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Review Article

Second Hit Phenomenon and Timing of Definitive Fracture Fixation After Damage Control Laparotomy: A Narrative Review

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ABSTRACT

Background: The second hit phenomenon describes the worsening of systemic inflammatory stress when major surgery is performed after severe trauma and remains a central concern in determining the timing of definitive fracture fixation in polytrauma patients. This issue is especially complex in patients undergoing damage control laparotomy, in whom the presence of an open abdomen has traditionally been viewed as a reason to defer definitive orthopaedic intervention. Objective: To review contemporary evidence on the second hit phenomenon and evaluate current concepts regarding the timing of definitive fracture fixation after damage control laparotomy, with emphasis on the transition from time-based to physiology-guided decision-making. Methods: A narrative review of approximately 12 peer-reviewed publications from 2016 to 2024 was undertaken, focusing on studies and conceptual papers addressing polytrauma physiology, damage control orthopaedics, early appropriate care, safe definitive surgery, open abdomen management, and factors influencing operative timing. Results: The reviewed literature demonstrated a clear shift away from rigid time-based fixation strategies toward individualized decisions guided by physiological markers such as lactate, base deficit, hemodynamic stability, coagulation status, and temperature. Although damage control orthopaedics remains appropriate in unstable patients, delayed fixation may increase instability-related and infectious complications. Limited but important evidence suggests that early definitive fixation can be performed safely in selected patients with an open abdomen when physiological recovery has been achieved. Conclusion: Definitive fracture fixation after damage control laparotomy should be guided primarily by physiological readiness rather than elapsed time or abdominal closure status alone. Keywords: Second hit phenomenon, polytrauma, damage control laparotomy, fracture fixation timing, damage control orthopaedics.

INTRODUCTION

Polytrauma remains one of the most demanding challenges in acute surgical care because management decisions must balance competing priorities across multiple organ systems while minimizing avoidable physiological deterioration. Among these decisions, the timing of definitive fracture fixation is particularly complex in severely injured patients, as operative intervention can either facilitate recovery through mechanical stabilization and early mobilization or aggravate post-traumatic inflammatory dysregulation when performed before adequate physiological recovery. This concern is commonly conceptualized through the “second hit” phenomenon, in which a major surgical procedure imposed on

an already primed inflammatory system amplifies systemic insult and increases the risk of adverse outcomes such as acute respiratory distress syndrome and multiple organ dysfunction syndrome (1).

Historically, early total care was adopted to achieve prompt definitive fixation and thereby reduce immobilization-related complications, prolonged ventilation, and extended hospitalization. Although this approach offered advantages in hemodynamically stable patients, its application in physiologically unstable polytrauma populations exposed important limitations, particularly the risk of exacerbating inflammatory and metabolic derangement through extensive early surgery. This led to the development of damage control orthopaedics, which emphasizes temporary stabilization as a means of reducing operative burden during the vulnerable post-injury phase (2). More recently, the concepts of early appropriate care and safe definitive surgery have shifted the decision-making framework from rigid time-based algorithms toward individualized assessment guided by markers such as lactate clearance, base deficit, coagulation status, temperature, and hemodynamic stability (3,4). These evolving paradigms reflect a broader movement in trauma care away from uniform sequencing and toward physiology-directed management.

The dilemma becomes more pronounced in patients undergoing damage control laparotomy, a subgroup that often represents the extreme end of physiological instability. The presence of an open abdomen has traditionally been interpreted as a practical and biological signal to defer definitive fracture fixation because of ongoing inflammation, fluid shifts, coagulopathy, contamination risk, and high intensive care dependency. However, emerging evidence suggests that delayed fixation may not always be protective and may, in selected patients, contribute to persistent instability, infectious complications, prolonged critical care requirements, and repeated surgical exposure. In particular, recent findings indicate that definitive fixation may be safely undertaken in carefully resuscitated multiply injured patients even in the presence of an open abdomen, challenging the conventional assumption that abdominal closure is a prerequisite for fracture fixation (5).

At the same time, the available literature remains clinically difficult to interpret because it spans heterogeneous study designs, different injury patterns, variable physiological thresholds, and distinct institutional practices. The “borderline” patient remains especially difficult to define, and uncertainty persists regarding how systemic inflammatory risk should be weighed against the local consequences of delayed stabilization, including fracture-related infection and prolonged mechanical instability (6-8). Additional complexity arises when polytrauma is accompanied by traumatic brain injury or spinal injury, both of which may alter operative priorities and modify the acceptable timing of fixation (9-12). Consequently, despite substantial conceptual progress, no clear consensus has been established regarding the optimal timing of definitive fracture fixation in polytrauma patients undergoing damage control laparotomy.

In this context, the present review was undertaken to synthesize contemporary evidence on the second hit phenomenon and the timing of definitive fracture fixation after damage control laparotomy, with particular emphasis on the transition from time-based paradigms to physiology-guided decision-making. The review also seeks to clarify whether an open abdomen should continue to be regarded as a relative contraindication to definitive fixation or whether physiological readiness should instead serve as the principal determinant of operative timing in this highly vulnerable patient population (1-12).

MATERIALS AND METHODS

This study was conducted as a narrative review with focused qualitative synthesis of peer-reviewed literature addressing the second hit phenomenon, damage control strategies, and the timing of fracture fixation in polytrauma patients, particularly those managed with damage control laparotomy. The review concentrated on publications from 2016 to 2024 in order to capture contemporary shifts in trauma care from traditional early total care and damage control orthopaedics models toward physiology-guided approaches such as early appropriate care and safe definitive surgery. Because the primary objective was

interpretive synthesis rather than pooled quantitative estimation, a narrative design was selected as the most appropriate method for integrating evidence derived from concept papers, retrospective cohort studies, and review-based literature within a clinically heterogeneous field (1-5).

The included literature was selected on the basis of direct relevance to four prespecified thematic domains: the immunophysiological basis of the second hit response after trauma, comparative damage control and definitive fixation paradigms in polytrauma, operative timing in patients undergoing damage control laparotomy or managed with an open abdomen, and the influence of physiological and injury-specific modifiers such as hemodynamic instability, metabolic derangement, traumatic brain injury, spinal trauma, and intensive care unit constraints on timing decisions. Studies were considered eligible when they contributed clinically meaningful evidence or conceptual insight into fracture fixation timing after severe trauma. Literature without direct relevance to fracture fixation timing, damage control strategy, or polytrauma physiology was not incorporated into the final synthesis.

Approximately 12 peer-reviewed articles were included in the final review corpus. These comprised retrospective cohort studies, conceptual analyses, systematic or narrative reviews, and clinically focused discussions relevant to trauma surgery and orthopaedic decision-making. Randomized controlled trials were not represented in the available body of literature, and substantial heterogeneity was observed across patient populations, injury profiles, outcome measures, and decision criteria. In view of this diversity, formal quantitative pooling was neither methodologically appropriate nor aligned with the study objective. Instead, the evidence was synthesized through a structured qualitative approach aimed at identifying recurring concepts, areas of agreement, conflicting interpretations, and unresolved clinical questions across the included studies (3-5,7-11).

Data extraction was oriented toward variables that directly informed operative timing and clinical interpretation. These included the described management paradigm, criteria used to define physiological readiness, outcomes associated with early versus delayed fixation, infection-related findings, intensive care considerations, and the effect of concomitant injuries on operative sequencing. Particular attention was paid to objective physiological markers repeatedly cited as relevant to safe fixation timing, including lactate level, base deficit, hemodynamic stability, temperature, and coagulation status, as these parameters underpin the contemporary shift toward physiology-directed decision-making. Evidence relating to the open abdomen was interpreted in the context of both systemic inflammatory vulnerability and the local consequences of prolonged skeletal instability (3-6).

To reduce interpretive bias, the review emphasized concordance of findings across studies rather than overreliance on any single publication and considered conclusions in light of study design limitations, patient selection issues, and probable institutional variation. Greater weight was given to findings that were mechanistically plausible and clinically consistent with modern trauma care principles, while retrospective evidence was interpreted cautiously because patients selected for earlier fixation are often physiologically more stable at baseline. This limitation was taken into account throughout the synthesis, particularly when evaluating apparent advantages of early definitive fixation in patients with open abdomen management (4,5,11).

The final narrative synthesis was organized around clinically relevant themes: the theoretical foundations of the second hit model, evolution of management paradigms from early total care to damage control and physiology-guided care, definitive fixation in the setting of damage control laparotomy, determinants of timing in borderline patients, and the interaction between systemic and local consequences of delayed fixation. This thematic structure was chosen to ensure interpretive clarity, preserve reproducibility of the review logic, and align the discussion with the central clinical question of whether definitive fixation after damage control laparotomy should be governed primarily by elapsed time or by demonstrable physiological readiness (1-12).

RESULTS

A total of approximately 12 peer-reviewed articles published between 2016 and 2024 were synthesized in this narrative review. The included literature consisted predominantly of retrospective cohort studies, conceptual reviews, and clinically oriented narrative or systematic discussions rather than randomized or prospective comparative trials. The evidence base was therefore heterogeneous in both design and scope, with most studies addressing one or more of the following domains: theoretical understanding of the second hit phenomenon, evolution of fracture fixation paradigms in polytrauma, physiological criteria guiding operative timing, fixation strategies in the setting of damage control laparotomy or open abdomen, and contextual modifiers such as infection risk, traumatic brain injury, spinal trauma, and intensive care unit constraints. Overall, the literature showed a clear shift from rigid time-based models of operative sequencing toward physiology-guided decision-making, although the strength of evidence remained limited by retrospective methodology and variable patient selection across studies.

The conceptual and historical literature consistently supported the view that the second hit phenomenon remains central to trauma decision-making, but its interpretation has evolved substantially. Earlier frameworks emphasized a vulnerable post-injury period during which major surgery could amplify systemic inflammation and precipitate organ dysfunction. More recent publications challenged the adequacy of time alone as a decision rule and instead emphasized physiological recovery as the more meaningful determinant of readiness for definitive fixation. Across the included studies, this transition was reflected in the progression from early total care to damage control orthopaedics and subsequently to early appropriate care or safe definitive surgery, with the latter approaches favoring individualized assessment using markers such as lactate, base deficit, hemodynamic stability, coagulation profile, and temperature rather than adherence to a fixed postoperative interval.

The evidence addressing patients with damage control laparotomy was narrower but clinically important. Traditional surgical practice generally treated the open abdomen as a reason to defer definitive fixation because it signified ongoing physiological instability, inflammatory burden, fluid shifts, and infectious vulnerability. However, the most directly relevant study in this subgroup reported that early definitive fixation in multiply injured patients with an open abdomen was associated with a markedly lower infection rate than delayed fixation, with reported rates of 3.1% versus 30.6%, respectively. This finding challenged the conventional assumption that abdominal closure must precede orthopaedic definitiveness and suggested that prolonged skeletal instability may itself perpetuate inflammatory and infectious complications when resuscitative targets have otherwise been met. Although this evidence was derived from a limited observational base and should be interpreted cautiously, it represented a major point of departure from traditional contraindication-based thinking.

A second dominant theme was the importance of local mechanical stability as a contributor to systemic and wound-related outcomes. The reviewed literature suggested that delayed fixation may reduce the immediate operative burden in unstable patients, but this benefit must be balanced against the consequences of prolonged fracture instability, repeated procedures, pin-site complications, soft tissue compromise, and higher fracture-related infection risk. In this context, delayed fixation was not uniformly protective and, in some scenarios, appeared to shift the burden of harm from systemic physiology to local mechanical and infectious complications. This broader interpretation of the second hit model implied that risk should not be understood solely as inflammatory amplification from surgery, but also as ongoing biological stress arising from untreated or insufficiently stabilized musculoskeletal injury.

The “borderline” patient emerged as one of the most poorly resolved areas in the literature. Several studies and conceptual discussions acknowledged that treatment decisions are often most difficult in patients who are neither overtly unstable nor clearly optimized for definitive surgery. While physiological surrogates such as lactate level, base deficit, vasopressor requirement, coagulation status,

and thermal regulation were repeatedly cited as practical indicators, no universally accepted threshold set was identified that could reliably resolve borderline cases across institutions. As a result, many decisions appeared to depend on local protocol, surgeon judgment, and multidisciplinary interpretation rather than on externally validated decision rules. This lack of standardization contributed substantially to variation in the timing of fixation across trauma systems.

Associated injuries also influenced the direction of timing decisions in a clinically meaningful way. In patients with concomitant traumatic brain injury, delayed fixation was often considered to avoid secondary neurological compromise, although this had to be weighed against increased pulmonary and infectious complications from immobilization. In contrast, spinal trauma literature generally favored earlier stabilization in carefully selected patients because of the potential neurological consequences of delay. These findings showed that fixation timing in polytrauma cannot be determined through a single framework alone, but must instead account for competing priorities between organ systems, including brain, spine, abdomen, and the musculoskeletal system. Similarly, intensive care unit factors such as vasopressor dependence, ventilatory support, coagulopathy, and incomplete resuscitation repeatedly appeared as barriers to early surgery, but these were interpreted less as logistical obstacles and more as indicators of persistent physiological unsuitability for definitive intervention.

Taken together, the included studies suggested that contemporary trauma care is moving toward a model in which definitive fixation after severe injury, including in selected patients with an open abdomen, may be feasible when objective physiological recovery is demonstrated. At the same time, the evidence did not support indiscriminate early fixation, because the adverse consequences of surgery in incompletely resuscitated patients remain a serious concern. The overall synthesis therefore favored a dynamic risk model in which both systemic inflammatory vulnerability and local consequences of delay are considered simultaneously. Rather than asking whether fixation should be early or delayed in absolute terms, the reviewed literature increasingly reframed the clinical question as whether the patient has achieved sufficient physiological readiness for a specific operation at a particular point in time.

Table 1. Characteristics of the Included Literature

Study Domain	Nature of Evidence	Main Contribution to Review
Second hit pathophysiology	Conceptual and review-based literature	Defined the biological rationale for deterioration after major surgery in recently traumatized patients
Management paradigms (ETC, DCO, EAC, SDS)	Reviews, conceptual analyses, retrospective evidence	Demonstrated the shift from time-based to physiology-guided operative timing
Open abdomen / DCL	Retrospective cohort evidence and interpretive discussion	Examined whether definitive fixation can be performed before abdominal closure in selected patients
Mechanical stability and infection	Review and trauma literature	Linked delayed or inadequate stabilization with higher infection risk and impaired healing
Borderline patient decision-making	Conceptual and case-oriented literature	Highlighted uncertainty in patients who are neither clearly unstable nor fully optimized
TBI and spinal injury modifiers	Injury-specific observational and review literature	Showed that associated injuries may alter acceptable timing thresholds
ICU-related constraints	Critical care literature	Identified vasopressor use, coagulopathy, ventilation, and incomplete resuscitation as barriers to fixation

The included literature was dominated by non-randomized evidence and conceptual analyses. Most publications contributed to more than one domain, but the largest concentration of evidence concerned evolving management paradigms and physiology-based timing frameworks, while direct evidence specific to damage control laparotomy remained comparatively sparse. This imbalance reinforces the importance of cautious interpretation when extrapolating broad trauma principles to the open-abdomen subgroup.

The synthesis demonstrated that no single paradigm adequately addresses all polytrauma scenarios. The strongest convergence across studies was seen in support for physiology-guided care, whereas the weakest area of consensus involved how to define and manage borderline patients. The literature also suggested that delayed fixation may protect against systemic deterioration in some patients while

simultaneously increasing local mechanical and infectious risk in others, underscoring the need for individualized assessment.

Table 2. Thematic Synthesis of Major Findings Across the Reviewed Literature

Theme	Direction of Findings	Overall Interpretation
Second hit concept	Consistently supported	Remains clinically relevant, but should be interpreted as dynamic rather than strictly time-bound
Early definitive fixation in stable patients	Generally favorable	Associated with mobilization benefits and lower immobilization-related complications
Damage control orthopaedics in unstable patients	Generally favorable	Reduces immediate physiological burden, but may increase later procedure burden
Physiology-guided timing	Strongly supported	More clinically useful than rigid time windows alone
Open abdomen as contraindication	Increasingly challenged	Not necessarily an absolute barrier when physiology is optimized
Delayed fixation and infection risk	Frequently associated	Prolonged instability may contribute to fracture-related infection and repeated intervention
Borderline patient classification	Inconsistently defined	Major unresolved problem limiting standardization
ICU-related delays	Commonly reported	Reflect persistent instability rather than merely logistical difficulty

Table 3. Narrative Comparison of Early and Delayed Fixation in Polytrauma

Consideration	Earlier Definitive Fixation	Delayed Fixation
Systemic inflammatory risk	Potentially higher if undertaken before resuscitative recovery	Lower immediate operative burden in unstable patients
Mechanical stability	Achieved sooner	Prolonged instability possible
Fracture-related infection	May be reduced when stable fixation is achieved early	May increase with repeated procedures, pin sites, and instability
ICU and hospital course	May shorten course in selected optimized patients	May prolong ICU dependency and staged operative exposure
Suitability	More appropriate in physiologically recovered patients	More appropriate in persistently unstable patients
Main clinical limitation	Harm if performed too early in unstable physiology	Harm from excessive delay and local complication burden

Table 1 comparative narrative table highlights the central message of the review: early and delayed fixation are not inherently superior strategies in isolation. Their relative safety depends on the interaction between the patient's current physiological condition and the local consequences of leaving the fracture insufficiently stabilized. The most appropriate timing strategy therefore appears to be conditional rather than categorical.

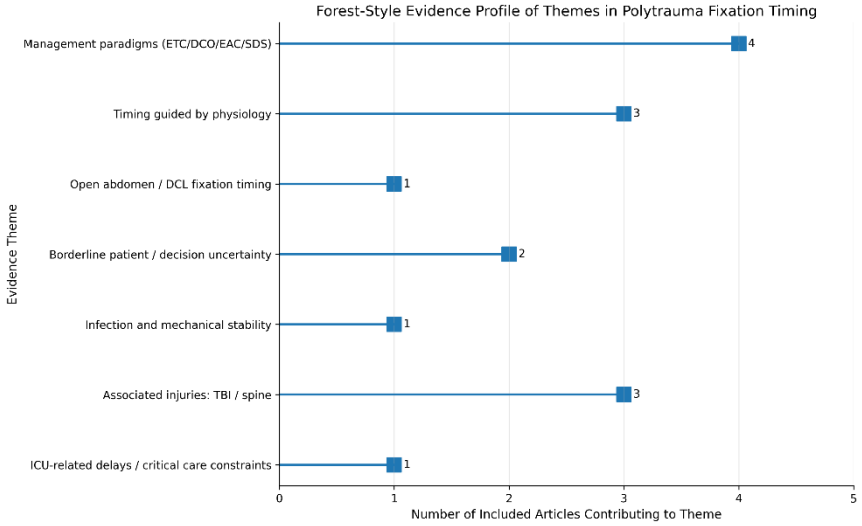

Figure 1. Evidence Density Across Clinical Decision Themes in Polytrauma Fixation Timing

The figure summarizes the number of included articles contributing to each major thematic domain identified in this narrative review. The largest concentration of evidence addressed management paradigms (n=4), followed by physiology-guided timing and associated injuries involving traumatic

brain or spinal trauma (n=3 each), whereas direct evidence specific to open abdomen/damage control laparotomy fixation timing, infection and mechanical stability, and ICU-related delays remained limited (n=1 each).

DISCUSSION

The present review shows that the concept of the second hit remains highly relevant in polytrauma care, but its practical interpretation has become more nuanced over time. Earlier trauma frameworks treated the early post-injury period as an inherently dangerous interval during which definitive fracture fixation could precipitate an exaggerated inflammatory response and increase the risk of acute respiratory distress syndrome, multiple organ dysfunction syndrome, and other systemic complications. Although this framework was clinically influential, the reviewed literature suggests that reliance on a fixed temporal window is increasingly insufficient for contemporary decision-making. Instead, a more individualized interpretation has emerged in which the magnitude of operative risk is determined less by elapsed time alone and more by the patient's evolving physiological readiness, including perfusion status, metabolic recovery, thermal balance, hemodynamic stability, and coagulation profile (1-4).

This shift has important implications for the historical progression from early total care to damage control orthopaedics and subsequently to early appropriate care or safe definitive surgery. Early total care offered clear benefits in stable patients by facilitating mobilization and limiting pulmonary and immobilization-related complications, yet the same approach could be hazardous in those with ongoing shock, coagulopathy, or systemic inflammatory activation. Damage control orthopaedics emerged as a protective strategy to reduce operative burden in unstable patients, but the literature reviewed here indicates that its benefits are not without cost. Temporary fixation, repeated procedures, prolonged instability, and delayed mechanical restoration may themselves create local biological stress and predispose patients to infection, extended critical care stay, and delayed recovery. Accordingly, more recent paradigms do not reject either early or staged fixation categorically; rather, they seek to match the scale and timing of surgery to objective indicators of physiological tolerance (2-4).

The most clinically provocative issue in this review concerns patients undergoing damage control laparotomy. Traditional teaching has generally treated the open abdomen as a practical marker of unresolved instability and therefore as a reason to delay definitive orthopaedic fixation. This position is understandable because the open abdomen often coexists with severe metabolic disturbance, ongoing resuscitative needs, contamination risk, and heightened inflammatory vulnerability. However, the reviewed literature also indicates that abdominal closure status alone may be an overly crude decision rule. The study by Glass et al. is particularly important in this regard because it reported substantially lower infection rates in patients undergoing early definitive fixation despite an open abdomen compared with those whose fixation was delayed, with rates of 3.1% versus 30.6%, respectively (5). Although this finding derives from observational data and must be interpreted cautiously, it challenges the assumption that an open abdomen should automatically preclude definitive fixation. Instead, it suggests that persistent fracture instability may itself sustain inflammatory stress and infectious susceptibility when local control is deferred for too long.

This interpretation broadens the second hit concept beyond its conventional systemic focus. The literature increasingly supports the view that delayed fixation is not a neutral strategy, as prolonged skeletal instability, repeated manipulations, pin-site problems, and soft tissue compromise may act as ongoing sources of biological insult. In this sense, the relevant clinical question is not simply whether surgery will deliver a second hit, but whether continued mechanical instability represents a persistent first hit that continues to drive inflammatory dysregulation and local morbidity. Such a perspective does not invalidate the rationale for damage control approaches; instead, it reframes operative timing as a balance between systemic vulnerability and the adverse consequences of leaving injury incompletely

stabilized. This more integrated view is consistent with current trauma surgery trends, in which local and systemic risks are weighed simultaneously rather than sequentially (3,6).

Another major finding of this review is the persistent uncertainty surrounding the so-called borderline patient. Across the included studies, physiological variables such as lactate, base deficit, vasopressor dependence, coagulation status, and temperature were repeatedly invoked as indicators of readiness, yet the literature does not offer a universally validated threshold set that can reliably determine when definitive fixation is safe in individual cases. This lack of standardization likely contributes to significant institutional variation in practice and explains why surgeon judgment and multidisciplinary interpretation remain central in trauma decision-making. From a methodological perspective, it also complicates comparison across studies because patients categorized as suitable for early fixation in one center may have been managed more conservatively elsewhere (4,7,8). The borderline group therefore remains one of the most important unresolved areas for future research.

The effect of associated injuries further demonstrates that fracture fixation timing in polytrauma cannot be governed by a single algorithm. In patients with traumatic brain injury, delayed fixation may be favored to avoid secondary neurological compromise or intracranial instability, yet excessive delay can also worsen pulmonary outcomes, immobility, and infection risk. Conversely, spinal injuries often require earlier stabilization because postponement may increase the risk of neurological deterioration and hinder overall trauma management (9,10,12). These observations show that timing decisions must account for competing physiological priorities across multiple organ systems. Similarly, intensive care unit variables such as ventilator dependence, vasopressor requirement, hypothermia, and coagulopathy are not merely logistical obstacles but important indicators that the patient has not yet achieved a state compatible with definitive operative stress (11). This reinforces the core conclusion of the review that operative timing should be driven by physiological readiness rather than by isolated procedural milestones.

The findings of this review should also be interpreted in light of the limitations of the available evidence. Most of the literature consisted of retrospective cohort studies, conceptual analyses, and review articles, with an absence of randomized controlled trials and a limited number of studies directly focused on patients with damage control laparotomy. Selection bias is therefore a major concern, particularly because patients chosen for earlier definitive fixation are often those who are already more physiologically stable. In addition, there is considerable heterogeneity in injury severity, associated trauma patterns, institutional protocols, and the physiological thresholds used to justify surgery. These factors limit the generalizability of current conclusions and reduce the precision with which evidence can be translated into universal decision algorithms. Nonetheless, despite these weaknesses, the reviewed literature consistently supports a transition away from rigid time-based doctrine toward more individualized, physiology-guided fracture fixation strategies.

Taken together, the discussion supports a contemporary interpretation of the second hit phenomenon as a dynamic continuum rather than a fixed postoperative interval. The safest timing of definitive fixation after severe trauma, including in selected patients with an open abdomen, appears to depend on the interaction between systemic resuscitative recovery and the local consequences of delaying mechanical stability. The review therefore does not support indiscriminate early fixation, nor does it support reflexive delay based solely on abdominal closure status or elapsed time. Rather, it supports individualized trauma care in which definitive fixation is considered when the patient demonstrates adequate physiological recovery and when the anticipated harms of continued instability begin to outweigh the operative inflammatory burden (1-12).

CONCLUSION

The timing of definitive fracture fixation after damage control laparotomy should no longer be governed by rigid temporal rules alone, as the reviewed evidence indicates that physiological readiness is a more

meaningful determinant of operative safety than elapsed time or abdominal closure status in isolation. While the second hit phenomenon remains a critical concept in polytrauma management, it is best understood as a dynamic interaction between systemic inflammatory vulnerability and the local consequences of prolonged skeletal instability. In carefully selected patients who demonstrate adequate resuscitative recovery, definitive fixation may be performed safely even in the setting of an open abdomen, whereas premature surgery in persistently unstable patients remains hazardous. Future research should focus on establishing more precise physiological thresholds and multicenter decision frameworks to improve consistency, reduce uncertainty in borderline cases, and better guide individualized fixation timing in complex trauma care (1-12).

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