Cureus
Part of SPRINGER NATURE

Open Access Review Article

ICU-Relevant Morbidity and Mortality Outcomes in Polytrauma Patients With Multiple Lower Extremity Long Bone Fractures: A Narrative Review

Review began 10/03/2026
Review ended 10/29/2026
Published 11/05/2026

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DOI: 10.7759/cureus.119169

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Abstract

Patients who sustain multiple lower extremity long bone fractures (LELBF) are at an increased risk for complications as polytrauma patients. Current literature focuses on outcomes associated with isolated fractures. However, the clinical impact of lower extremity fracture burden on intensive care unit (ICU) outcomes in polytrauma patients remains incompletely characterized. This narrative review synthesizes current literature evaluating LELBF and critical care outcomes in polytrauma patients, often relying on studies that compare timing and triage strategies, as well as unilateral versus bilateral fractures. The primary outcomes of interest are mortality, ICU length of stay (LOS), and acute respiratory distress syndrome (ARDS) or other pulmonary dysfunction. Secondary outcomes include multiple organ dysfunction syndrome (MODS), sepsis, and thromboembolic events. Across comparative studies, bilateral fractures were directionally associated with a longer ICU stay and more pulmonary complications, although these differences were not statistically significant in every study. Mortality was also higher, but independent of injury severity in only one of the studies that adjusted for it. Early or single-stage fixation was associated with a shorter or similar ICU stay in each study that reported it, with inconsistent effects on mortality, ARDS, and sepsis; the one randomized trial stratified by physiologic status found more acute lung injury after primary nailing in borderline patients only. This review aims to summarize existing evidence about fracture burden and critical care outcomes in polytrauma patients with multiple LELBF and to identify areas needing further investigation.

Categories: Trauma, Orthopedics
Keywords: icu patient outcomes, intensive care unit (icu), long-bone fractures, narrative review, polytrauma

Introduction And Background

Trauma is one of the leading causes of death and disability in patients under the age of 45, with lower extremity long bone fractures (LELBFs) being one of the most common orthopaedic manifestations; femoral shaft fractures have been shown to have an incidence of 10-20 per 100,000 person-years [1,2]. Patients in the polytrauma setting, either with multiple long bone injuries or one long bone injury and an additional traumatic organ injury, are a distinct, more severely injured population compared to an isolated long bone injury [3]. The Berlin definition of polytrauma requires an Abbreviated Injury Scale (AIS) score of 3 or greater in at least two body regions plus at least one physiologic derangement [4]; bilateral femoral fractures alone do not satisfy it, as both femora are assigned to the same region. Bilateral femur fractures (BFFs) are one of the most studied subpopulations in this context, with literature published over the last two to three decades reporting mortality rates ranging from 6% to 32% [5,6].

Patients with multiple LELBFs are recognized to be at heightened risk for systemic complications. Acute respiratory distress syndrome (ARDS) is widely regarded as a high-risk pulmonary complication in this population, secondary to adipose tissue and marrow embolization from long bone fracture sites compounded by an amplified systemic inflammatory response [7-10]. Alongside ARDS, this population also faces elevated risk for sepsis, multiple organ dysfunction syndrome (MODS), and thromboembolic events, such as deep vein thrombosis (DVT) and pulmonary embolism (PE); the latter is a well-recognized and potentially preventable cause of morbidity and mortality after major trauma [11,12]. Multiple studies comparing unilateral to bilateral or multiple long bone fracture patterns have reported meaningfully higher rates of these complications as fracture burden increases, though the degree to which this risk is attributable to fracture burden itself, as opposed to the severity of associated injuries, remains debated [13-15].

The debate over triage and fixation strategy in orthopaedic trauma centers on comparing early fixation, commonly regarded as early total care (ETC) or early definitive fixation (EDF), with delayed fixation, commonly regarded as damage control orthopaedics (DCO) or delayed definitive fixation (DDF) [9]. EDF has historically been preferred because it has been shown to reduce ventilation requirements, shorten hospital stay, and enable earlier mobility [16]. However, DCO focuses on temporizing measures, such as placement of

external fixation, and is used to stabilize the fracture while other resuscitative efforts are prioritized. Once the patient is stabilized, definitive fixation is pursued [17]. Support for DCO relies on considering the physiologic burden of immediate definitive fixation in patients already in a weakened state. Data supporting DCO generally rely on improved outcomes in unstable or highly injured patients [18]. However, fully characterizing and delineating these two major philosophies remains inconclusive, as studies often contradict each other, and meta-analyses find minimal differences or low-confidence results [16,19]. Contemporary practice no longer treats this as a binary choice. Patients are classified as stable, borderline, unstable, or in extremis, and resuscitation parameters (e.g., lactate, base excess, pH) determine when definitive fixation can proceed, an approach termed early appropriate care or safe definitive surgery [20-23]. Under the early appropriate care protocol (i.e., fixation within 36 hours once lactate is below 4.0 mmol/L, pH is 7.25 or greater, or base excess is -5.5 or greater), complication rates fell from 22.1% to 16.3% relative to a historical cohort [22].

In summary, the existing literature establishes that patients with multiple LELBF face elevated risks of ARDS, MODS, sepsis, and thromboembolic complications relative to patients with isolated long bone injury, but this body of work is fragmented. Critically, the specific clinical impact of lower extremity (LE) fracture burden on intensive care unit (ICU) outcomes in polytrauma patients remains incompletely characterized, and the optimal timing and triage strategy for these patients continues to be debated. This narrative review synthesizes the current literature evaluating multiple LELBF and critical care outcomes in polytrauma patients, with particular attention to studies comparing unilateral to bilateral or polytrauma fracture patterns, and to studies examining timing and triage strategy. The primary outcomes of interest are mortality, ICU length of stay (LOS), and ARDS. MODS, sepsis, and thromboembolic events are examined as key secondary outcomes.

Review

Materials and methods

Search Strategy

A structured literature search was conducted using PubMed in March 2026 and re-run with a refined search string in October 2026. The search was limited to articles published between January 2006 and March 2026, with an English-language filter applied. The complete search string is provided in Table *1*, and the updated search identified 968 records. Three pre-2006 studies identified through backward citation searching met all other criteria and were retained [13,24,25]. Eligible study designs included retrospective registry studies, retrospective database studies, single-center and multicenter retrospective studies, randomized controlled trials (RCTs), and secondary analyses of said study designs. Studies of predominantly adult populations with multiple LELBF were included if they reported one or more of the outcomes of interest, including: mortality, ICU LOS, ARDS, MODS, sepsis, or thromboembolic events. Studies were excluded if they were case reports, case series without a defined cohort design, systematic reviews and meta-analyses without extractable data, editorials, animal studies, studies involving pediatric populations, or studies not published in English. Studies that did not evaluate the outcomes of interest were excluded.

Search strategy
Database: PubMed
Date of search: March 2026; re-run October 2026
Search string: ((polytrauma OR "poly trauma" OR multiple trauma OR injury severity score) AND (multiple fractures OR bilateral fractures OR bilateral femur fractures OR bilateral tibia fractures) AND (femur OR femoral OR tibia OR tibial) AND fracture) AND (ICU length of stay OR ventilator days OR ARDS OR mortality OR MOF OR MODS OR sepsis OR morbidity OR ICU OR multiple organ dysfunction syndrome OR acute respiratory distress syndrome OR outcomes)
Filters: English language, publication date: 01/01/2006-03/31/2026
Records identified: 968 (updated search); supplemented by backward citation searching of included full texts

TABLE 1: Search strategy.

The inclusion criteria were studies published between January 2006 and March 2026, as well as older studies identified through backward citation searching; written in English; and employing a retrospective registry study, retrospective database study, single-center or multicenter retrospective study, RCT, or secondary analysis of these designs. Eligible studies evaluated patients with multiple LELBF and reported one or more outcomes of interest, including mortality, ICU LOS, ARDS, MODS, sepsis, or thromboembolic events. Studies involving predominantly adult or skeletally mature populations were eligible, although adolescents could be

included. The exclusion criteria were non-human studies; non-English publications; case reports or case series, systematic reviews and meta-analyses, editorials, and dissertations; studies that did not evaluate populations with multiple LELBF; studies that did not evaluate the outcomes of interest or for which data could not be extracted; and studies involving pediatric or skeletally immature populations.

Study Selection and Data Extraction

Articles were screened by title and abstract, with full-text review for potentially eligible articles. Screening and data extraction were performed by two authors, with uncertainties resolved by discussion. Full texts were excluded if they used an ineligible study design (including systematic reviews), included pediatric or skeletally immature populations, did not report any outcome of interest, or did not report outcomes by lower extremity fracture pattern and were not retained as indirect evidence. Figure *1* summarizes the study identification process.

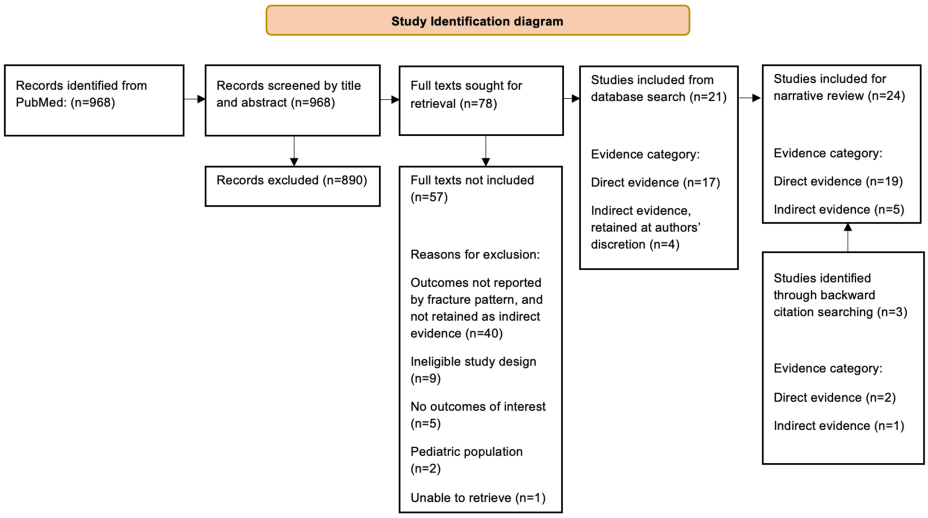


FIGURE 1: Flow diagram demonstrating the study identification strategy.

Outcome Measures

Primary outcomes were mortality, ICU LOS, and ARDS or other pulmonary dysfunction. Secondary outcomes were MODS, sepsis, and thromboembolic events, including DVT, PE, and fat embolism syndrome (FES). Outcomes were extracted as reported by each study. Mortality was recorded as in-hospital mortality unless otherwise stated. ICU LOS was recorded as the mean or median number of days reported. Two registry studies reported ICU stay for survivors only [14,15], and one study reported a combined ICU and high-dependency unit stay [13]. Pulmonary outcomes were recorded as defined in each study. ARDS was defined by the American-European Consensus Conference criteria, a PaO_2/FiO_2 ratio of 200 mmHg or less, or by other oxygenation-based criteria. Acute lung injury (ALI) is a historic term used in some of the studies and reflects the same pathology as ARDS but to a less severe degree. Pulmonary organ failure was defined in some studies as a respiratory Sequential Organ Failure Assessment (SOFA) score of 3-4; some registry-based studies used coded complications; and several studies did not state a definition. Where a definition was given, multiple organ failure (MOF) and MODS were defined as dysfunction of at least three organ systems. Comparisons across studies with different definitions are therefore interpreted with caution.

Evidence Classification and Appraisal

Because bilateral femoral fractures alone do not satisfy the Berlin definition [4], the term polytrauma is used in this review in the broader sense applied by the source studies (multiply injured patients). Included studies were classified as direct or indirect evidence. Direct evidence included studies reporting outcomes for patients with multiple LELBF, either as a distinct comparison group (i.e., unilateral versus bilateral fractures) or as the study population (i.e., bilateral or multiple fracture cohorts); 19 studies met this criterion. Five additional studies that did not report outcomes for multiple LELBF separately, or did not report fracture pattern, were retained at the authors' discretion as indirect evidence because they inform the effect of fracture burden or fixation strategy. These were selected for relevance and are not intended as a comprehensive account of the broader polytrauma femoral fracture literature; the synthesis rests primarily on the direct evidence. Consistent with the narrative design, no formal risk-of-bias tool was applied. Evidence quality for the purposes of interpretation was highlighted in the discussion, as no formal statistical

tool was used due to high heterogeneity of reporting between studies. Publications drawing on overlapping patient populations were identified to highlight caution in treating them as independent. The manuscript was prepared with reference to the six items of the Scale for the Assessment of Narrative Review Articles (SANRA) [26].

Results

Article Selection

We included 24 studies reporting the outcomes of interest in the study population of LE long bone fractures, 21 identified through the database search and three through backward citation searching [5,7-9,11,13-15,24,25,27-40]. Retrospective studies comprised the vast majority (20 of 24), with two RCTs and two secondary analyses of RCT data making up the remainder. Comparative population sizes ranged from 23 patients in a single-center retrospective study to 199,592 in a large retrospective database study. Nine studies focused on ICU outcomes when comparing unilateral versus bilateral LE long bone fractures. Ten studies compared triage modalities/philosophies for LE long bone fractures. Two studies reported ICU outcomes of polytraumatized patients with long bone fractures without a clear relevant comparator. Lastly, three studies examined polytrauma-related risk factors for specific clinical outcomes. Nineteen studies were classified as direct evidence and five as indirect evidence. Table *2* describes the design, focus, and evidence type of the studies included. Several publications draw on overlapping patient populations and cannot be treated as independent corroboration: Pape et al. (2007), Pfeifer et al. (2012), and Dienstknecht et al. (2013) analyze the same 165-patient European Polytrauma Study on the Management of Femur Fractures (EPOFF) trial cohort [9,31,37]; Kobbe et al. (2013), Lichte et al. (2014), and Steinhausen et al. (2014) draw on the TraumaRegister DGU over overlapping time periods [14,15,39]; the two Flagstad et al. (2021a,b) studies originate from the same 10 centers [5,32]; Arnold et al. (2024), Miller et al. (2023), and Moffitt et al. (2026) draw on the Trauma Quality Improvement Program or its Michigan collaborative over overlapping years (2016-2020) [8,28,35].

Author, year	Design	Category	n	Focus
Alobaidi et al., 2016 [27]	Retrospective single-center cohort study†	Triage/timing	307	12h vs ≥12h rIMN
Arnold et al., 2024 [28]	Retrospective cohort study with propensity score matching (multicenter national database)	Triage/timing	1,118	EDF vs DDF timing
Flagstad et al., 2021a [5]	Retrospective multicenter cohort study	Triage/timing	328	EDF vs DDF timing
Flagstad et al., 2021b [32]	Retrospective multicenter review	Triage/timing	246	Simultaneous vs staged IMN of ≥2 LE long bone fractures
Mansour et al., 2023 [34]	Retrospective single-center cohort study	Triage/timing	23	Triage: OpR vs ICU vs Ward
Miller et al., 2023 [35]	Retrospective multicenter registry-based cohort study	Triage/timing	146	Simultaneous vs staged IMN of ≥2 LE long bone fractures
Moffitt et al., 2026 [8]	Retrospective cohort study with propensity score matching	Triage/timing	3,202	Simultaneous vs staged IMN of ≥2 LE long bone fractures
Pape et al., 2007 [9]	Prospective randomized controlled multicenter trial†	Triage/timing	165	Ex-fix vs IMN
Rixen et al., 2016 [38]	Prospective randomized controlled multicenter trial†	Triage/timing	34	Ex-fix vs IMN
Steinhausen et al., 2014 [39]	Retrospective multicenter registry-based cohort study	Triage/timing	379	DCO vs ETC in BFF
Copeland et al., 1998 [24]	Retrospective single-center registry-based cohort study	Unilateral vs bilateral	885	UFF vs BFF
Cosgrove et al., 2022 [30]	Retrospective registry-based cohort study	Unilateral vs bilateral	119,213	UFF vs BFF
Denis-Aubrée et al., 2021 [7]	Retrospective single-center cohort study	Unilateral vs bilateral	201	UFF vs BFF
Giannoudis et	Retrospective single-center case-control study	Unilateral vs	54	UFF vs BFF

al., 2000 [13]		bilateral		
Kobbe et al., 2013 [14]	Retrospective multicenter registry-based cohort study	Unilateral vs bilateral	894	UFF vs BFF
Lichte et al., 2014 [15]	Retrospective multicenter registry-based cohort study	Unilateral vs bilateral	2,074	UTF vs BTF
O'Toole et al., 2014 [36]	Retrospective single-center cohort study	Unilateral vs bilateral	515	UFF vs BFF; mortality trend vs historical cohort
Pfeifer et al., 2012 [37]	Secondary analysis of prospective multicenter RCT data (Pape et al., 2007)	Unilateral vs bilateral	165	UFF vs BFF
Willett et al., 2010 [40]	Retrospective multicenter registry-based cohort study	Unilateral vs bilateral	22,882	UFF vs BFF, with or without associated injuries
Cannada et al., 2008 [29]	Retrospective multicenter cohort study	No comparator	89	Retrograde IMN outcomes
Lane et al., 2015 [33]	Retrospective single-center cohort study	No comparator	72	Complications with BFF
Dienstknecht et al., 2013 [31]	Secondary analysis of prospective multicenter RCT data (Pape et al., 2007)†	Risk factor analysis	165	Long bone fracture as predictors of complications
Godzik et al., 2014 [11]	Retrospective registry-based cohort study (National Trauma Data Bank)	Risk factor analysis	199,592	PE risk with multiple fractures
Handolin et al., 2004 [25]	Retrospective single-center cohort study†	Risk factor analysis	61	Pulmonary complications comparing LE fracture with intramedullary fixation vs no LE fracture

TABLE 2: Design and focus of the studies used for data extraction.

BFF: bilateral femoral fracture(s); BTF: bilateral tibial fracture(s); DDF: delayed definitive fixation; EDF: early definitive fixation; Ex-fix: external fixation; ICU: intensive care unit; IMN: intramedullary nailing; LE: lower extremity; n: sample size; OpR: operating room; PE: pulmonary embolism; RCT: randomized controlled trial; rIMN: reamed intramedullary nailing; UFF: unilateral femoral fracture(s); UTF: unilateral tibial fracture(s); DCO: damage control orthopaedics; ETC: early total care; LELBF: lower extremity long bone fracture

† Indirect evidence: polytrauma long bone fracture cohorts that included patients with multiple LELBF without reporting their outcomes separately, or that did not report fracture pattern.

Mortality

Twenty studies reported mortality, defined as in-hospital mortality unless indicated otherwise (Table *3*). Within the studies comparing unilateral and bilateral fractures, bilateral injuries were generally associated with higher mortality rates. Larger retrospective studies reported mortality ranges of 9.4%-11.7% for unilateral groups and 16.9%-25.9% for bilateral groups (p=0.022 and <0.001, respectively) [14,24]. One study reported 0% mortality in unilateral and BFFs [7]. A case-control study by Giannoudis et al. (2000) found a large variation in mortality between groups: 0% (unilateral) compared to 14.2% (bilateral) (p>0.05). This study also examined systemic complications, suggesting that increased fracture burden may contribute to greater physiological compromise beyond mortality alone [13]. Lichte et al. (2014) looked specifically at unilateral vs bilateral tibial shaft fractures and reported mortality rates of 16.3% and 20.0%, respectively (p=0.20) [15]. Additional comparative studies showed the same direction. O'Toole et al. (2014) reported in-hospital mortality of 2% for unilateral and 7% for bilateral femoral fractures (p=0.04), a decline from 26% for bilateral fractures at the same center in 1984-1990 [36]. Willett et al. (2010) reported mortality of 9.8% for isolated bilateral femoral fractures and 31.6% when associated injuries were present, compared with 3.4% and 12.8% for unilateral fractures; an isolated bilateral fracture was associated with three-fold higher adjusted odds of death (OR 3.07, 95% CI 1.36-6.92) [40]. Cosgrove et al. (2022) reported in-hospital mortality of 1.5% versus 2.4% (RR 1.58, 95% CI 1.35-1.85), but the difference was not independent of age and Injury Severity Score (ISS), with an adjusted RR of 1.04 (95% CI 0.89-1.20) [30].

Author, year	Focus	Mortality	ICU stay	ARDS/ALI/pulmonary dysfunction
Alobaidi et			2 vs 7d	

al., 2016 [27]	12h vs ≥12h rIMN	0.6% vs 0% (p=0.32)	(p=0.009)	ARDS: 0.6% vs 1.3% (p=0.54)
Arnold et al., 2024 [28]	EDF vs DDF timing	1.8% vs 2.2% (p=0.76)	5 vs 7d (p<0.001)	ARDS: 1.4% vs 2.2% (p=0.52)
Flagstad et al., 2021a [5]	EDF vs DDF timing	3.0% vs 8.5% (p=0.03)	5.9 vs 11.3d (p<0.01)	ARDS: 3.7% vs 12.3% (p<0.01)
Flagstad et al., 2021b [32]	Bilateral nailing (1 stage) vs one at a time (2 stage)	2.7% vs 0% (p=0.22)	7.6 vs 11.8d (p=0.02)	ARDS: 5.9% vs 13.8% (p=0.05); 78% reduced risk with single stage on multivariate analysis
Mansour et al., 2023 [34]	Triage: OpR vs ICU vs Ward	0 vs 14.3% vs 0 (p>0.05)	4.0 vs 9.0 vs 2.5d (p>0.05)	ARDS: 37.5% vs 28.6% vs 0% (p>0.05)
Miller et al., 2023 [35]	Simultaneous vs staged IMN of ≥2 LE long bones	NR	NR	ARDS (registry-coded): 1.7% vs 7.1% (p=0.166)
Moffitt et al., 2026 [8]	Simultaneous vs staged IMN of ≥2 LE long bones	3.2% vs 2.1% (after propensity matching; p=NR)	6 vs 7d (median; p=0.053)	ARDS (registry-coded): 1.4% vs 2.6% (p=0.10)
Pape et al., 2007 [9]	Ex-fix vs IMN	0.6% pooled*	12.4 vs 8.2d (p=0.617)	ARDS: 10% vs 8.6% (p=0.972); borderline patients: adjusted OR 6.69 for ALI with IMN vs ex-fix (p<0.05), no difference in stable patients
Rixen et al., 2016 [38]	Ex-fix vs IMN	1 vs 2 deaths, intention to treat (as treated, all deaths in the ex-fix group)	21.8d vs 12.4d (p=0.037)	ARDS: 0% vs 11.8% (p>0.05)
Steinhausen et al., 2014 [39]	DCO vs ETC in BFF	13.5% vs 8.4% (p=NR)	19.4 vs 11.5d (p<0.001)	NR
Copeland et al., 1998 [24]	UFF vs BFF	11.7% vs 25.9% (p<0.001)	NR	ARDS: 7.3% vs 15.7% (p=0.014)
Cosgrove et al., 2022 [30]	UFF vs BFF	1.5% vs 2.4% (RR 1.58, 95% CI 1.35–1.85); not independent after age and ISS adjustment	2.4 vs 5.3d; adjusted 2.6 vs 3.8d (p<0.0001)	NR
Denis-Aubrée et al., 2021 [7]	UFF vs BFF	0% vs 0% (p=NR)	11.7 vs 18.4d (p=0.029)	ARDS: 4% vs 36% (p<0.001); not independent of ISS on multivariate analysis
Giannoudis et al., 2000 [13]	UFF vs BFF	0% vs 14.2% (p>0.05)*	0.8 vs 4.0d (p<0.05)	ARDS: 5.0% vs 42.8% (p<0.05)
Kobbe et al., 2013 [14]	UFF vs BFF	9.4% vs 16.9% (p=0.022)	12.7 vs 17.0d (p=0.012)	Pulmonary organ failure (SOFA-based): 20.6% vs 34.7% (p=0.01); OR 1.97 on multivariate analysis
Lichte et al., 2014 [15]	UTF vs BTF	16.3% vs 20.0% (p=0.20)	12.2 vs 14.7d (p=0.12)	Pulmonary organ failure (SOFA-based): 23.1% vs 29.5% (p=0.076); OR 1.56 on multivariate analysis
O'Toole et al., 2014 [36]	UFF vs BFF	2% vs 7% (p=0.04)	4 vs 8d (p=0.006)	NR
Pfeifer et al., 2012 [37]	UFF vs BFF	NR	12.2 vs 18.2d (p=0.008)	Pooled: ALI 24%, ARDS 9%
Willett et al., 2010 [40]	UFF vs BFF ± associated injuries	UFi 3.4%, UFa 12.8% vs BFi 9.8%, BFa 31.6%; isolated BFF adjusted OR 3.07	UFi 5.1, UFa 6.7 vs BFi 6.8, BFa 7.8d	NR
Cannada et al., 2008 [29]	Retrograde IMN outcomes	5.6%	NR	ARDS: 14.6%

Lane et al., 2015 [33]	Complications with BFF	6.9%**	NR	ARDS: 0%
Dienstknecht et al., 2013 [31]	Long bone fracture as predictors of complications	NR	NR	ARDS: 0%, ALI: 21%
Handolin et al., 2004 [25]	Pulmonary complications comparing LE fracture with intramedullary fixation vs no LE fracture	4% vs 9% (p=NR)	NR	ARDS: 4% vs 6% (p>0.05)

TABLE 3: Primary outcomes of the studies used for data extraction.

ALI: acute lung injury; ARDS: acute respiratory distress syndrome; BFF: bilateral femoral fracture(s); BTF: bilateral tibial fracture(s); d: days; DDF: delayed definitive fixation; EDF: early definitive fixation; Ex-fix: external fixation; ICU: intensive care unit; IMN: intramedullary nailing; ISS: injury severity score; LE: lower extremity; NR: not reported; OpR: operating room; OR: odds ratio; p: p-value; rIMN: reamed intramedullary nailing; SOFA: Sequential Organ Failure Assessment; UFF: unilateral femoral fracture(s); UTF: unilateral tibial fracture(s); BFa/BFi: bilateral femoral fracture with associated injuries/isolated; CI: confidence interval; DCO: damage control orthopaedics; ETC: early total care; RR: relative risk; UFa/UFi: unilateral femoral fracture with associated injuries/isolated

* death reported timeframe not identified; ** included prefixation deaths.

For studies without a clearly relevant comparator, mortality ranged from 5.6% to 6.9%. Cannada et al. (2008) analyzed the fixation of bilateral femoral shaft fractures using retrograde intramedullary fixation, reporting a mortality rate of 5.6% [29]. This finding was notably lower than the bilateral-fracture mortality rates reported in the comparator studies above, particularly among those examining polytrauma patients. In a similar study of bilateral femoral fractures but with heterogeneous fixation methods, a 6.9% mortality rate was reported [33].

For studies evaluating different triage approaches in the context of LE fractures, the mortality rates ranged from 0% to 14.3%. A prospective RCT by Rixen et al. (2016) comparing external fixation to intramedullary nailing (IMN) reported three deaths (9%), one in the external fixation arm and two in the IMN arm; both IMN-arm deaths occurred in patients treated with external fixation after protocol deviation, so on an as-treated basis all three deaths occurred in the external fixation group [38]. One study examining retrograde intramedullary fixation before or after 12 hours reported a mortality rate of 0.6% in the <12 h group and 0% in the >12 h group (p=0.32) [27]. In a study comparing early versus delayed definitive treatment for BFFs, the mortality rates were 1.8% and 2.2%, respectively (p=0.76) [28]. A similar study by Flagstad et al. (2021a) reported a mortality of 3.0% for EDF and 8.5% for DDF (p=0.03) [5]. One prospective RCT reported a pooled overall mortality rate of 0.6% when comparing external fixation vs IMN [9]. Flagstad et al. (2021b), a larger retrospective study looking at patients with BFFs treated with IMNs, reported a mortality rate of 2.7% in patients who had both fractures treated in the same surgery, while patients treated in a staged manner (two surgeries, one femur fixation per surgery) had a mortality rate of 0% (p=0.22) [32]. Mansour et al. (2023) reported mortality data based on where the patient was triaged on arrival: 0% operating room (OpR), 14.3% ICU, and 0% ward (p>0.05) [34]. After propensity score matching, Moffitt et al. (2026) reported mortality of 3.2% with simultaneous fixation and 2.1% with staged fixation of multiple LE long bone fractures [8]. Steinhausen et al. (2014) reported mortality of 13.5% after damage control and 8.4% after ETC in patients with bilateral femoral shaft fractures, but standardized mortality ratios (0.74 vs 0.79) showed no difference after adjustment for injury severity [39].

One study evaluated how LE long bone fractures affected a specific clinical outcome [25]. Handolin et al. (2004) compared IMN of LE long bone fracture versus no LE fracture in the context of known chest trauma (pulmonary contusion), and found a mortality rate of 4% in the IMN fixation group, compared to 9% in the no fracture group [25].

ICU LOS

Seventeen studies reported ICU LOS (Table *3*). Nine studies examined ICU LOS in relation to triage and timing approach comparators. Mansour et al. (2023), a study of bilateral femoral fractures, found that when triaged directly to the OpR versus ICU versus non-ICU inpatient care, times were as follows: 4 days vs 9 days vs 2.5 days [34]. Alobaidi et al. (2016) examined the effect of immediate to delayed fixation of 12 hours as a cut-off time in a mixed group of single and multiple LE fractures, reporting two days ICU LOS when fixated within 12 hours of admission and seven days if fixation was performed after 12 hours of admission (p=0.009) [27]. Studies comparing early versus delayed fixation for bilateral fractures show wide variation. Flagstad et al. (2021a) found an ICU LOS of 5.9 days vs 11.3 days when comparing immediate vs delayed fixation (p<0.01) [5]. However, this study examined timing and delays to fixation across 10 different level one trauma centers; as such, timing may have varied between sites [5]. A larger study by Arnold et al. (2024) found a

shorter ICU LOS, reporting five and seven days for early and delayed groups (p<0.001) [28]. Of note, Rixen et al. (2016) found a large variance between external fixation and IMN groups for femoral shaft fractures in polytrauma, reporting 21.8 vs 12.4 days, respectively, when comparing polytrauma patients (p=0.037) [38]. With a similar study design, Pape et al. (2007) found an ICU LOS of 12.4 days in the external fixation group compared to 8.2 days in the IMN group (p=0.617) [9]. Flagstad et al. (2021b) found a difference of 7.6 days vs 11.8 days when comparing single vs two-stage fixation of bilateral femoral fractures with IMN (p=0.02) [32]. Moffitt et al. (2026) reported a median ICU stay of six versus seven days for simultaneous versus staged fixation (p=0.053) [8]. Steinhausen et al. (2014) reported an ICU stay of 19.4 days after damage control versus 11.5 days after ETC (p<0.001); notably, the damage control group was more severely injured [39].

In the nine studies directly comparing single fractures and multiple fractures, eight reported ICU LOS. The multiple-fracture group was consistently reported as having higher ICU LOS. Kobbe et al. (2013) found 12.7 days vs 17 days (p=0.012), while a larger study of tibial shaft fractures (n=2,074), Lichte et al. (2014), found a similar trend of 12.2 vs 14.7 days (p=0.12) [14,15]. The most notable difference was reported by Denis-Aubrée et al. (2021), with 11.7 vs 18.4 days (p=0.029) [7]. However, this study focused on polytrauma patients and whether IMN could be done emergently. This is further supported by Pfeifer et al. (2012), who reported 12.2 days in the unilateral femur fracture (UFF) group compared to 18.2 days in the BFF group (p=0.008) [37]. However, when looking specifically for bilateral fractures as an independent predictor in multivariate regression, significance was not found (p=0.06), and that borderline condition was in fact the strongest predictor (p=0.002) [37]. Giannoudis et al. (2000) compared bilateral femoral fracture complications with unilateral fractures, reporting a combined ICU LOS of 4 days vs 0.8 days (p<0.05) [13]. Three additional comparative studies had similar findings: O'Toole et al. (2014) reported 4 versus 8 days (p=0.006) [36], Willett et al. (2010) reported 5.1 to 6.7 days for unilateral and 6.8 to 7.8 days for bilateral fractures depending on associated injuries [40], and Cosgrove et al. (2022) reported 2.4 versus 5.3 days (p<0.0001), which remained after adjustment for age and ISS (2.6 vs 3.8 days) [30].

Acute Respiratory Distress/Pulmonary Failure

Nineteen studies reported ARDS or a similar version of pulmonary failure (Table *3*); definitions differed between studies and are described in the Methods. Among the nine triage/timing studies that reported pulmonary outcomes, EDF generally had a lower rate of ARDS than delayed fixation. Specifically, two studies comparing EDF to DDF found ranges from 1.4%-3.7% in EDF groups and 2.2%-12.3% in DDF groups [5,28]. One of these, Flagstad et al. (2021a), showed statistical significance (p<0.01) [5]. Two studies comparing external fixation to immediate IMN showed ARDS ranges of 0%-10% in the external fixation group and 8.6%-11.8% in the immediate IMN group, though neither showed statistical significance [9,38]. The pooled rates obscure the principal finding of the EPOFF trial: among borderline patients, the adjusted odds of ALI were 6.69 times greater after primary nailing than after external fixation (p<0.05), with no difference among stable patients [9]. Alobaidi et al. (2016) found rates of 0.6% and 1.3% (p=0.54) when comparing IMN fixation of femoral shaft fractures before or after 12 hours of admission [27]. Flagstad et al. (2021b) reported ARDS rates of 5.9% versus 13.8% when comparing single- to two-staged IMN treatment of bilateral femoral fractures (p=0.05) [32]. Lastly, Mansour et al. (2023) reported ARDS rates based on whether the patient went directly to the OpR vs ICU vs ward, with rates of 37.5%, 28.6%, and 0%, respectively (p>0.05) [34]. Two simultaneous versus staged studies of multiple LE long bone fractures reported lower registry-coded ARDS rates after simultaneous fixation, without statistical significance: 1.7% versus 7.1% (p=0.166) in Miller et al. (2023) and 1.4% versus 2.6% (p=0.10) after propensity score matching in Moffitt et al. (2026) [8,35].

Six of the nine unilateral versus bilateral comparator studies reported pulmonary outcomes. Three studies on UFF compared to BFF reported ARDS rates of 4%-7.3% and 15.7%-42.8%, respectively, with statistical significance found in all three studies [7,13,24]. Notably, Lichte et al. (2014) examined unilateral tibial fractures (UTF) and bilateral tibial fractures (BTF) in polytrauma patients, reporting pulmonary organ failure rates of 23.1% and 29.5%, respectively (p=0.076, OR 1.56) [15]. Kobbe et al. (2013) also examined pulmonary organ failure rates in UFF and BFF, reporting rates of 20.6% compared to 34.7%, respectively (p=0.01, OR 1.97) [14]. Pfeifer et al. (2012) reported pooled rates of 24% ALI and 9% ARDS [37].

In two studies examining bilateral femoral fractures without a unilateral comparison group, ARDS rates varied widely, with Cannada et al. (2008) reporting 14.6% and Lane et al. (2015) reporting 0% [29,33]. When comparing the effect of LE fracture burden with the addition of pulmonary contusion, Handolin et al. (2004) reported ARDS rates of 4% in those with LE fractures compared to 6% in those without (p>0.05) [25]. Lastly, Dienstknecht et al. (2013) reported an ARDS rate of 0% and an ALI rate of 21% in an analysis of predictors of complications in a LE long bone polytrauma cohort [31].

Multiple Organ Dysfunction Syndrome (MODS)

Eight studies examined MODS and/or multi-organ failure (MOF) (Table *4*). Pape et al. (2007) reported MODS at 5% in both the external fixation group and the IMN group (p=0.953) [9]. Kobbe et al. (2013) reported rates of 14.6% vs 25.0% in UFF vs BFF groups (p=0.034) [14]. Looking only at BFFs, Lane et al. (2015) reported only a 2.9% rate in their polytrauma setting [33]. Similarly, Pfeifer et al. (2012) reported a 5% rate when pooling

UFF and BFF [37]. When comparing UTF to BTF, Lichte et al. (2014) found higher rates of MODS, reporting 25.3% vs 31.6% (p=0.087) [15]. Interestingly, Handolin et al. (2004) reported MOF at 4% in a LE fracture group with IMN treatment, compared with 15% in a LE non-fracture group [25]. Dienstknecht et al. (2013) reported 0% of MODS in their secondary analysis looking for predictors of complication in LE polytrauma patients [31], which differs from the 5% reported by Pape et al. (2007) for the same cohort; the discrepancy was unclear from the text and is discussed in further detail in the limitations. Steinhausen et al. (2014) reported MOF in 40.2% after damage control, compared with 25.3% after ETC (p=0.016) [39].

Author, year	Focus	MODS	Sepsis	PE/DVT/FES
Alobaidi et al., 2016 [27]	12h vs ≥12h rIMN	NR	0.6% vs 1.3% (p=0.54)	FES: 0.6% vs 0.7% (p=1.00)
Arnold et al., 2024 [28]	EDF vs DDF timing	NR	NR	DVT: 2.2% vs 6.5% (p=0.012), PE: 3.9% vs 5.4% (p=0.42)
Flagstad et al., 2021a [5]	EDF vs DDF timing	NR	3.9% vs 8.1% (p=0.25)	DVT: 4.3% vs 9.3% (p=0.07), PE: 3.0% vs 4.3% (p=0.56), FES: 4.9% vs 5.5% (p=0.80)
Flagstad et al., 2021b [32]	Bilateral nailing (1 stage) vs one at a time (2 stage)	NR	4.9% vs 7.0% (p=0.53)	DVT: 5.4% vs 10.3% (p=0.18), PE: 3.7% vs 6.9% (p=0.31), FES: 5.9% vs 10.3% (p=0.24)
Mansour et al., 2023 [34]	Triage: OpR vs ICU vs Ward	NR	NR	Embolic event: 12.5% vs 14.3% vs 12.5% (p>0.05)
Miller et al., 2023 [35]	Simultaneous vs staged IMN of ≥2 LE long bones	NR	NR	PE: 3.4% vs 3.6% (p=1.00)
Moffitt et al., 2026 [8]	Simultaneous vs staged IMN of ≥2 LE long bones	NR	NR	DVT: 4.4% vs 4.8% (p=0.71), PE: 3.3% vs 2.9% (p=0.66)
Pape et al., 2007 [9]	Ex-fix vs IMN	5% vs 5% both (p=0.953)	11.7% vs 13.4% (p=0.621)	0% FES
Rixen et al., 2016 [38]	Ex-fix vs IMN	NR	23.5% vs 11.8% (p>0.05)	NR
Steinhausen et al., 2014 [39]	DCO vs ETC in BFF	40.2% vs 25.3% (p=0.016)	21.6% vs 12.0% (p=0.081)	NR
Copeland et al., 1998 [24]	UFF vs BFF	NR	NR	NR
Cosgrove et al., 2022 [30]	UFF vs BFF	NR	NR	NR
Denis-Aubrée et al., 2021 [7]	UFF vs BFF	NR	NR	PE: 2.8% vs 12% (p=0.06)
Giannoudis et al., 2000 [13]	UFF vs BFF	NR	NR	NR
Kobbe et al., 2013 [14]	UFF vs BFF	14.6% vs 25.0% (p=0.034); not independent on multivariate analysis	10.3% vs 17.6% (p=0.08)	NR
Lichte et al., 2014 [15]	UTF vs BTF	25.3% vs 31.6% (p=0.087)	12.9% vs 14.6% (p=0.60)	NR
O'Toole et al., 2014 [36]	UFF vs BFF	NR	NR	NR

Pfeifer et al., 2012 [37]	UFF vs BFF	Pooled: 5%	Pooled: 13%	NR
Willett et al., 2010 [40]	UFF vs BFF ± associated injuries	NR	NR	NR
Cannada et al., 2008 [29]	Retrograde IMN outcomes	NR	NR	PE/DVT: 6.7%, FES: 4.5%
Lane et al., 2015 [33]	Complications with BFF	2.9%	2.9%	DVT: 10%, PE: 2.9%
Dienstknecht et al., 2013 [31]	Long bone fracture as predictors of complications	0%	11%	NR
Godzik et al., 2014 [11]	PE risk with multiple fractures	NR	NR	PE: 0.46% overall; multiple fractures OR 1.89 for PE (p<0.001)
Handolin et al., 2004 [25]	Pulmonary complications comparing LE fracture with intramedullary fixation vs no LE fracture	4% vs 15% (p>0.05)	19% vs 12% (p>0.05)	PE: 0% vs 0% (p=NR), FES: 0% vs 3% (p=NR)

TABLE 4: Secondary outcomes of the studies used for data extraction.

BFF: bilateral femoral fracture(s); BTF: bilateral tibial fracture(s); DDF: delayed definitive fixation; DVT: deep vein thrombosis; EDF: early definitive fixation; Ex-fix: external fixation; FES: fat embolism syndrome; ICU: intensive care unit; IMN: intramedullary nailing; LE: lower extremity; MODS: multiple organ dysfunction syndrome; NR: not reported; OpR: operating room; OR: odds ratio; p: p-value; PE: pulmonary embolism; rIMN: reamed intramedullary nailing; UFF: unilateral femoral fracture(s); UTF: unilateral tibial fracture(s); DCO: damage control orthopaedics; ETC: early total care; MOF: multiple organ failure

Sepsis

Of the 12 studies that reported sepsis, variability was high, ranging from 0.6% to 23.5% (Table *4*). Alobaidi et al. (2016) reported 0.6% vs 1.3% (p=0.54) when comparing early vs late IMN for femoral shaft fracture [27]. Flagstad et al. (2021a), when comparing EDF to DDF, found sepsis rates of 3.9% vs 8.1% (p=0.25) [5]. Similarly, in a different work by Flagstad et al. (2021b) comparing single-stage vs two-stage IMN, sepsis rates were 4.9% and 7.0%, respectively [32]. Notably, these three studies did not look exclusively at the polytrauma population. In comparing external fixation with IMN, Pape et al. (2007) found sepsis rates of 11.7% in the external fixation group and 13.4% in the IMN group (p=0.621); Dienstknecht et al. (2013) and Pfeifer et al. (2012) reported pooled sepsis rates of 11% and 13%, respectively, using the same cohort [9,31,37]. Rixen et al. (2016), in a similar study comparing external fixation to IMN, reported sepsis rates of 23.5% and 11.8%, respectively (p>0.05) [38]. Studies comparing unilateral to bilateral fractures reported similar results: Lichte et al. (2014) reported 12.9% vs 14.6% in tibial fracture polytrauma patients (p=0.60), and Kobbe et al. (2013) yielded 10.3% vs 17.6% for UFF and BFF, respectively (p=0.08) [14,15]. Notably, Lane et al. (2015) found a 2.9% sepsis rate for BFFs, much lower than previously reported [33]. Handolin et al. (2004) found septic rates of 19% vs 12% in LE fractures with known pulmonary contusions when fixed with IMN vs without LE fractures [25]. Steinhausen et al. (2014) reported sepsis in 21.6% after damage control versus 12.0% after ETC (p=0.081) [39].

Thromboembolic Events

Thirteen studies reported on thromboembolic events including DVT, PE, and FES (Table *4*). Alobaidi et al. (2016) reported FES rates of 0.6% in the <12 h IMN group versus 0.7% in the >12 h group (p=1.00) [27]. When comparing immediate bilateral fixation versus staged IMN, Flagstad et al. (2021b) found DVT rates of 5.4% vs 10.3% (p=0.18), PE rates of 3.7% vs 6.9% (p=0.31), and FES rates of 5.9% vs 10.3% (p=0.24), respectively [32]. In a similar study by Pape et al. (2007), they did not report PE or DVT rates, but reported a pooled FES rate of 0% [9]. Mansour et al. (2023) pooled thromboembolic events and found rates of 12.5% for the immediate OpR group, 14.3% for the immediate ICU group, and 12.5% for the immediate ward group (p>0.05) [34]. Two studies comparing EDF to DDF regarding thromboembolic events reported: DVT ranges from 2.2% to 4.3% in the EDF groups and 6.5% to 9.3% in the DDF groups; for PEs, the ranges were 3.0% to 3.9% in the EDF groups and 4.3% to 5.4% in the DDF groups [5,28]. Of those two studies, Flagstad et al. (2021a) reported FES rates of 4.9% in the EDF group and 5.5% in the DDF group (p=0.80) [5]. Denis-Aubrée et al. (2021), when comparing UFF to BFF, found PE rates of 2.8% and 12%, respectively (p=0.06) [7]. Cannada et al. (2008) reported a combined DVT/PE rate of 6.7% and an FES rate of 4.5% in their cohort of BFFs, while Lane et al. (2015) reported a DVT rate of 10% and a PE rate of 2.9% in a similar BFF cohort [29,33]. Interestingly, Handolin et al. (2004) found a 0% PE and FES rate in their LE fracture with fixation

cohort, and a 0% PE rate, but a 3% FES rate in their no LE fracture cohort [25]. Lastly, Godzik et al. (2014) reported an overall PE rate of 0.46%, with an odds ratio of 1.89 for PE in patients with multiple fractures (p<0.001) [11]. In the two simultaneous versus staged studies, PE rates were similar: 3.4% versus 3.6% (p=1.00) in Miller et al. (2023) and 3.3% versus 2.9% (p=0.66) in Moffitt et al. (2026), with DVT in 4.4% versus 4.8% (p=0.71) in the latter [8,35].

Discussion

Across the nine studies comparing unilateral to bilateral femoral fractures, or tibial in the case of Lichte et al. (2014), the direction of effect was largely consistent: the bilateral group had equal or worse outcomes than the unilateral group for every outcome reported, although many of these differences were not statistically significant, several studies draw on overlapping cohorts, and outcome definitions varied [7,13-15,24,30,36,37,40]. ICU LOS and ARDS/severe pulmonary dysfunction were the most robust findings, with longer ICU stay in all eight studies with data and statistical significance in six, and higher ARDS/severe pulmonary dysfunction with significance in four of five studies that reported it comparatively. Mortality followed the same direction but was less consistent, with significance in five of eight studies; among studies that adjusted for injury severity, bilaterality was independently associated with mortality in Willett et al. (2010) (isolated bilateral fracture OR 3.07) but not in Cosgrove et al. (2022) after adjustment for age and ISS [30,40]. Cannada et al. (2008) and Lane et al. (2015), two bilateral femoral fracture-only cohorts, reported notably lower absolute mortality (5.6% and 6.9%, respectively) than most bilateral arms in the previously mentioned comparative studies, reflecting likely narrower inclusion criteria [29,33]. Likewise, a systematic review by Stavlas et al. (2009) of only bilateral femoral fracture cohorts reported similar mortality to the two aforementioned studies (6%), with findings of MODS, PE, and FES trending in the same direction as well [6]. The largest unilateral versus bilateral comparison, 119,213 operatively treated femoral shaft fractures in the National Trauma Data Bank, showed the same pattern: bilateral fractures were associated with a longer ICU stay (5.3 versus 2.4 days unadjusted; 3.8 versus 2.6 days after adjustment for age and ISS), more ventilator days (3.1 versus 1.3; 2.0 versus 1.4 adjusted), and more complications, but not with higher mortality after adjustment [30].

Among the 10 studies comparing triage or fixation timing, ICU LOS showed the most consistent pattern: earlier, single-stage, or IMN-first management had a shorter or equal ICU stay in every study that reported it, with statistical significance in six of nine. Thromboembolic events generally, but not uniformly, favored earlier or single-stage fixation: DVT was significantly lower in one study, whereas PE was marginally more frequent after simultaneous fixation in Moffitt et al. (2026) (3.3% vs 2.9%, p=0.66) [5,8,9,27,28,32,34,35,38,39]. Mortality, ARDS, and sepsis did not share this consistency, and each reversed direction in at least one study. Rixen et al. (2016), though indirect evidence, is the clearest example: its external-fixation arm had a longer ICU stay but fewer deaths on an intention-to-treat basis (one versus two) and markedly lower ARDS (0% vs 11.8%) than its IMN arm [38]. Because allocation was randomized, these differences cannot reflect patient selection; with 17 patients per arm and early termination, chance is the more probable explanation, and the investigators calculated that a mortality endpoint would require approximately 1,300 patients per arm [38]. The observational studies carry a different limitation: the most severely injured patients are preferentially temporized, biasing the comparison against delayed fixation, whereas patients who die before definitive fixation are excluded from the delayed group altogether, as were 23 eligible patients (7%) in Denis-Aubrée et al. (2021) [7]. Propensity score matching, as applied by Arnold et al. (2024), addresses the first bias but not the second [28]. Consistent with this, Steinhausen et al. (2014) found in the TraumaRegister DGU that external fixation was applied to the more severely injured half of 379 patients with bilateral femoral shaft fractures, with no mortality difference between damage control and ETC after adjustment for injury severity [39], and Moffitt et al. (2026) found no increase in ARDS, ventilator-associated pneumonia, or acute kidney injury with simultaneous compared with staged nailing after propensity score matching [8]. Mansour et al.'s (2023) comparison of patients triaged to the OpR, ICU, or non-ICU inpatient care can be interpreted similarly: because triage destination reflected presenting severity rather than a randomized strategy, its finding of worse outcomes in ICU-triaged patients more plausibly reflects severity driving triage location rather than triage location driving outcomes [34]. This same pattern appears outside the two comparator categories above: Dienstknecht et al. (2013) found that standard clinical parameters failed to predict complications in stable multiply injured patients, with severe head and thoracic injury driving complications rather than fracture pattern [31]. Interestingly, Handolin et al. (2004) found that fixation of an LE fracture in patients with chest trauma was not associated with worse ARDS, MODS, or mortality than no fracture at all [25]. Both reinforce that associated injury, more than the fracture or its treatment, drives much of the risk in this population, the same treatment-follows-presentation pattern seen in Mansour et al. (2023) [34]. Similarly, in a systematic review of 38 studies of multiply injured patients with femur fractures, Nahm et al. (2012) found that EDF was generally associated with a shorter hospital LOS and lower rate of ARDS, with no consistent difference in mortality, aligning with the trends noted in fixation timing/triage studies evaluated in this review [41].

MODS and sepsis were comparatively under-reported and trended in the same direction but reached significance only in Kobbe et al. (2013), where the difference did not survive multivariate adjustment [14], and in Steinhausen et al. (2014), where MOF was more frequent after damage control in a more severely injured group [39]. The single strongest secondary-outcome finding in this review came from Godzik et al.'s (2014) national registry of 199,592 patients, which found multiple LE/pelvic fractures independently

increased PE risk (OR 1.89, p<0.001) [11]. Because studies defined pulmonary outcomes differently, rates are best compared within studies rather than between them.

In summary, fracture laterality showed a consistent direction of effect across outcomes, although statistically supported and independently adjusted associations were limited mainly to ICU stay and pulmonary dysfunction, while fixation timing was similarly consistent only for ICU LOS, suggesting fracture burden itself carries a more reliable risk signal across outcome domains than the specific timing or method of fixation. This contrast warrants caution: laterality is an exposure and fixation timing a treatment decision, and the two literatures are confounded differently, so the difference in consistency reflects study design as much as the relative importance of the two factors. These directional patterns derive from fewer independent datasets than publications and should not be read as definitive evidence.

A limitation of the ISS bears on every adjusted comparison in this review. The ISS uses the highest AIS score in each of the three most severely injured body regions, and both femora fall in the same region, so a contralateral femoral shaft fracture adds nothing: unilateral and bilateral femoral shaft fractures each contribute 9 points [42], whereas the New Injury Severity Score (NISS), which sums the squares of the three highest AIS scores irrespective of region, would score them 9 and 18 [43]. The same limitation applies to ipsilateral femoral and tibial fractures (floating knee), which fall within a single body region despite carrying greater risk than either fracture alone. Adjustment for ISS therefore removes the effect of other injuries but leaves the second fracture within the bilateral variable, as Kobbe et al. (2013) and Lane et al. (2015) noted [14,33]. Where bilaterality remained significant after adjustment, as for pulmonary failure and ICU stay, part of the association is attributable to the scoring system; where it did not, as for mortality in most studies, the associated injuries accounted for the outcome. Future studies should report the NISS alongside the ISS.

This review has several limitations. Study designs, comparator definitions, and sample sizes (from n=23 to n=199,592) are highly heterogeneous, precluding formal quantitative pooling. The analysis is qualitative and directional. Confounding by injury severity and by indication recurs throughout: several associations significant on univariate analysis did not survive multivariate adjustment, while others reached independent significance despite a non-significant univariate result. The unilateral versus bilateral comparison carries a further, structural version of this problem: a bilateral fracture satisfies several of the earlier polytrauma definitions in isolation, although not the Berlin definition [4,44], so the bilateral arm of every comparator study is a guaranteed polytrauma population set against a unilateral arm with variable, generally lower, polytrauma prevalence. This likely inflates the apparent effect of laterality itself. Secondary outcomes were reported far less completely than mortality, ICU stay, and ARDS, and pulmonary complications were defined inconsistently across studies. Additionally, Pape et al. (2007) reported an MOF incidence of 5%, while Dienstknecht et al. (2013), drawing on the same 165-patient EPOFF cohort and the same definition (dysfunction of at least three organ systems), reported none; Pape et al. observed MOF only among borderline patients. The discrepancy cannot be resolved from the published reports, and no conclusion is drawn from these figures [9,31]. Lastly, the literature spans nearly three decades, during which fixation practice and venous thromboembolism prophylaxis have evolved considerably. The included studies are also less independent than their number suggests: several draw on the same trial cohort, registries, or centers, so the 24 publications represent fewer than 24 independent cohorts (see Article Selection). The search was limited to a single database (PubMed), so relevant studies indexed elsewhere may have been missed. Five included studies were classified as indirect evidence because outcomes were not reported by fracture pattern, and several studies enrolled small numbers of adolescents (from age 13 to 16 years) or did not state an age limit; these were retained because their populations were predominantly adult. Future work should prioritize prospective, standardized, severity-adjusted studies that vary fracture laterality and fixation timing independently, and should extend beyond the femur-dominant cohorts that dominate this literature.

Conclusions

Patients with multiple LELBFs in the polytrauma setting had a longer ICU stay in every comparative study that reported it, and generally higher, though less consistently significant, rates of mortality, ARDS, and other complications than patients with a single LELBF; in the largest adjusted analysis, the mortality difference was not independent of injury severity. Early or single-stage fixation was associated with shorter or similar ICU stays in every study that reported them, and with less DVT in one of two propensity-matched studies, but its effect on mortality, ARDS, and sepsis is considerably less uniform, reversing direction entirely in at least one trial. Injury severity and confounding by indication likely underlie several of these associations, and the heterogeneity of study design and outcome reporting limits how confidently any of them can be read causally. Prospective, standardized, severity-adjusted research is needed to clarify optimal ICU-level management in this population. The debate has shifted from ETC versus damage control to physiology-guided timing, and the unresolved question is whether a second long bone fracture should alter the physiologic threshold for definitive fixation.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the

work.

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Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

Generative AI (Claude, Anthropic, OpenEvidence) was utilized for manuscript preparation, namely proofreading, outlining, editing, data verification, and citation management. All AI-assisted content was manually reviewed and verified for accuracy by the authors.

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