical cost from other years (2000-2012) were first converted into 2013 values in Renminbi (RMB) adjusting for inflation [14], using the GDP deflator of China [15], and were then converted to US dollars (USD) at the exchange rate equaling USD 1 = 6.196 RMB for 2013.

Statistical analysis

Statistical analysis was performed using the RStudio, version 1.4.1717 (GNU General Public License) and SPSS 22.0 (IBM Corporation, Armonk, NY, USA). Mann-

Whitney test was applied for quantitative variables, the $\chi 2$ test for categorical variables and the Kruskal-Wallis rank sum test for continuous variables. Statistical significance was set at 0.05. We used the Bonferroni test for multiple corrections. Since direct medical cost barely complies with the assumptions of the ordinary least squares (OLS) regression, and they, usually, are skewed to the right. Thus, a generalized linear method (GLM) with gamma family, log-link function was used to assess the association of direct medical costs with clinical characteristics.

Patient and public involvement

No patients were involved.

Results

Clinical Characteristics of Patients by Management

Table 1 shows the clinical characteristic of patients with splenic injury managed with NOM or OM. A total of 8083 patients had splenic injury from 2000 to 2013 were identified. Most of the patients managed with NOM or OM were men, 80% or 83.1% respectively. Patients in two groups were typically in their prime of life, most ranging in age from 18 to 40 years old. Car collision was the main factor that causes splenic injury. Patients with high splenic injury grade (III-V) and high NISS are more likely to undergo an operation. There was no difference between secondary hospitals and tertiary hospitals adopting the treatment strategies on patients. Compared with patients in NOM, patients in OM had longer LOS, more blood transfusion, higher mortality, and total direct medical cost.

In addition, the ratio of patients with OM decreased from 65.3% in 2000 to 44.1%

in 2013, while patients with NOM increased from 34.7% in 2000 to 55.9% in 2013 (Fig 1A). In 2000, the mean DMC per-patient with NOM and OM was $2256 and $3089, respectively. However, the mean DMC per-patient has risen to $3627 (NOM) and $5312 (OM), respectively, in 2013 (Fig 1B).

Clinical Features and DMC of Patients by Age

As is shown in table 2, car collision was frequent cause of splenic injury for all ages. After correction to Bonferroni, length of stay (LOS) was the longest in the advanced age group (>65 years) (median 14 days) than any other groups ($p < 0.001$), except 18-40 years group ($p = 1$), while children group (<18 years) was the shortest LOS (median 11 days) than other groups. Compared with 18-40 years patients and children group, advanced age patients had higher mortality. The total DMC for patients in different age group were statistically significantly different ($p < 0.001$), and the advanced age group had higher DMC (US $3,187) than any other groups ($P = 0.001$), except 45-60 years group ($p = 1$). The cost of drug accounted for a major proportion of the DMC in all groups (children: 31.6%, 18-40 years: 40%, 40-65 years: 42.9%, advance age: 40.3%, respectively). There were significantly differences ($p < 0.001$) between the groups in categories of expenditure of laboratory tests and transfusion, which increased with age after correction to Bonferroni. As to cost of surgery differences, compared with the children, 18-40 years, and advanced age group, the 40-65 years group had a significantly highest payments, while both of children and advanced age patients had relatively low cost on surgery.

Structure of Direct Medical Cost

Figure 2 has shown that the distribution of various DMC by different management. Drug cost is the main expenditure in DMC, accounting for 46% (US$ 1612) of total DMC, followed by hospitalization (18%, USD$ 633). Patients with NOM and OM had similar patterns structure of DMC, but transfusion and surgery costs are higher in patients with OM than patients with NOM.

Predicators of Direct Medical Cost

Table 3 shows the results of GLM with gamma distribution and the log-link function performed to determine the variables affecting direct medical costs. Female patients cost 5.9% less than men (p=0.002). LOS was predicted to increase the DMC by 2.2% ($p < 0.01$). Alive was associated with 34.6% increase in DMC ($p<0.001$). The higher grade of splenic injury patients had, the more the DMC they cost ($p<0.001$). Overall, patients with splenic injury with OM cost 50.5% more than patients with NOM ($p<0.001$). Admission to the ICU was associated with a 59.9% increase in DMC ($p<0.001$). Transfusion more than twice was associated with a 51.2% increase in DMC. Overall, DMC for adult patients were higher from 27.1% to 44.1% than children ($p<0.001$). Patients with severe NISS cost 6.3% more than mild ones (p=0.0046), while there was no significant difference between mild and moderate NISS. In addition, patients in tertiary hospitals spent more money than in secondary hospitals.

Discussion

Using a large military fund database from China, we can obtain the clinical data of patients with splenic injury and calculate direct medical cost resulting from splenic injury. To our knowledge, this is the first description of the multicenter clinical features

and direct medical cost of splenic injury in China. Currently, NOM is the standard of treatment in hemodynamically patients with splenic injury, and the success rate of this produces exceeds 80-90% [3]. In this retrospective study, we showed the changes in the treatment of splenic trauma and its related direct medical cost in China over the decades. Interestingly, the ratio of NOM had increased gradually in Chinese hospitals, while the DMC of patients with splenic injury had increased sharply after 2010 since the Chinese government issued new rounds of health care system reforms in 2009 [11].

In this study, the rate of patients with splenic injury with OM was higher than patients with NOM before 2010, which contrasted with many studies [5, 7, 9]. However, patients undergoing NOM vastly outnumbered patients with OM after 2010, which made a sharp contrast to the modality of management for patients before 2010, but the rate of patients with NOM in this study is still lower than any other studies [7, 16]. Several reasons may be explained this phenomenon. First, young Chinese doctors are bored with their careers [17, 18]. Some doctors have symptoms of depression, stress, anxiety, burnout, and insomnia when they go to work due to low job titles, low wages, long work hours, and poor policy support from the government [17], which may affect their performance on decision of clinical treatment. Second, because of large population in China, the healthcare resources are seriously insufficient, and inequalities exist everywhere. Unfortunately, medical care insurance also cannot cover the health expenditure, and hospital expenses are usually very large. Even worse, many doctors in large Chinese hospitals expend large amounts of efforts to do research to get high academic title, with a little care about the level of humanitarianism during the medical

service process [19]. Therefore, the relationship between doctors and patients is usually strained [20]. Although Rosenberg, G, et al. reported in their study that readmission rates of patients with splenic injury after initial management strategies did not differ [21], readmission is unacceptable for many poor Chinese patients and their families, which can impose heavy financial burdens on their families. To avoid medical conflicts whenever possible, some Chinese doctors must choose a safe and conservative treatment. The truth behind the issue is that there have been many violent events against medical personnel in Chinese hospital over the decades [22, 23], some of the doctors even lost their lives in these medical disputes. Chinese healthcare system barely exists regulations to protect medical staff from intended violence [24], so it is hard to be free for doctors to make the decision that patients benefit most from under this circumstance. Comfortingly, Doctor Law of the People's Republic of China was revised recently, which is the first time to enact laws to protect doctors' practice, and doctors' human dignity [25]. Third, Chinese government has introduced a new healthcare reform since 2009. Five main domains were reformed in China's health system reform: social health security, essential medicines, primary healthcare, basic public health service package, and public hospitals [26]. These measures improved access to healthcare and reduced health inequality, to a certain extent. Moreover, it, in some degree, reduced the contradiction between doctors and patients, and promoted the progress of medical level [26]. However, in public hospitals, medical expenditure per-patient discharged increased by 22.1% between 2010 and 2013 [27, 28]. The proportion of out-of-pocket payments for healthcare decreased, but the financial burden of healthcare did not fall

much. Moreover, the proportion of drug cost in total hospital expenditure has decreased, but total hospital expenditure is still rising [28]. Thus, splenic injury patients with low splenic grade and mild NISS were more likely to be adopted by NOM, but the per-patient direct medical cost was higher than before whatever management doctors took.

The mechanism of splenic injury in this study is typically car collision and fall, which is consistent with other studies [4, 29]. In our study, most patients underwent NOM were splenic injury grade Ⅰ/Ⅱ, with mild NISS, while patients with OM were higher splenic injury grade and moderate or severe NISS. Although this modality of treatment strategies of splenic injury in Chinese hospitals runs counter to the mainstream view, the fact is doctors in China must make an optimal medical plan to juggle effective treatment and harmonious doctor-patient relationship within a short time when facing large amounts of inpatients. In addition, Chinese surgeons should keep the one-time successful rate of management as possible as they can, or they may have troubles from unit leadership and patients [24].

China has already entered the aging society since 1999 and is one of the fastest-aging countries in the world [30]. Injury is the fifth leading cause of death in the elderly. Compared to younger patients, advanced age patients who sustain major trauma have been shown to experience higher mortality rates and higher economic burden on families and societies. In our study, age over 65 years had a longer length of stay, higher DMC, and mortality, but lower rate of OM and surgery cost than any other groups. Management of splenic injury in the elderly population remains controversial. Tsugawa et al. believed initial operative intervention in the elderly, as signs of shock and severe

injuries are not obvious in elderly patients [31]. However, Warnack E, et al. advocated for which modality of management doctors choose depends on the actual situation of the patient [32]. Considering the high mortality and cost in elderly patients, we believe multiple disciplinary team (MDT) is needed to identify and assess worst-off senile patient's condition. Drugs are the major cost in all age groups, followed by hospitalization cost. The two categories of medical cost made up most of direct medical cost in splenic injury, which were the two main sources of Chines hospitals' profit at that time.

Consistent with previous studies, NOM of splenic injury has contributed to a substantial decrease in DMC, mortality, and LOS [9]. In addition, there were significant differences in DMC by splenic injury grade types, gender, number of transfusions, and age. In our study, male patients with high splenic injury grade had higher DMC than female with low splenic injury. The older the patients are, the higher DMC are. Old patients are more likely to experience a higher rate of complications, such as pneumonia, subphrenic abscesses, and heart disease after NOM [31, 32], which increases the length of stay and expenditure in hospital. Therefore, decision for a proper management for old patients with splenic injury should be considered the economic burden factor. Since higher prevalence and incidence of splenic injury in males than females, combined with higher medical expenditures for old male patients, preventative and public education of traffic safety programs aimed at men are cost-effective health interventions. Plus, the traffic laws and construction of facilities in cities should be improved to protect citizens from injury.

In our study, drug cost was the main contributor to average splenic injury-related DMC in NOM or OM, followed by hospitalization costs (figure 2). This phenomenon might be explained from two sides. From the supply side, Chinese doctors can obtain 15% profit margin from the monetary values of drugs they prescribed according to the drug mark-up policy [33]. From 2009 to 2015, this policy was gradually ended in hospitals of all sizes, but overall hospital expenditure is still increasing [26]. From the demand side, patients in China are obsessed with medication therapy when they are ill [34]. Also, traditional Chinese medications are widely welcomed by patients and doctors in China, not only can it bring benefit for hospitals but also it does work in some patients [35].

There are some limitations in our study. First, we cannot tell what type of NOM was adopted in patients due to lack of related code in CTDB. Second, because of flaws of CTDB, the categories of DMC cannot be extracted from 2010 to 2013, we just extracted the total DMC of patients during that period. Third, patients' comorbidities and concomitant injury were not included in CTDB, so we cannot further evaluate the impact of these indicators on DMC. Fourth, because the insurance types were not recorded in this database, we cannot estimate patients-related medical care utilization or provide comprehensive cost analysis of patients with splenic injury. Despite these limitations, the strengths of our study provide a valuable data on clinical profile of splenic injury in China, and useful health economic information to future research on economic burden of splenic injury in China.

Conclusions

This study is the first, to our knowledge, to describe direct medical cost for splenic injury in China. China's health system always bares amounts of economic burden, coupled with lack of effective incentives to improve health workers' motivation and laws to protect doctors from violence, which may have a significant influence on the management and cost of patients with splenic injury. With the new round of Chinese health care reform in 2019, there has been some progress in contained rising medical expenditures and reshaped hospitals' revenue structures [11]. This research will be useful for government and health administration services to reform the health care policies to contain trauma-related medical costs, and it provides useful evidences for management of splenic trauma in China.

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Not applicable.

Authors' contributions

Y.C. and Q.Z. conceived and designed the study. L.L., YB.M., and Y.Q. participated in data collection and analysis. Y.C. participated in writing. J.H.Z. and Y.C. were responsible for statistical analysis. All authors read and approved the final manuscript.

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Availability of data and materials

The database used and/or analyzed during the study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Table 1 Characteristics of study population by management

	NOM n=2782	OM n=5301	*P* value
Male	2217(80%)	4405(83.1%)	<0.001
Age			<0.001
<18	324(11.6%)	421 (7.9%)	
18-40	1630 (58.6%)	3131 (59.1%)	
41-65	754(27.1%)	1635 (30.8%)	
>65	74(2.7%)	114 (2.2%)	
Trauma cause			<0.001
Car collision	1046 (37.6%)	2092 (39.5%)	
Motorcycle or Cycling Collision	126 (4.5%)	268 (5.2%)	
Fall from heights	365 (13.3%)	811 (15.3%)	
Fall and hurt oneself	208 (7.5%)	465 (8.8%)	
Crush injury	34 (1.2%)	50 (0.9%)	
Penetrating injuries	385 (13.5%)	798 (15.1%)	
Sports	112 (4%)	157 (3%)	
Personal assault	340 (12.2%)	533 (10.1%)	
Others	166 (6%)	127 (2.4%)	
Splenic grade			<0.001
I/II	2707 (97.4%)	1280 (24.1%)	
III/IV	57 (2%)	3512 (66.3%)	
V	18 (0.6%)	509 (9.6%)	
NISS			<0.001
Mild <15	1722 (61.9%)	1666 (31.4%)	
Moderate 15-25	784 (28.2%)	2209 (41.7%)	
Severe > 25	276 (9.9%)	1426 (26.9%)	
Hospital level			0.727
Secondary hospitals	569 (20.5%)	1067 (20.1%)	
Tertiary hospitals	2213 (79.5%)	4234 (79.9%)	
Blood transfusion >1	539 (19.4%)	3474 (65.5%)	<0.001
LOS, median (IQR)	11 (7-18)	14 (10-12)	<0.001
Mortality	76 (2.7%)	200 (3.8%)	<0.001

Direct medical cost, median (IQR)	1223 (595-2542)	3062 (2104-4619)	<0.001

IQR, interquartile range

Table 2 Clinical features and DMC of splenic injury by age

	<18	18-40	41-65	>65	P value
n	745	4761	2389	188	
Trauma cause					
Car collision	268 (40%)	1884 (39.6%)	911 (38.1)	75 (40%)	
Motorcycle or Cycling collision	43 (5.8%)	172 (3.6%)	166 (6.9%)	13 (6.9%)	
Fall from heights	105 (14.1%)	685 (14.4%)	361 (15.1%)	25 (13.3%)	
Fall and hurt oneself	83 (11.1%)	356 (7.5%)	207 (8.7%)	27 (14.4%)	
Crush injury	9 (1.2%)	40 (0.8%)	35 (1.5%)	0	
penetrating injuries	111 (14.9%)	711 (14.9%)	333 (13.9)	28 (14.9%)	
Sports	35 (4.7%)	155 (3.3%)	77 (3.2%)	2 (1%)	
Personal assault	69 (9.3%)	593 (12.5%)	202 (8.5%)	9 (4.8%)	
Others	22 (3%)	165 (3.5%)	97 (4.1%)	9 (4.8%)	
Splenic grade					<0.001
I/II	429 (57.6%)	2311 (48.5%)	1145 (47.9%)	102 (54.2%)	
III/IV	282 (37.9%)	2159 (45.2%)	1056 (44.2%)	72 (38.3%)	
V	34 (4.6%)	291 (6.1%)	188 (7.9%)	14 (7.4%)	
NISS					0.15
Mild <15	347 (46.6%)	1976 (41.5%)	986 (41.3%)	79 (42%)	

Moderate 15-25	272 (36.5%)	1787 (37.5%)	874 (36.6%)	60 (31.9%)	
Severe > 25	126 (16.9%)	998 (21%)	529 (22.1%)	49 (26.1%)	
LOS, median (IQR)	11 (8-16)	13 (9-21)	13 (9-23)	14 (9-22)	<0.001
Mortality	16 (2.1%)	143 (3%)	99 (4.1%)	13 (6.9%)	0.001
Direct medical cost ($), median (IQR)	1701 (847-2700)	2467 (1420-3942)	2779 (1640-4533)	3949 (1668-5043)	<0.001
Drugs	538 (261-1128)	987 (474-1867)	1192 (597-2252)	1329 (603-2247)	<0.001
Laboratory tests	95 (54-158)	121 (69-202)	141 (80-239)	180 (95-322)	<0.001
Imaging	9 (0-67)	15 (0-80)	23 (0-102)	32 (0-122)	<0.001
Surgery	268 (0-483)	339 (9-529)	378 (83-555)	298 (0-474)	<0.001
Transfusion	0 (0-187)	80 (0-294)	131 (0-372)	196 (0-456)	<0.001
Hospitalization	264 (113-525)	366 (166-706)	413 (186-803)	451 (176-1014)	<0.001
Others	173 (91-336)	230 (117-458)	259 (132-510)	362 (126-592)	<0.001

Table 3 Results of generalized linear model with gamma distribution

Variables	β	SE	P	EXP (β)	95% CI
Gender					
Male	Reference			1	
Female	-0.061	0.0194	0.0016**	0.941	0.906-0.977
LOS	0.022	0.0004	<0.001***	1.022	1.021-1.023
Mortality					
Death	Reference			1	
Alive	0.297	0.5200	<0.001***	1.346	1.240-1.464
Splenic injury grade					
Ⅰ/Ⅱ	Reference			1	
Ⅲ/Ⅳ	0.076	0.0217	<0.001***	1.079	1.034-1.124
Ⅴ	0.193	0.0349	<0.001***	1.212	1.133-1.298
Management					
NOM	Reference			1	
OM	0.409	0.0235	<0.001***	1.505	1.440-1.573
ICU					
No	Reference			1	
Yes	0.422	0.0244	<0.001***	1.599	1.525-1.678
Blood transfusion ＞ 2					
No	Reference			1	
Yes	0.413	0.0170	<0.001***	1.512	1.465- 1.561
Age					
<18	Reference			1	
18-40	0.239	0.0265	<0.001***	1.271	1.206-1.338
41-65	0.323	0.0283	<0.001***	1.382	1.307-1.460
>65	0.365	0.0550	<0.001***	1.441	1.295-1.607
NISS					
<15	Reference			1	
15-25	0.012	0.0173	0.673	1.012	0.978-1.046
>25	0.061	0.0216	0.005**	1.063	1.020-1.109
Hospital					
Secondary hospitals	Reference			1	
Tertiary hospitals	0.364	0.0187	<0.001***	1.439	1.387-1.492

Exp(B), Exponential of coefficients; CI, confidence intervals; SE, standard error. P value: ***P<0.001; **P<0.01.

Figure 1. A. Overall trend in splenic management over time from 2000-2013. B. Mean per-patient direct medical cost from 2000-2013.

Figure2. Direct medical cost subtypes of patients with splenic injury by management from 2000-2008 (percentages).

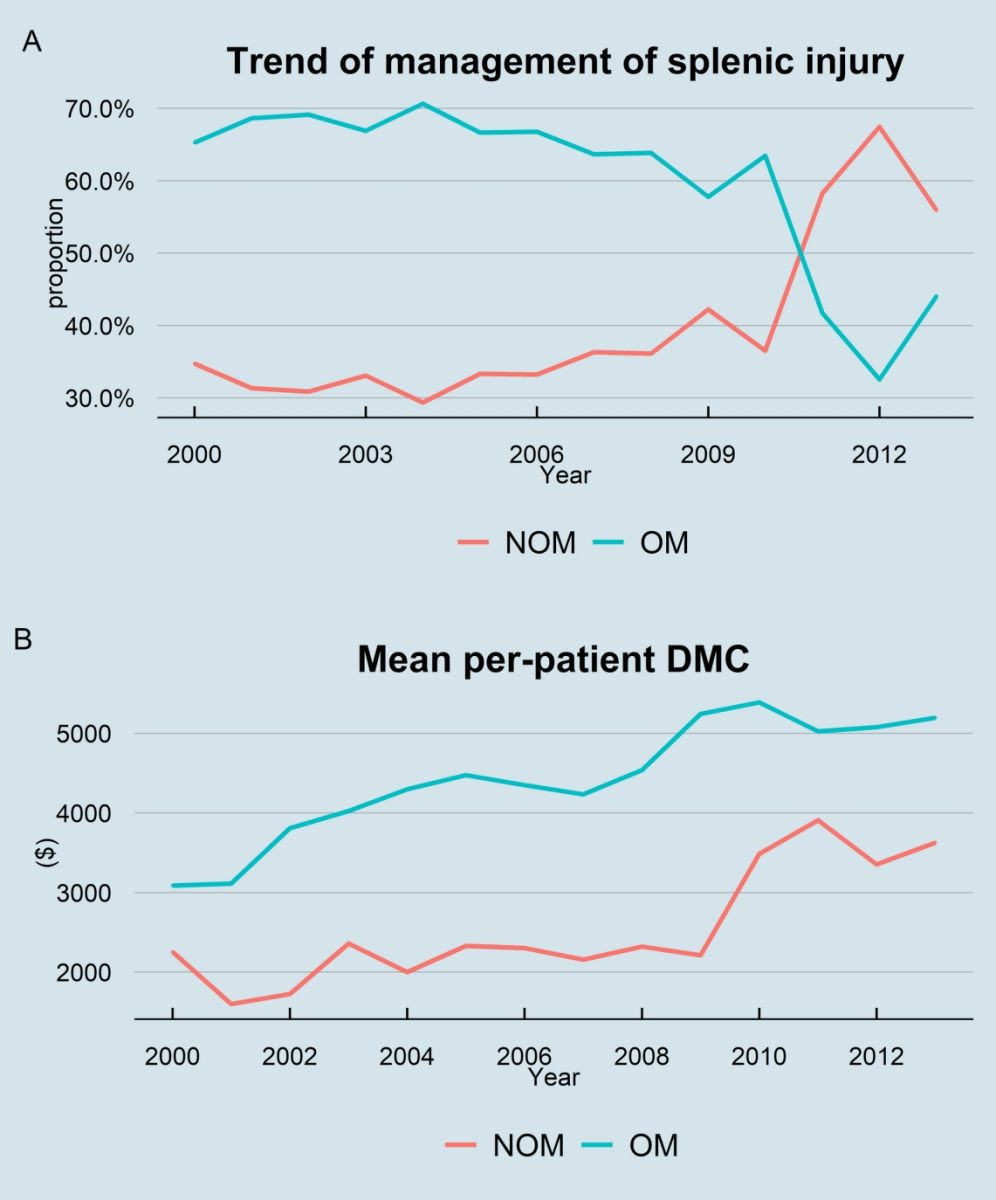

Figure 1. A Overall trend in splenic management over time from 2000-2013. B Mean per-patient direct medical cost from 2000-2013.

156x188mm (300 x 300 DPI)

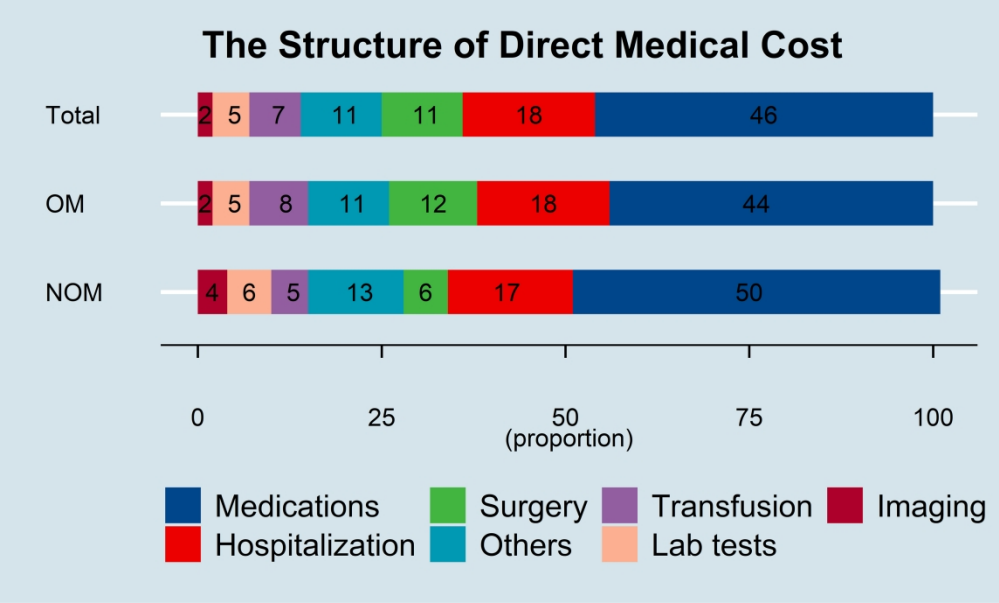

Figure 2. Direct medical cost subtypes of patients with splenic injury by management from 2000-2008 (percentages).

156x94mm (600 x 600 DPI)

Reporting checklist for economic evaluation of health interventions.

Based on the CHEERS guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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	Reporting Item	Page Number
Title		
#1	Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.	1

Abstract			
	#2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions	2
Introduction			
Background and objectives	#3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions	3
Methods			
Target population and subgroups	#4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	5-6
Setting and location	#5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	5-6
Study perspective	#6	Describe the perspective of the study and relate this to the costs being evaluated.	5-6
Comparators	#7	Describe the interventions or strategies being compared and state why they were chosen.	6-7
Time horizon	#8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	5-6
Discount rate	#9	Report the choice of discount rate(s) used for costs and	6

		outcomes and say why appropriate	
Choice of health outcomes	#10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed	7
Meaurement of effectiveness	#11a	Single study-based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data	7
Measurement of effectiveness	#11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data	7
Measurement and valuation of preference based outcomes	#12	If applicable, describe the population and methods used to elicit preferences for outcomes.	7
**Estimating resources and costs **	#13a	Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs	6

Methods

Estimating resources and costs	#13b	Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	6
Currency, price date, and conversion	#14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	6
Choice of model	#15	Describe and give reasons for the specific type of decision analytical model used. Providing a figure to show model structure is strongly recommended.	7
Assumptions	#16	Describe all structural or other assumptions underpinning the decision-analytical model.	7
Analytical methods	#17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	7

Results			
Study parameters	#18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	7-8
Incremental costs and outcomes	#19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	8-9
Characterising uncertainty	#20a	Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	9
Characterising uncertainty	#20b	Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	9
Characterising heterogeneity	#21	If applicable, report differences in costs, outcomes, or cost effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	9

Discussion			
Study findings, limitations, generalisability, and current knowledge	#22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	9-15
Other			
Source of funding	#23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support	15
Conflict of interest	#24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations	15

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Clinical Features and Direct Medical Cost of Splenic Injury in China: a cross-sectional study

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Abstract

Objectives: This study analyzes the clinical features and direct medical cost of splenic injury during 2000-2013 in China.

Design This was a cross-sectional study.

Methods: We used ‘The No. 1 Military Medical Project’ information system to conduct a retrospective study. Patients’ information from 2000 to 2013 were identified. Demographic data, treatment, clinical data, and direct medical cost (DMC) were collected. We performed a generalized linear method (GLM) using gamma distribution to assess the drivers of direct medical costs.

Results: We included 8083 patients with splenic injury who met the study criteria. Over the 14-year study period, 2782 (34.4%) patients were treated with NOM (non-operative management), 5301 (65.6%) with OM (operative management). From 2000 to 2013, the rate of NOM increased from 34.7% to 55.9%, while OM decreased from 65.3% to 44.1%. Mean per-patient DMC in both NOM and OM increased from 2000 to 2013. In GLM analysis, male, old age, LOS (length of stay), severe splenic injury grade, OM, ICU (intensive care unit), blood transfusion, and tertiary hospitals were associated with higher DMC, while female and NOM was associated with lower DMC.

Conclusions： In China, management of splenic injury was the most important factor impacting the total direct medical cost. Proper management and public policy could curtail the burden of splenic injury.

Keywords: Splenic injury, Clinical features, Direct medical cost, Non-operative,

Operative, China, Healthcare system reform

Strengths and limitations of this study

We provided the most comprehensive description of clinical features of splenic injury and its related direct medical cost in China.

This study is useful for government and health administration services to reform the health care policies to contain trauma-related medical costs, and it provides useful evidence for management of splenic trauma in China.

This research cannot tell what type of NOM was adopted in patients due to the lack of related code in CTDB (Chinese Trauma Databank).

The insurance types were not recorded in this database, we cannot estimate patients-related medical care utilization or provide comprehensive cost analysis of patients with splenic injury

Introduction

The spleen is an organ found in all vertebrates. Similar in structure to a large lymph node, its function is to alternatively get rid of immune complexes, circulating pathogens, and senescent, dysfunctional, or infected red blood cell[1,2]. Trauma is a leading cause of death, with approximately 5 million deaths reported each year globally. According to reports, splenic injuries take up to 16% to 23.8% of trauma, with a mortality rate of 9.3%, mainly in response to associated injuries and treatment[3]. Recently, management paradigms for splenic injury are always controversial. Although nonoperative management (NOM) has been recognized as a standard of treatment in

hemodynamically stable patients (an estimated success rate exceeding 80-90%)[3,4], some literature contends old age, high grade of splenic trauma, the sign of a large hemoperitoneum, contrast extravasation on admission, high ISS value, low systolic blood pressure on admission, transfusion of more than one packed cells, and the presence of brain injury associated trauma may increase the probability of failure of NOM[5,6].

At present most of the studies on splenic injuries focused on the comparison of the safe and clinical outcomes of operative versus nonoperative management[4,7]. The direct medical cost is a factor that cannot be neglected in evaluating if treatment strategies are proper from a health care economy point of view. The study of the cost of managing splenic injuries has rarely been reported in multicenter studies[8-10]. Moreover, there is no data on the cost of management of splenic injuries in China, and the studies on the characteristic of splenic injuries in Chinese hospitals were rarely reported.

The issues of medical cost in China are notably complicated due to its changing public medical insurance policy features[11]. Therefore, it is necessary to understand the association of structure of medical cost with the different modalities of strategies, which may provide some useful data and evidence for health care workers and health care policymakers, to a certain extent.

Until now, there is no study on DMC of splenic injury. To fill the gap, we explored the related factors of the total direct medical cost of splenic injury based on a database. These results will provide an insight into the potential factors that contribute to direct medical cost and support useful evidence for making a public policy to reduce the

burden of splenic injury.

Materials and Methods

Data source

Data for this study was obtained from 'The No. 1 Military Medical Project' information system, which is part of the Chinese Trauma Databank (CTDB)[12-15]. It was built and maintained by the Information Center of the Medical Department under the Ministry of General Logistics of the Chinese People's Liberation Army (PLA), possessing a lot of users' groups in China, and covering more than 200 military hospitals and 90 public hospitals. The database collects large amounts of trauma care data aiming to help the research, prevention, and treatment of trauma**.**

inpatients' information was included in the CTDB. Data handling in this system-based study are performed without revealing the identity of any participants and therefore obtaining ethical approval is not required.

Study Design

This was a retrospective study using the data from the No. 1 Military Medical Project information system to identify 8038 inpatients with splenic injury (ICD9-CM 865.00-865.19) in 8 hospitals (6 tertiary, three army medical hospitals of the PLA in Chongqing, the fourth people's hospital of Chongqing, affiliated hospital of Chengdu medical college, NO. 324 hospital of the army, and 2 secondary hospitals, No. 22 hospital of the army, and NO. 477 hospital of the army) between January 2000 and December 2013. Patients who underwent splenectomy, splenorrhaphy and partial splenectomy were all defined as the operative management group, while the others were

identified as the NOM group.

Basic demographic data, direct medical cost, the total length of hospital stay (LOS), injury pattern, trauma mechanism, transfusion, mortality, New Injury Severity Score (NISS)[16], and splenic injury grade[17] were collected. Exclusion criteria included patients who were dead on arrival at the hospital and those patients for whom complete data are unavailable (Figure 1).

Estimation of costs

In our study, we extracted the direct medical cost (DMC) of each patient from the database, which includes medications, laboratory tests, imaging, surgery, transfusion, hospitalization (medical consumables, diagnostic procedures, material, etc.), and other costs (room costs, nursing care cost, etc.). However, there were only records of total direct medical costs in 2010-2013, the expenses category was missing during that period in CTDB.

The total direct medical cost from other years (2000-2012) was first converted into 2013 values in Renminbi (RMB) adjusting for inflation [18], using the GDP deflator of China[19], and was then converted to US dollars (USD) at the exchange rate equaling USD 1 = 6.196 RMB for 2013.

Statistical analysis

Statistical analysis was performed using the RStudio, version 1.4.1717 (GNU General Public License) and SPSS 22.0 (IBM Corporation, Armonk, NY, USA). Mann-Whitney test was applied for quantitative variables, the $\chi 2$ test for categorical variables, and the Kruskal-Wallis rank-sum test for continuous variables. Statistical significance

was set at 0.05. We used the Bonferroni test for multiple corrections. Because direct medical cost barely complies with the assumptions of the ordinary least squares (OLS) regression, they, usually, are skewed to the right. Thus, a generalized linear method (GLM) with gamma family, log-link function was used to assess the factors impacting on the direct medical costs of splenic injury.

Patient and public involvement

No patients were involved.

Results

Characteristics of Patients by Management

Table 1 shows the demographic and clinical characteristics of patients with splenic injury managed with NOM or OM. In this study, a total of 8083 patients with splenic injury from 2000 to 2013 were included. Most of the patients managed with NOM or OM were men, 80% or 83.1% respectively. Patients in the age group 18-40 years took up most of the population in NOM and OM. Car collision was the main factor that causes splenic injury. There was no difference between secondary hospitals and tertiary hospitals adopting the treatment strategies on patients. Compared with patients in NOM, patients in OM had longer LOS, more blood transfusion, higher splenic injury grade, NISS, mortality, and total direct medical cost.

In addition, the proportion of patients with OM decreased from 65.3% in 2000 to 44.1% in 2013, while patients with NOM increased from 34.7% in 2000 to 55.9% in 2013 (Fig 2A). In 2000, the mean DMC per-patient with NOM and OM was $2256 and $3089, respectively. However, the mean DMC per-patient has risen to $3627 (NOM)

and $5312 (OM), respectively, in 2013 (Fig 2B).

Structure of Direct Medical Cost

Figure 3 has shown that the distribution of various DMC by different management. Drug cost is the main expenditure in DMC, accounting for 46% (US$ 1612) of total DMC, followed by hospitalization (18%, USD$ 633). Patients with NOM and OM had similar patterns structure of DMC, but transfusion and surgery costs are higher in patients with OM than patients with NOM.

Predictors of Direct Medical Cost

Table 2 shows the results of GLM with gamma distribution and the log-link function performed to determine the variables affecting direct medical costs. The cost of treating splenic injury in female patients was 6.3% lower compared to that of men ($p=0.002$). LOS was predicted to increase the DMC by 2.2% ($p < 0.01$). The cost of patients improved after treatment was 34.6% higher compared to that of those who were dead ($p<0.001$). Patients with a high splenic injury grade, blood transfusion, OM, admission to ICU, old age, and high NISS (>25) from tertiary hospitals had to bear higher total DMC. While there was no significant difference between mild and moderate NISS. Compared with 2000, the mean per-patient DMC increased 2002-2013.

Discussion

Using a large military fund database from China, we can obtain the clinical data of patients with splenic injury and calculate direct medical cost resulting from the splenic injury. To our knowledge, this is the first description of the multicenter clinical features and direct medical cost of splenic injury in China. Currently, NOM is the standard of

treatment in hemodynamically stable patients with splenic injury, and the success rate of this produces exceeds 80-90%[3]. In this retrospective study, we showed the changes in the treatment of splenic trauma and its related direct medical cost in China from 2000 to 2013. Interestingly, the ratio of NOM had increased gradually in Chinese hospitals, while the DMC of patients with splenic injury had increased sharply after 2010.

In this study, the rate of patients with splenic injury with OM was higher than patients with NOM before 2010, which contrasted with many studies[5,7,9]. However, patients undergoing NOM vastly outnumbered patients with OM after 2010. We suppose there are several reasons for this phenomenon. First, before the reform of the Chinese healthcare system in 2009, the healthcare resources are seriously insufficient, and inequalities exist everywhere. Moreover, the relationship in China between doctors and patients is usually strained[20]. Thus, to avoid medical conflicts whenever possible, some Chinese doctors must choose a safe and conservative treatment to improve the one-time success ratio of treatment. Second, the Chinese government has introduced a new healthcare reform since 2009. Five main domains were reformed in China's health system reform: social health security, essential medicines, primary healthcare, basic public health service package, and public hospitals. These measures improved access to healthcare and reduced health inequality, to a certain extent. Moreover, it, to some degree, reduced the contradiction between doctors and patients and promoted the progress of medical level[21]. However, in public hospitals, medical expenditure per-patient discharged increased by 22.1% between 2010 and 2013[22,23]. The proportion of out-of-pocket healthcare payments decreased, but the financial burden of healthcare did

not fall much. The proportion of drug cost in total hospital expenditure has decreased, but total hospital expenditure is still rising[23]. Thus, splenic injury patients with low splenic grade and mild NISS were more likely to be adopted by NOM, but the per-patient direct medical cost was higher than before whatever management doctors took. Previous studies have reported that nonsurgical treatment of blunt splenic injury is cost effective due to patients undergoing OM tend to have a longer length of stay, drug, caregiving, more blood transfusions, and more medical consumables[9,24], which is similar to our results. Although the rate of patients with NOM is higher than OM in this study after 2010, the DMC of NOM in our study is much lower than OM.

China has already entered the aging society since 1999 and is one of the fastest aging countries in the world[25]. Injury is the fifth leading cause of death in the elderly. Compared to younger patients, advanced age patients who sustain major trauma have been shown to experience higher mortality rates and higher economic burdens on families and societies. In our study, age over 65 years had a longer length of stay, higher DMC, and mortality. Management of splenic injury in the elderly population remains controversial. Tsugawa et al. believed initial operative intervention in the elderly, as signs of shock and severe injuries are not obvious in elderly patients[26]. However, Warnack E, et al. advocated for which modality of management doctors choose depending on the actual situation of the patient[27]. Considering the high mortality and cost in elderly patients, we believe a multiple disciplinary team (MDT) is needed to identify and assess the worst-off senile patient's condition.

In this study, drug cost was the main contributor to average splenic injury-related

DMC in NOM or OM, followed by hospitalization costs (Figure 2). This phenomenon might be explained from two sides. From the supply side, Chinese doctors can obtain a 15% profit margin from the monetary values of drugs they prescribed according to the drug mark-up policy[28]. From 2009 to 2015, this policy was gradually ended in hospitals of all sizes, but overall hospital expenditure is still increasing [26]. From the demand side, patients in China are obsessed with medication therapy when they are ill[29]. Before 2009, pharmaceuticals accounted for above 40% of public hospitals' revenue in China. After healthcare system reforms in 2009, the rate of revenue began to slowly decline due to mark-up removal but still accounted for about 39% of public hospitals' revenue[30].

There are some limitations in our study. First, we cannot tell what type of NOM was adopted in patients due to the lack of related code in CTDB. Second, the categories of DMC cannot be extracted from 2010 to 2013 due to this part of the data was missing at that time in the datasets, we just extracted the total DMC of patients during that period. Third, patients' comorbidities and concomitant injury were not included in CTDB, so we cannot further evaluate the impact of these indicators on DMC. Fourth, because the insurance types were not recorded in this database, we cannot estimate patients-related medical care utilization or provide a comprehensive cost analysis of patients with splenic injury. Despite these limitations, this study estimates to analyze direct medical costs of splenic injury and potential factors affecting the costs, as well as to provide evidence to develop specific and cost-effective interventions based on the cost estimations in this study.

Conclusions

This study is the first, to our knowledge, to describe direct medical cost for splenic injury in China. China's health system always bears amounts of economic burden, coupled with a lack of effective incentives to improve health workers' motivation and laws to protect doctors from violence, which may have a significant influence on the management and cost of patients with splenic injury. This research will be useful for government and health administration services to reform the health care policies to contain trauma-related medical costs in the future and provides useful evidence for the management of splenic trauma in China.

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Authors' contributions

Y.C. and Q.Z. conceived and designed the study. L.Y., YB.M., and Y.Q. participated in data collection and analysis. Y.C. participated in writing. J.H.Z. and Y.C. were responsible for statistical analysis. All authors read and approved the final manuscript.

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Availability of data and materials

The database used and/or analyzed during the study are available from the

corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics committee of Army Medical Center of PLA (2022-63). Since the claims data were an anonymized database and had no influence on patient care, the Ethics Committee waived the requirement for patient consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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1

Table 1 Demographic and clinical characteristics of the study population by management

	NOM n=2782	OM n=5301	*P-value*
Male	2217(80%)	4405(83.1%)	<0.001
Age			<0.001
<18	324(11.6%)	421 (7.9%)	
18-40	1630 (58.6%)	3131 (59.1%)	
41-65	754(27.1%)	1635 (30.8%)	
>65	74(2.7%)	114 (2.2%)	
Trauma cause			<0.001
Car collision	1046 (37.6%)	2092 (39.5%)	
Motorcycle or Cycling Collision	126 (4.5%)	268 (5.2%)	
Fall from heights	365 (13.3%)	811 (15.3%)	
Fall and hurt oneself	208 (7.5%)	465 (8.8%)	
Crush injury	34 (1.2%)	50 (0.9%)	
Penetrating injuries	385 (13.5%)	798 (15.1%)	
Sports	112 (4%)	157 (3%)	
Personal assault	340 (12.2%)	533 (10.1%)	
Others	166 (6%)	127 (2.4%)	
Splenic grade			<0.001
Ⅰ/Ⅱ	2707 (97.4%)	1280 (24.1%)	
Ⅲ/Ⅳ	57 (2%)	3512 (66.3%)	
Ⅴ	18 (0.6%)	509 (9.6%)	
NISS			<0.001
Mild <15	1722 (61.9%)	1666 (31.4%)	
Moderate 15-25	784 (28.2%)	2209 (41.7%)	
Severe > 25	276 (9.9%)	1426 (26.9%)	
Hospital level			0.727
Secondary hospitals	569 (20.5%)	1067 (20.1%)	
Tertiary hospitals	2213 (79.5%)	4234 (79.9%)	
Blood transfusion >1	539 (19.4%)	3474 (65.5%)	<0.001
LOS, median (IQR)	11 (7-18)	14 (10-12)	<0.001
Mortality	76 (2.7%)	200 (3.8%)	<0.001
Direct medical cost, median (IQR)	1223 (595-2542)	3062 (2104-4619)	<0.001

2 IQR, interquartile range

Table 2 Results of a generalized linear model with gamma distribution

Variables	β	SE	P	EXP (β)	95% CI
Gender					
Male	Reference			1	
Female	-0.065	0.019	0.002**	0.937	0.903-0.972
LOS	0.022	0.000	<0.001***	1.022	1.021-1.023
Mortality					
Death	Reference			1	
Alive	0.268	0.041	<0.001***	1.308	1.208-1.419
Splenic injury grade					
Ⅰ/Ⅱ	Reference			1	
Ⅲ/Ⅳ	0.074	0.021	<0.001***	1.077	1.034-1.121
Ⅴ	0.190	0.034	<0.001***	1.208	1.132-1.291
Management					
NOM	Reference			1	
OM	0.431	0.023	<0.001***	1.539	1.474-1.605
ICU					
No	Reference			1	
Yes	0.444	0.024	<0.001***	1.559	1.488-1.633
Blood transfusion ＞ 2					
No	Reference			1	
Yes	0.440	0.016	<0.001***	1.553	1.506-1.602
Age					

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<18	Reference			1	
18-40	0.242	0.026	<0.001***	1.274	1.211-1.339
41-65	0.299	0.027	<0.001***	1.349	1.277-1.423
>65	0.347	0.053	<0.001***	1.414	1.275-1.572
NISS					
<15	Reference			1	
15-25	0.024	0.017	0.154	1.024	0.991-1.058
>25	0.055	0.021	0.095**	1.056	1.014-1.100
Hospital					
Secondary hospitals	Reference			1	
Tertiary hospitals	0.351	0.018	<0.001***	1.420	1.370-1.471
Year					
2000	Reference			1	
2001	0.049	0.046	0.279	1.05	0.960-1.148
2002	0.268	0.046	<0.001***	1.308	1.195-.1.429
2003	0.397	0.045	<0.001***	1.488	1.360-1.624
2004	0.416	0.046	<0.001***	1.516	1.395-1.657
2005	0.474	0.046	<0.001***	1.606	1.466-1.757
2006	0.447	0.045	<0.001***	1.563	1.429-1.707
2007	0.413	0.045	<0.001***	1.511	1.381-1.650
2008	0.392	0.046	<0.001***	1.480	1.351-1.618
2009	0.569	0.069	<0.001***	1.766	1.544-2.023
2010	0.526	0.076	<0.001***	1.693	1.461-1.968
2011	0.596	0.073	<0.001***	1.816	1.575-2.099
2012	0.688	0.071	<0.001***	1.991	1.735-2.289

2013	0.616	0.079	<0.001***	1.851	1.589-2.165

Exp(B), Exponential of coefficients; CI, confidence intervals; SE, standard error. P value: ***P<0.001; **P<0.01.

Figure 1. Flow chart of the study.

Figure 2. A. Overall trend in splenic management over time from 2000-2013. B. Mean per-patient direct medical cost from 2000-2013.

Figure 3. Direct medical cost subtypes of patients with splenic injury by management from 2000-2009 (percentages).

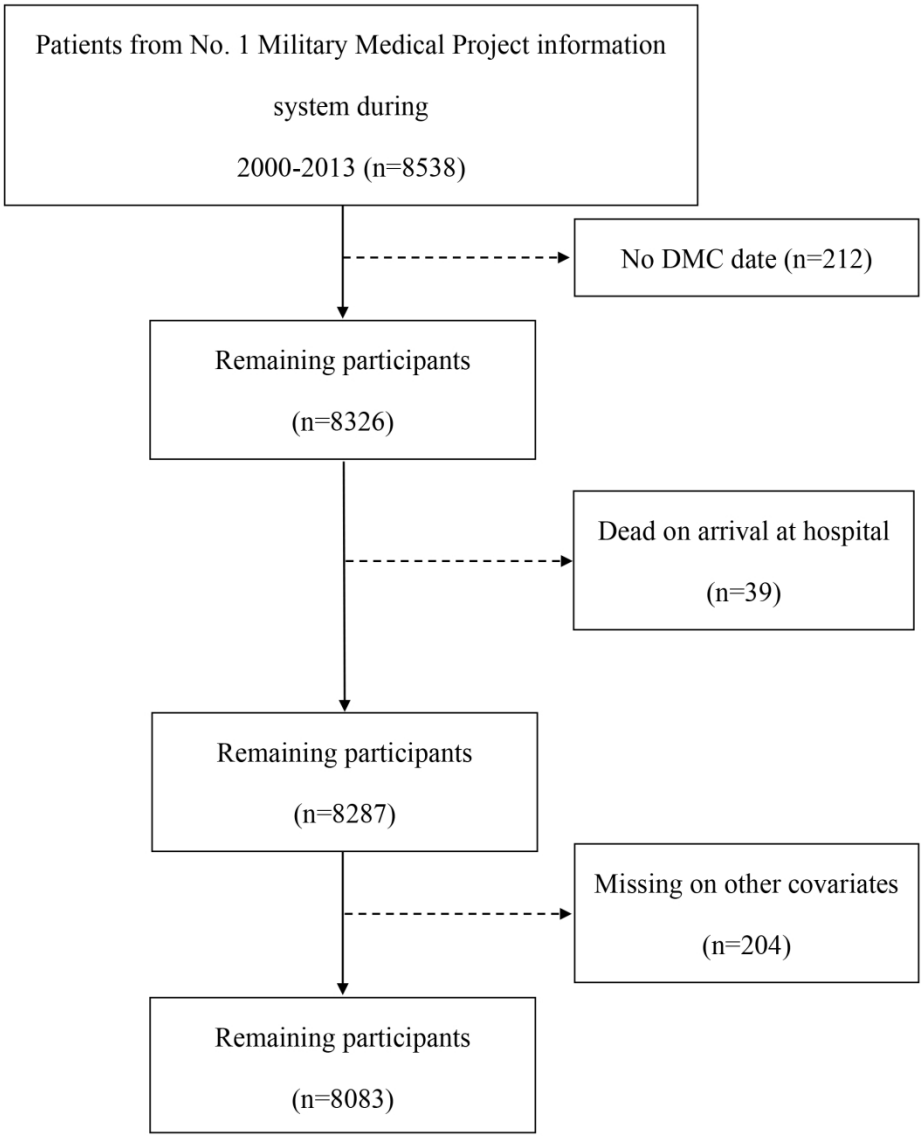
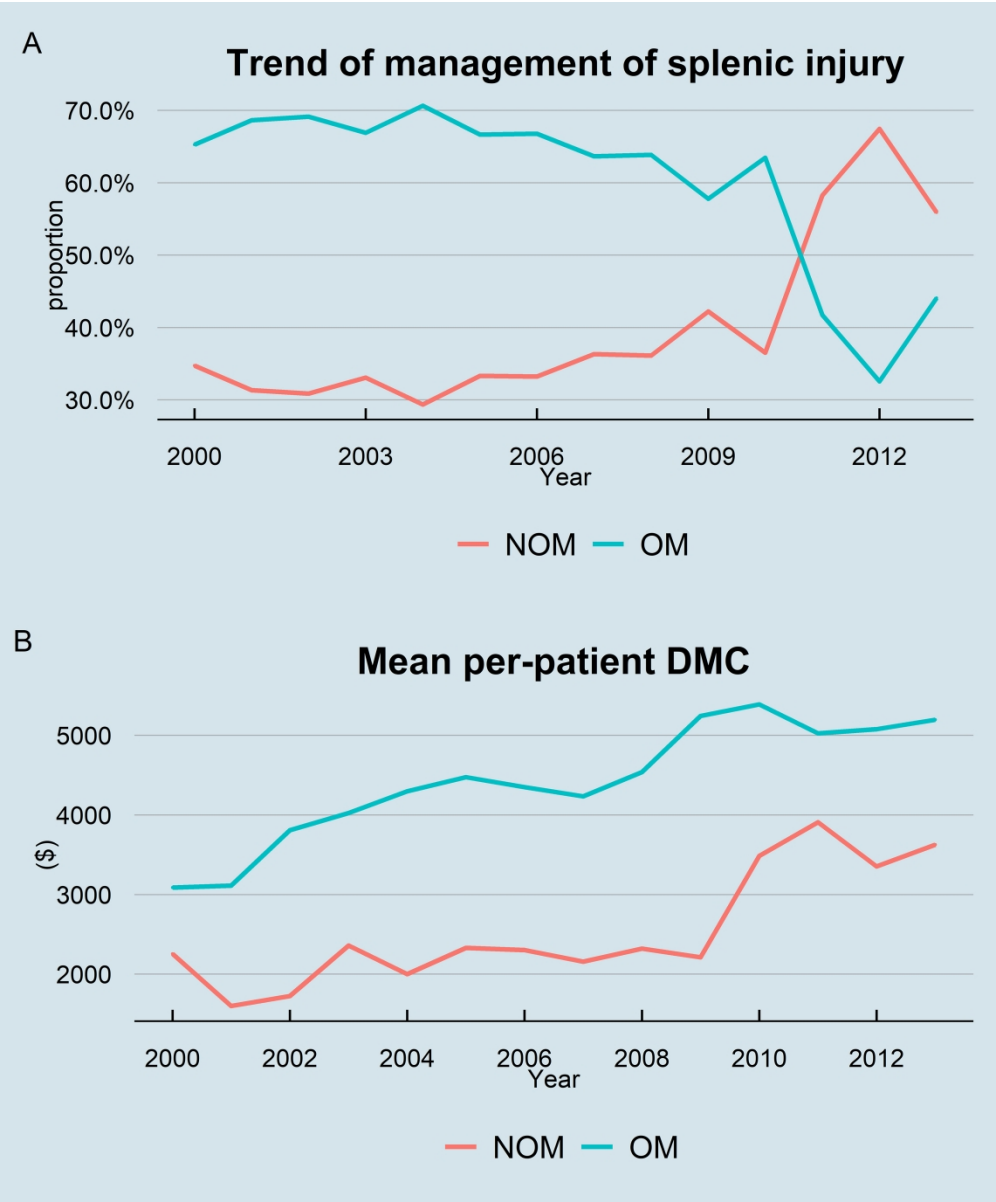


Figure 1. Flow chart of the study



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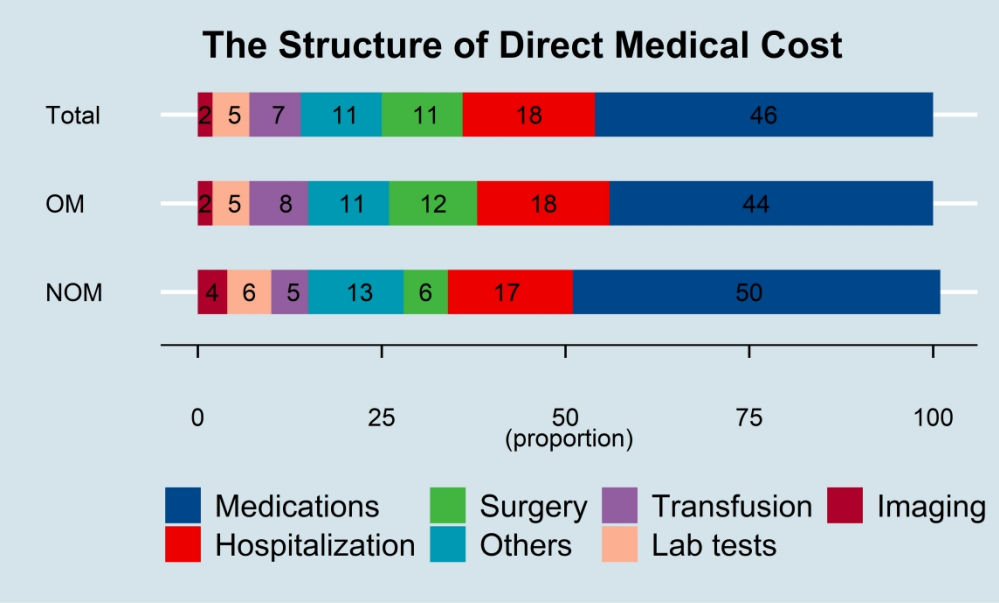

Figure 3. Direct medical cost subtypes of patients with splenic injury by management from 2000-2009 (percentages).

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Reporting checklist for economic evaluation of health interventions.

Based on the CHEERS guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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	Reporting Item	Page Number
Title		
#1	Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.	1

Abstract			
	#2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions	2
Introduction			
Background and objectives	#3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions	3
Methods			
Target population and subgroups	#4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	5-6
Setting and location	#5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	5-6
Study perspective	#6	Describe the perspective of the study and relate this to the costs being evaluated.	5-6
Comparators	#7	Describe the interventions or strategies being compared and state why they were chosen.	6-7
Time horizon	#8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	5-6
Discount rate	#9	Report the choice of discount rate(s) used for costs and	6

		outcomes and say why appropriate	
Choice of health outcomes	#10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed	7
Meaurement of effectiveness	#11a	Single study-based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data	7
Measurement of effectiveness	#11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data	7
Measurement and valuation of preference based outcomes	#12	If applicable, describe the population and methods used to elicit preferences for outcomes.	7
**Estimating resources and costs **	#13a	Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs	6

Methods

Estimating resources and costs	#13b	Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	6
Currency, price date, and conversion	#14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	6
Choice of model	#15	Describe and give reasons for the specific type of decision analytical model used. Providing a figure to show model structure is strongly recommended.	7
Assumptions	#16	Describe all structural or other assumptions underpinning the decision-analytical model.	7
Analytical methods	#17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	7

Results

Study parameters	#18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	7-8
Incremental costs and outcomes	#19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	8-9
Characterising uncertainty	#20a	Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	9
Characterising uncertainty	#20b	Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	9
Characterising heterogeneity	#21	If applicable, report differences in costs, outcomes, or cost effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	9

Discussion			
Study findings, limitations, generalisability, and current knowledge	#22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	9-15
Other			
Source of funding	#23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support	15
Conflict of interest	#24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations	15