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REVIEW ARTICLE

A methodological systematic review of early versus late stabilization of thoracolumbar spine fractures

Dan Xing · Yang Chen · Jian-Xiong Ma · Dong-Hui Song · Jie Wang · Yang Yang · Rui Feng · Jun Lu · Xin-Long Ma

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Abstract
Objective The optimal timing of stabilization in patients with traumatic thoracolumbar fractures remains controversial. There is currently a lack of consensus on the timing of surgical stabilization, which is limited by the reality that a randomized controlled trial to evaluate early versus late stabilization is difficult to perform. Therefore, the objective of this study was to determine the benefits, safety and costs of early stabilization compared with late stabilization using data available in the current literature.
Methods An electronic literature search was performed in Medline, Embase, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials for relevant studies evaluating the timing of surgery in patients with thoracolumbar fractures. Two reviewers independently analyzed and selected each study on the basis of the eligibility criteria. The quality of the included studies was assessed using the Grading of Recommendations Assessment, Development, and Evaluation system (GRADE). Any disagreements were resolved by consensus.
Results Ten studies involving 2,512 subjects were identified. These studies demonstrated that early stabilization shortened the hospital length of stay, intensive care unit length of stay, ventilator days and reduced morbidity and hospital expenses for patients with thoracic fractures. However, reduced morbidity and hospital expenses were not observed with stabilization of lumbar fractures. Owing to the very low level of evidence, no conclusion could be made regarding the effect of early stabilization on mortality.
Conclusions We could adhere to the recommendation that patients with traumatic thoracolumbar fractures should undergo early stabilization, which may reduce the hospital length of stay, intensive care unit length of stay, ventilator days, morbidity and hospital expenses, particularly when the thoracic spine is involved. Individual patient characteristics should be concerned carefully. However, the definite conclusion cannot be made due to the heterogeneity of the included studies and low level of evidence. Further prospective studies are required to confirm whether there are benefits to early stabilization compared with late stabilization.

Keywords Thoracolumbar · Fracture · Spine · Timing of surgery · Systematic review

D. Xing and Y. Chen contributed equally to this work.

D. Xing · Y. Chen · Y. Yang · X.-L. Ma (✉)
Department of Orthopaedics Institute, Tianjin Hospital, 406 Jiefang Nan Street, Hexi District, Tianjin 300211, China
e-mail: tjmuld@gmail.com

D. Xing · J.-X. Ma · J. Wang · R. Feng · X.-L. Ma
Department of Orthopaedics, Tianjin Medical University General Hospital, 154 Anshan Street, Heping District, Tianjin 300052, China

D. Xing · D.-H. Song · J. Lu (✉)
Department of Orthopaedics, Tianjin Gongan Hospital, 78 Nanjing Street, Heping District, Tianjin 300042, China
e-mail: junlu0419@yahoo.com.cn

Introduction

The timing of surgery in patients with traumatic thoracolumbar fractures, with or without spinal cord injury (SCI), remains controversial. There are several advantages to early surgery in patients with thoracolumbar fractures. Quicker patient mobilization with shorter hospital stays

and a lower incidence of thromboembolic and pulmonary complications are two major benefits [5, 6]. Early mobilization is also thought to decrease mortality and morbidity, which is described in the evolution of the management of femur fractures. However, early surgery may be associated with hypotension, increased neurological complications and operative hemorrhages. Other potential disadvantages include operating in a setting of potentially missed or underestimated multiple injuries, operating without a full understanding of the overall injury, and operating under non-ideal conditions relative to the complexity of the surgery and resources required. Later surgery avoids the above complications or disadvantages and allows for surgical intervention under more controlled conditions.

Currently, there have been no adequate studies that investigate whether the timing of surgery affects surgical outcomes. Although several retrospective studies have reported that early surgery was associated with a lower incidence of complications and a decreased hospital length of stay (HLOS), these studies exhibited methodological deficits and a higher risk of bias because of poor study design. The underlying problem is the difficulty in the design and execution of a randomized controlled trial to determine the clinical outcomes and complications because of the ethical concerns and logistics of scheduling a major spine surgery in an urgent manner [3].

The purpose of this systematic review was to evaluate the benefits, safety and costs of early stabilization compared with late stabilization after traumatic thoracolumbar fractures, with or without SCI, and to evaluate the evidence according to the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system. This will provide a foundation of evidence from which a clinical decision may be made to guide the surgeon and to determine the optimal timing of surgery.

Materials and methods

Search strategy and eligibility criteria

An electronic search using the keywords thoracolumbar, thoracic or lumbar, spine or spinal, trauma and surgery was performed in Medline, Embase, Sciencedirect, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials through June 2012. Manual searches were performed in addition to the electronic search for the reference lists of all of the retrieved articles. Moreover, all of the relevant conference databases, which provide gray literature, were also searched. In studies where there were overlapping patients and the criteria included the hospital, study period, and participation information, we retained only the largest study to avoid any duplication of information. In addition, the selected studies had to compare the early with late surgical stabilization in adult patients ($\geq$18 years) with traumatic thoracolumbar fractures. Owing to time, the early surgery was described as ranging between 8 and 72 h [4, 11, 14, 15]. Studies that defined early surgery as greater than 72 h were excluded. Exclusion criteria included cervical fractures, a sample size $<$10 in each treatment group and studies without sufficient outcome data. Articles published in languages other than English were also excluded.

Study selection

Two reviewers (DX and JXM) independently analyzed each title and abstract on the basis of the eligibility criteria and then met to discuss any discrepancies. Articles that were not excluded from our study on the basis of the title and abstract were independently retrieved for full-text review by the same two reviewers.

Data extraction

The two independent reviewers (DX and JXM) extracted data from the qualifying articles. A previously piloted data extraction form was used to record information regarding the population, study design, sample size, spine segment, the number of ventilator (VENT) days, HLOS, intensive care unit of stay (ICULOS), respiratory complications, morbidity, mortality and in-hospital costs. The corresponding author of each study was then contacted to obtain any additional information that was required. In the case of discrepancies, a third reviewer (JW) was involved.

Methodological quality and rating the evidence of each article

The quality of the studies was independently assessed by two authors (JXM and YC). The method used to evaluate the quality of evidence of the individual studies and the overall quality of the body of evidence incorporated aspects of the rating scheme developed by the Oxford Centre for Evidence-based Medicine [18], which was used with modifications by *The Journal of Bone and Joint Surgery American Volume* (*J Bone Joint Surg Am*) [23], with precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group [1] and with recommendations made by the Agency for Healthcare Research and Quality (AHRQ) [22]. Each included study was rated against prior criteria that were classified into four levels (level of evidence I, II, III, and IV) for each of the four different study types (i.e., therapeutic, prognostic, diagnostic, and economic or decision modeling). The basic principle behind the level of evidence

was that some articles were more influential than others based solely on the nature of their study design because improved study methods decreased the potential for error and minimized the sources of bias [21]. Previous studies have shown that a higher level of evidence is associated with increased rates of citation in orthopedic literature [16]. Furthermore, the concept of the level of evidence has recently gained widespread acceptance in the orthopedic community. A third author (XLM) was the adjudicator when conflicting evaluations were needed to be resolved.

Analysis

We pooled the number of VENT days, HLOS, ICULOS, respiratory complications, hospital expenses and mortality cases. A qualitative analysis [20] was performed considering the following three domains: quality of studies, quantity of studies and consistency of results across the studies [22]. The quality of studies is associated with the level of evidence, which has been described above. The quantity of studies is defined by the number of published studies that are similar in population, outcome and medical condition. The consistency refers to whether the results of the different studies lead to a similar conclusion (similar values and in the same direction). We judged whether the body of literature represented a minimum standard for each of the three domains using the following criteria: for study quality, at least 80 % of the studies reported were required to be rated as a level of evidence I or II; for the study quantity, at least three published studies were needed that were adequately powered to answer the study question; and for study consistency, at least 70 % of the studies were required to have consistent results. The definition of the overall strength of the evidence is presented in Table 1, which used the concepts obtained from the GRADE Working Group [1]. An overall strength of "high" meant that "further research is very unlikely to change our confidence in the estimate of the effect." The overall strength of "moderate" meant that "further research is likely to have an important impact on our confidence in the estimate of the effect." However, an overall strength of evidence rating of "low" meant that "further research is very likely to have an important impact on our confidence in the estimate of the effect and is likely to change the estimate." Moreover, "very low" meant that "any estimate of the effect is very uncertain."

Results

Study identification

On the basis of our research, we identified 1,160 potential citations after the duplications were excluded. After screening of the citation titles and abstracts, we identified 98 publications for full-text reading. On the basis of the full-text screening, 10 studies that provided a comparison of early versus late thoracolumbar fracture stabilization were included in the present review. The most frequent reason for exclusion was the inclusion of only cervical fractures or the absence of stratification for results by spine level. Figure 1 depicts the flow diagram of the selection process for relevant studies.

Study characteristics included in the analysis

The characteristics of the studies are presented in Table 2. A total of 10 studies [2, 4–6, 8, 10–12, 15, 19] were included, consisting of 2,512 patients with thoracolumbar fractures. These articles were published between 1999 and 2012. The number of total study subjects ranged from 27 [4, 15] to 1,126 [2]. All of the investigations compared early and late surgical stabilization in adult patients with traumatic thoracolumbar fractures. The majority of the studies used 72 h as the separation time point between early and late intervention. In addition, there were 2 studies that used 24 or 8 h to separate early versus late surgery. Half of the included studies reported whether the patients were with or without SCI.

Quality assessment

The results of the study quality assessment are presented in Table 2. Two studies [2, 4] were graded as level II, whereas the remaining eight studies were graded as level III. Only one study [4] was a quasi-randomized controlled trial. One observational study [15] was a prospective cohort study, and the remaining eight studies were retrospective cohort studies. Although the quasi-randomized controlled trial was single-blinded to the evaluators, it did not have a concealed sequence allocation and had used an inaccurate randomized method. The prospective cohort study lacked an independent assessment of complications and did not control for potential confounding factors. Propensity score modeling (PSM) was applied in one retrospective study to mitigate imbalances in variables known to be associated with an assignment for an intervention, which offsets any confounding factors between the treatment groups and improved the comparison of outcomes.

Clinical outcomes

The outcome parameters available and evaluated in each of the ten studies are summarized in Table 3. Conclusions from each study are summarized in Table 4. Nine of the studies reported the HLOS. Four of the nine studies [6, 10–12] presented data for thoracic and lumbar fractures, one study

Table 1 Definition of overall strength of evidence

Overall strength of evidence	Further research impact	Domain criterion met		
		Quality	Quantity	Consistency
High	Very unlikely to change our confidence in the estimate of the effect	+	+	+
Moderate	Likely to have an important impact on our confidence in the estimate of the effect and may change the estimate	+	−	+
		+	+	−
Low	Very likely to have an important impact on our confidence in the estimate of the effect and is likely to change the estimate	+	−	−
		−	+	+
Very low	Any estimate of the effect is very uncertain	−	+	−
		−	−	+
		−	−	−

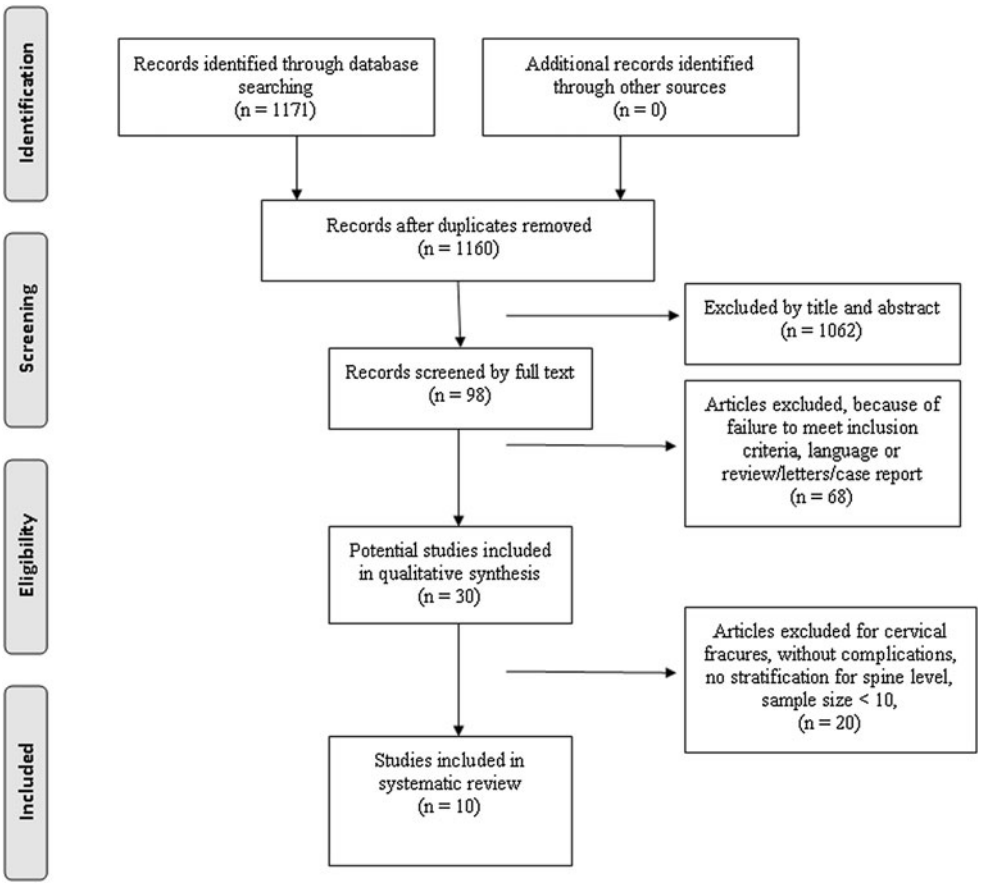

Fig. 1 The study selection and inclusion process

[19] included only thoracic fractures, and two studies [4, 5] included only thoracolumbar fractures and divided the patients into subgroups according to injury severity score (ISS). One study [8] divided all of the patients into an early and a late group with comparable ISS, equal laboratory parameters at admission, and comparable demographics. The mean HLOS with thoracic fractures ranged from 10.1 to 38.3 days in the early group compared with 14.4 to 42.6 days in the late group. The mean HLOS with lumbar fractures ranged from 9.4 to 33.8 days in the early group compared with 14.1 to 36.4 days in the late group. The range of the mean HLOS with thoracic/lumbar/thoracolumbar was 8.1 to 70 days in the early group compared with 15 to 108 days in the late group. The HLOS was significantly lower in the early group compared with the late group in all of the included studies. However, some of these studies reported that the ICULOS was significantly lower in the early group than in the late group. Six studies reported the VENT days for thoracic, lumbar or thoracolumbar fractures. In three of the included studies [6, 12, 19],

Table 2 Studies characteristics

Study	Years	Study design	Country	Date collection	Level	Number		Age		Gender (female)		SCI		ISS		Early time point (h)	Level of evidence
						Early	Late	Early	Late	Early	Late	Early	Late	Early	Late		
Kerwin et al. [12]	2008	Cohort	USA	Retrospective	Thoracic	137	108	36	39	NA	NA	NA	NA	22.1	21.3	<72	III
					Lumbar	80	63	33.8	36.4	NA	NA	NA	NA	17.8	19.1		
Kerwin et al. [10]	2007	Cohort	USA	Retrospective	Thoracic	18	59	NA	NA	NA	NA	72.2 %	47.5 %	23.4	22.3	<72	III
					Lumbar	22	48	NA	NA	NA	NA	45.5 %	20.1 %	19.1	22.8		
Cengiz et al. [4]	2008	RCT	Turkey	Prospective	Thoracolumbar	12	15	39.67	41.44	25 %	33.3 %	NA	NA	ASIA 2.00	ASIA 1.93	<8	II
Schinkel et al. [19]	2006	Cohort	Germany	Retrospective	Thoracic	156	49	36.7	38.1	24 %		NA	NA	28.5	30.9	<72	III
Kerwin et al. [11]	2005	Cohort	USA	Retrospective	Thoracic (with SCI)	31	15	37.6	38	NA	NA	63.3 %	36.6 %	30.5	30.5	<72	III
					Thoracic (without SCI)	18	26	34.7	42.2	NA	NA			18.7	19.7	<72	
					Lumbar	24	44	35	44	NA	NA	0	0	17	18	<72	
Chipman et al. [5]	2004	Cohort	USA	Retrospective	Thoracolumbar (ISS <15)	32	26	34.3	46.2	15.6 %	34.6 %	NA	NA	10.0	10.6	<72	III
					Thoracolumbar (ISS ≥15)	37	51	29.9	35.7	35.1 %	33.3 %	NA	NA	25.8	29.1	<72	
Croce et al. [6]	2001	Cohort	USA	Retrospective	Thoracic	30	49	26	35	27 %		50 %	61 %	23	25	<72	III
					Lumbar	29	20	33	33			31 %	30 %	19	21	<72	
McLain and Benson [15]	1999	Cohort	USA	Prospective	T, L, and TL	14	13	27.5	30.0	21.4 %	23.1 %	71 %	54 %	42	36	<24	III
Boakye et al. [2]	2012	Cohort	USA	Retrospective	T and TL	563	563	NA	NA	29.5 %	31.1 %	NA	NA	40	50	<72	II
Frangen et al. [8]	2010	Cohort	Germany	Retrospective	T, L, and TL	57	103	40	42	28.8 %		44 %	28 %	16	13	<72	III

T Thoracic, *L* lumbar, *TL* thoracolumbar, *NA* not available, *SCI* spinal cord injury, *ISS* injury severity score

the patients with thoracic fractures had significantly lower VENT days in the early group, as presented in Table 3. Frangen et al. [8] reported that patients with thoracic, lumbar or thoracolumbar fractures have significantly lower VENT days in the early group compared to patients with ISS (26–37), as well as less complete paraplegia or preoperative lung failure. There was no significant difference in the VENT days in patients with lumbar fractures only.

The rate of morbidity as measured by the incidence of respiratory complications and mortality are also presented in Table 3. Seven out of all of the included studies reported the incidence of respiratory complications. Four studies [2, 6, 11, 19] reported that patients with thoracic fractures had a lower rate of respiratory complications in the early group. Kerwin et al. [11] identified a significantly lower incidence of respiratory complications in patients with SCI with thoracic fractures. However, there was no significant difference in the incidence of respiratory complications in patients with lumbar or thoracolumbar fractures only. The mean mortality varied among studies that ranged in thoracic fractures from 0 to 11.1 % in the early group compared with 0 to 17 % in the late group. There was only one study that reported a statistically lower rate of mortality in the early group than the late group (6.2 vs. 17 %) [19]. When stratified by ISS, those in the early group continued to have a lower rate of mortality despite injury severity. However, a study by Kerwin et al. [10] reported that there was a slightly higher rate of mortality in patients with thoracic fractures treated within 48 h compared with those treated after 48 h (5.6 vs. 0 %), but this did not reach statistical significance. Another study conducted by Kerwin et al. [11] in 2005 compared patients with thoracic fractures, with or without SCI, using 72 h as a separation time point for early and late surgeries. There were no deaths reported in patients with SCI. In the subgroup without SCI, a slightly higher rate of mortality was found in the early group, but with no significant difference (11.1 vs. 0 %). These findings indicated that early surgery might be associated with higher mortality. In a later study in 2008, Kerwin et al. [12] reported that there were no deaths in patients with thoracic fractures after reviewing 245 patients from a trauma database. There was no significant difference in mortality between the early and late groups in four studies investigating lumbar fractures only, in one study focused on thoracolumbar fractures, or in three studies reporting on thoracic, lumbar, and thoracolumbar fractures.

Three studies [2, 6, 12] included data on the costs of surgery for patients. One of the three studies [6] demonstrated lower costs for patients with thoracic fractures undergoing early surgery compared with late surgery. Boakye et al. [2] reported that patients with thoracic/thoracolumbar fractures had significantly lower costs in early stabilization after reviewing 1,126 patients from an inpatient database. However, there were no significant differences in the hospital expenses between the groups in two studies that examined lumbar fractures.

Evidence summary and recommendation strengths

The overall strength of evidence to assess whether early surgery in thoracolumbar fractures reduces HLOS, ICULOS, and VENT days is "high" such that the estimate of the effect is very certain. However, the overall strength of evidence to assess whether early surgery reduces in-hospital costs and morbidity is "moderate" such that further research is likely to have an important impact on our confidence in the estimate of the effect. The overall strength of evidence to assess mortality is "very low" of which the estimate of the effect is very uncertain. Therefore, these findings may lower the confidence in recommendations.

Discussion

The optimal timing of surgical stabilization of thoracolumbar injuries, whether early or late, remains controversial, particularly because major traumatic thoracolumbar fractures are commonly associated with polytrauma. Removal of damaged bone, disk and ligament fragments that decompress the swollen spinal cord limits secondary injury and improves the outcome. Several studies have evaluated the neurological outcome, but there is no consensus on the timing of surgery. The timing of stabilization is usually classified as early (<72 h) or late (>72 h). Although early stabilization has been described as ranging anywhere from 8 to 72 h, the 72-h stratification point is based on preclinical studies, which demonstrated that early decompression of acute SCI results in improved neurological recovery [9]. However, there is no clear evidence to support early surgery in decreased mortality and morbidity. A prospective randomized controlled trial on thoracic fractures showed that there was no significant difference in mortality and morbidity [4]. Therefore, we performed a systematic review aimed toward contributing to the planning of the optimal timing and effect of this time interval on the HLOS, ICULOS, VENT days, hospital expenses, morbidity, and mortality.

The shorter HLOS, ICULOS, and VENT days in the early group may be partly attributed to the study design in that the late group, by definition, had a longer hospitalization stay. Moreover, these shorter times may be preserved by avoiding complications, quick recovery, and treatments. A significant large number of late surgery patients required ventilator support for noninfectious reasons, which may reflect the need to sedate and control patients to support additional injuries. The use of ventilator

Table 3 HLOS, ICULOS, VENT days, morbidity, mortality, and hospital charges comparing early versus late thoracolumbar fractures stabilization

References	Fracture location	HLOS (days)			ICULOS (days)			VENT (days)			Respiratory (%)			Mortality (%)			Expenses ($)		
		Early	Late	*P*	Early	Late	*P*	Early	Late	*P*	Early	Late	*P*	Early	Late	*P*	Early	Late	*P*
Kerwin [12]	Thoracic	11.6	22.3	<0.001	4.1	7.5	<0.001	1.6	4.5	0.013				0	0	NS	27,975	105,205	0.046
	Lumbar	12.2	20.1	0.0018	4.1	6.7	0.0094	1.8	3.6	0.1087				2.5	0	NS	97,093	85,715	0.6012
Kerwin [10]	Thoracic	10.2	14.4	<0.01	2.1	5.2	NS	1.8	3.8	NS				5.6	0	NS			
	Lumbar	9.4	14.1	<0.01	1.7	2.6	NS	1.3	1.1	NS				4.5	0	NS			
Cengiz et al. [4]	Thoracolumbar	12.5	26	<0.001	0	0	NS				0	20	NS	0	0	NS			
Schinkel et al. [19]	Thoracic	38.8	42.6	0.048	12.7	20.1	0.001	7.0	12.9	0.022	19	31	0.016	6.2	17	<0.05			
Kerwin et al. [11]	Thoracic with SCI	10.1	30.5	0.001	2.3	13.1	0.0079	1.2	1.4	NS	6.5	33.3	0.0291	0	0	NS			
	Thoracic without SCI	13.4	17.8	NS	5.9	6.9	NS	4.6	8.1	NS	17	23	NS	11.1	0	NS			
	Lumbar	10.4	18	0.0054	3.3	2.7	NS	1.8	1	NS	16.7	6.8	NS	0	0	NS			
Chipman et al. [5]	Thoracolumbar with ISS <15	8.1	15.5	<0.001	2.9	4.7	NS				6.3	7.7	NS						
	Thoracolumbar with ISS ≥15	11.5	20.7	<0.001	4.1	10.5	0.003				13.5	17.6	NS						
Croce et al. [6]	Thoracic	13.0	30.0	<0.001	7.0	15.1	<0.001	1.2	7.6	<0.001	3	37	<0.001	0	2	NS	84,011	146,087	<0.001
	Lumbar	11.2	16.7	<0.001	4.1	7.1	NS	0.6	1.0	NS	3	0	NS	0	0	NS	70,200	82,472	NS
McLain et al. [15]	T, L, and TL										0	8	NS	7	8	NS			
Boakye et al. [2]	T and TL	10.0	15.0	<0.0001							10.1	17.2	0.0005	0.5	1.4	NS	213,031	251,151	<0.0001
Frangen et al. [8]	T, L, and TL with ISS ≤25			NS			NS			NS				3	1	NS			
	T, L, and TL with 25 < ISS ≤ 37							0	3	<0.05				8	7	NS			
	T, L, and TL with ISS >37	56	108	<0.05	14	20	<0.05	15	14.5	NS				28	19	NS			
	T, L, and TL with PLF	63	108	<0.05	15	24	<0.05	14	19	<0.05				14	6	NS			
	T, L, and TL with CP	70	101	<0.05	9	16	<0.05	5	12	<0.05				20	13	NS			

HLOS Hospital length of stay, *ICULOS* intensive care unit length of stay, *VENT* ventilator, *NS* no significance, *SCI* spinal cord injury, *ISS* injury severity score

Table 4 Summary of study conclusions

Study	Conclusions
Kerwin et al. [12]	The majority of patients with spinal fractures underwent operative fixation within 3 days, and these patients had less complications and required less resources
Kerwin et al. [10]	Spinal fixation within 48 h after vertebral fractures and dislocations appears to increase mortality despite similar anatomical and physiological parameters in the later operative group. Incomplete resuscitation of patients before surgery may have contributed to this result. The shorter HLOS may have been due to the higher number of early deaths
Cengiz et al. [4]	Early surgery may improve neurological recovery and decrease HLOS and also additional systemic complications in patients with thoracolumbar spinal cord injuries. Thus, early stabilization of thoracolumbar spine fractures within 8 h after trauma appears to be favorable
Schinkel et al. [19]	Early stabilization of thoracic spine in trauma patients reduced the overall HLOS and ICULOS and improved outcomes. Early stabilization of thoracic spine injuries within 3 days after trauma appeared to be favorable
Kerwin et al. [11]	There is a significantly lower complication rate in early surgical patients compared with late surgical patients. Patients with thoracic spine trauma and a spinal cord injury had the greatest benefit in the reduction of morbidity, HLOS and ICULOS from early stabilization. A 20 % reduction of costs in the early group was observed compared to the late group
Chipman et al. [5]	Patients with thoracolumbar spine injuries undergoing early surgery had shorter HLOS. Patients with ISS $\geq$15 undergoing early surgery had less complications and shorter ICULOS. No differences were observed in terms of the complication rates and ICULOS in patients with ISS $<$ 15
Croce et al. [6]	Early fixation was associated with a lower incidence of pneumonia, a shorter ICULOS, fewer VENT, and lower expenses in patients with thoracic fractures
Mclain et al. [15]	In patients who required segmental instrumentation for spinal fractures with an ISS greater than 26, there was no difference in the rate of complications or mortality between patients who had urgent ($\leq$24 h) or early surgery (between 24 and 72 h). The study reported that a large proportion of patients in the urgently treated group had a trend toward improved neurological improvement compared with the early surgery group
Boakye et al. [2]	Early surgery ($<$72 h) for traumatic thoracic/thoracolumbar fractures was associated with a significantly lower overall complication rate, decreased HLOS and resource utilization
Frangen [8]	Severely injured patients (ISS $\geq$ 38) with early stabilization had a significantly shorter ICULOS and overall shorter HLOS

support may increase the risk of pneumonia and may be one factor that increases the risk of respiratory complications in the late group.

From the present systematic review, patients with early surgery had a lower incidence of respiratory complications and shorter ICULOS and HLOS, which resulted in lower hospital expenses. This was a clear advantage for spinal stabilization within 72 h of injury. Moreover, earlier patient mobilization and its advantages to overall patient care were achieved by early stabilization, resulting in lower rates of pneumonia and less resource utilization. In particular, it was extremely significant in patients with pulmonary injuries. However, much of the controversy in the treatment of thoracolumbar fractures originates from inadequate knowledge regarding the pathophysiology of the disease as well as the timing of specific treatments. Kerwin et al. [10] reported that early surgery of thoracic fractures can result in higher mortality, but without exhibiting a significant difference. Croce et al. [6] found a significantly higher mortality in patients with ISS $>$25 who underwent early spine fixation. This may indicate that proper surgical time and careful consideration of each individual patient's condition by the surgeon are very important. Pape et al. [17] suggested that early spinal stabilization may not be appropriate for all patients. Severely injured patients may receive an initial injury followed by surgery, which may amplify their previous injuries. The surgery may come too early, adding stimulation to the already activated inflammatory cascade, which may result in deterioration and subsequent increased mortality. Therefore, ISS, in the most included studies, was higher in the late group than in the early group, which may affect patients' needing on HLOS, ICULOS, VENT days. Furthermore, deaths may still be related to ongoing impairment of immune function resulting from spinal fractures that are difficult to detect during the early period after injury. Kerwin et al. [10] suggested that better recognition of patients with persistent acidosis and inadequate organ perfusion and patients on whom early stabilization should not be performed will improve the outcome and reduce mortality.

Although most fractures were in the thoracolumbar (T11–L2) area, several included studies performed their analysis separately according to the lumbar and thoracic area. However, several included studies did not divide their patients into a thoracic and lumbar group. As a transitional area, there may be no difference in optimal timing for surgery in T12 and L1. Therefore, it may be inappropriate to divide the fracture area into thoracic and lumbar, which might not be applied in all patients with thoracolumbar fractures.

For patients who are neurologically intact, immediate early surgery to stabilize the patient is very attractive. However, for patients who are not neurologically normal, some surgeons fear that some factors, such as operative stress, blood gas changes and hypotension, might worsen neurological injury. Surgeons are very eager for patients to be stabilized prior to surgery, which may postpone the surgery date. Magerl [13] considered only the presence of a partial or progressive neurological lesion as an unstable condition and treated the lesion by spinal stabilization after decompression of neurological elements. Fehlings et al. [7] reported that decompression early after SCI may be performed safely and is associated with improved neurological outcome in patients with cervical SCI. However, the timing of surgical decompression after an SCI remains a controversial topic. Clinical signs after thoracolumbar fractures with SCI may depend on the location of the lesion and the amount of damage to the gray and white matter. Furthermore, several included studies of the present review did not report whether the patients were with or without SCI. Many factors, such as morbidity, mortality, pulmonary condition and physical recovery, were also affected by the presence or absence of neurological injury. Therefore, the patients with or without neurological injury of the included studies might influence the effect size of the outcomes. Although it is better to analyze patients separately with or without SCI, it was unrealistic to collect individual patient characteristics from the included studies.

To a certain degree, the difference of HLOS between early and late surgery seems to be affected by a delay of surgery. Late surgery may result in the prolongation of HLOS directly. Patients without SCI or with low ISS may also be operated lately. Additionally, the timing of surgery may depend on different indications for different surgical approaches and on subjective factors of patients and surgeons. Therefore, the HLOS, which could be easily affected by various confounding factors, may not be an impressive outcome. In a similar way, VENT days may also be affected by ISS and SCI. Patients with severe injuries or with SCI mostly need more VENT days before or after surgery. Hence, selection bias for patients may exert an influence on the accuracy of summarized results, especially in the non-randomized controlled trials.

The limitations of this systematic review primarily include the following: (1) The information obtained from the medical record review did not identify differences in patient groups as an unidentified reason for delaying surgery. (2) Only one quasi-randomized controlled trial was identified in the systematic review. Most of the included studies were a retrospective evaluation of prospectively collected registry data that limited the examination of confounding factors that may have affected the mortality and morbidity. These include the presence of associated injuries, patient baseline medical comorbidities, patients with or without SCI, ISS and surgeon or operation room scheduling conflicts. (3) The registry data may be subject to bias, which affects their internal validity. Furthermore, a specific institution's clinical volume affects the patient outcomes. (4) Selection biases were introduced in the present review because the database was regional and different hospitals applied different indications for early surgery and criteria for inclusion or exclusion. (5) As confounding factors, associated injuries, neurologic impairment, ISS with or without SCI in patients of the included studies may exert an influence on the homogeneity of the present systematic review. Furthermore, some variables, such as HLOS and data costs of surgery, may be affected by different economic conditions of different regions or countries, which may exert influence on the homogeneity of the included studies.

Despite the above limitations, this review has made a significant contribution in evaluating the timing of surgical intervention in patients with traumatic thoracolumbar fractures. The results of the review represent the best available literature, which suggest that early stabilization most likely decreases complications, facilitates early rehabilitation, decreases hospital expenses, and reduces HLOS, ICULOS, and VENT days. However, no comments can be made about mortality from the present review, as it exhibited a "very low" level of evidence.

Conclusion

This systematic review provided an overview of the current knowledge regarding the timing of stabilization for patients with thoracolumbar fractures. Early surgery may shorten the HLOS, ICULOS, and VENT days for patients with thoracolumbar fractures. Furthermore, early stabilization may also reduce morbidity and hospital expenses when the thoracic spine is involved. However, the present review does not provide evidence that early stabilization of lumbar fractures exhibits benefits other than fewer HLOS, ICULOS and VENT days. Owing to the very low level of evidence, no conclusion can be made in terms of the effect of early stabilization on mortality. Therefore, we could adhere to the recommendation that patients with traumatic thoracolumbar fractures may undergo surgery prior to 72 h to reduce HLOS, ICULOS, VENT days, hospital expenses, morbidity, or potentially mortality, particularly when the thoracic spine is involved. Owing to the underlying heterogeneity of the included studies, the exact conclusion of the present systematic review cannot be made based on the present evidence. Because randomized controlled trials in injured patients are ethically not suitable for investigative study, further prospective and homogeneous studies are

required to confirm whether there is a benefit of early stabilization compared with late stabilization.

Conflict of interest None.

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