ICM on Open Injuries - Submission of the Consensus Recommendation

RQ: Does concomitant traumatic brain injury significantly accelerate fracture union in open injuries?

Section 1: Background

Traumatic brain injury (TBI) has been associated with enhanced fracture healing in several clinical and experimental studies. Patients sustaining fractures along with TBI have been reported to demonstrate earlier callus formation, greater callus volume, and faster radiological progression of union, especially in closed long-bone fractures. This phenomenon is thought to be mediated by systemic osteogenic responses following brain injury, including the release of humoral factors, inflammatory cytokines, neuropeptides, bone morphogenetic proteins, fibroblast growth factors, circulating osteoprogenitor cells, and alterations in neuroendocrine signalling.

However, the biology of open fracture healing is more complex than that of closed fractures. In open injuries, union is influenced not only by systemic factors but also by the severity of local tissue damage and contamination. Soft-tissue loss, periosteal stripping, vascular compromise, infection, segmental bone loss, repeated debridement, instability, and delays in definitive fixation or soft-tissue coverage are critical determinants of healing. These adverse local factors may diminish or negate the potential osteogenic benefit associated with TBI.

Thus, while TBI may promote callus formation in fractures overall, its role in accelerating union in open injuries remains uncertain. Evidence from closed-fracture studies should therefore not be directly extrapolated to open fractures.

Section 2: Data Extraction Table

S.no	Author, year of publication, Country	Study Design	Sample Size	Study population (Inclusion and exclusion criteria)	Groups compared	Results
1	Perumal R, Sivakumar SP, Vijay Shankar CBS, Gaddam SR, Jayaramaraju D, Rajasekaran S. 2018, India	Retrospective comparative study	146 patients. Closed fractures: 74/146 (50.7%); open fractures: 72/146 (49.3%). TBI group: 34 closed, 32 open; control group: 40 closed, 40 open.	Patients with lower-limb fractures with or without TBI. This was the only included study that clearly reported open and closed fracture distribution and directly evaluated open fractures.	Group IA: closed fractures with TBI (n=34); Group IB: closed fractures without TBI (n=40); Group IIA: open fractures with TBI (n=32); Group IIB: open fractures without TBI (n=40).	TBI was associated with faster union in closed fractures, particularly in patients who underwent craniotomy. No acceleration of union was seen in open fractures. Mean union time in open fractures with TBI was 9 months compared with 7.3 months without TBI.
2	Newman RJ, Stone MH, Mukherjee SK. 1987, UK	Clinical observational study	11 patients with 13 long-bone fractures	Patients with long-bone fractures and severe head injury. Open/closed fracture status was not clearly reported.	Fractures in patients with severe head injury.	Reported unusually rapid union and exuberant callus formation in association with severe head injury. Results were based on long-bone fractures and cannot be directly applied to open injuries.
3	Perkins R, Skirving AP. 1987, UK	Comparative clinical study	Femoral fracture patients with and without head injury; exact open/closed distribution not clearly reported.	Patients with femoral fractures with or without head injury. Open/closed fracture status was not clearly reported.	Femoral fractures with head injury vs femoral fractures without head injury.	Head injury group showed increased callus formation and faster healing. Findings appear to relate mainly to closed femoral fractures/general femoral fracture cohorts, with no open-fracture-specific analysis.

S.no	Author, year of publication, Country	Study Design	Sample Size	Study population (Inclusion and exclusion criteria)	Groups compared	Results
4	Spencer RF. 1987, UK	Quantitative clinical assessment	53 patients with limb fractures and severe head injury compared with 30 patients with limb fractures without head injury.	Patients with limb fractures with or without severe head injury. Open/closed fracture status was not clearly reported.	Severe head injury group vs non-head-injury controls.	Patients with head injury had greater healing response and faster union. The study did not separately analyse open fractures.
5	Giannoudis PV, Mushtaq S, Harwood P, et al. 2006, UK	Clinical review / observational evidence	Not applicable	Patients with femoral fracture and head injury; open/closed fracture distribution not clearly reported.	Femoral fractures associated with head injury.	Reported accelerated bone healing and excessive callus formation in femoral fractures with head injury. Evidence is supportive for TBI-associated healing but indirect for open injuries.
6	Shim DW, Chung YH, Kim H, et al. 2022, Korea	Case-control study	48 tibial fracture patients: 12 with TBI and 36 without TBI.	Tibial fracture patients treated with plate fixation or intramedullary nailing. Severe open fractures (Gustilo-Anderson type III or higher) were excluded.	TBI group vs non-TBI group.	Tibia fractures with TBI showed shorter time to callus formation and thicker callus ratio. However, severe open injuries were excluded and the study does not establish accelerated union in open fractures.

Section 3: Results Summary

Six articles were included. Only Perumal et al. directly assessed both closed and open fractures and clearly reported the distribution of fractures. In this study, TBI was associated with faster union in closed fractures, particularly in patients who underwent craniotomy, but no accelerated union was seen in open fractures. Open fractures with TBI had a mean union time of 9 months, compared with 7.3 months in open fractures without TBI.
All other included articles reported accelerated healing, increased callus formation, or faster radiological union after head injury, but their results were based mainly on closed fractures or general long-bone fracture cohorts. Apart from Perumal et al., the articles did not clearly mention whether the included fractures were open or closed and did not analyze open fractures separately. Therefore, these findings cannot be directly extrapolated to open injuries.
Key gap: Direct evidence for open fractures is limited to Perumal et al. No other included study clearly reported open versus closed fracture status or provided open-fracture-specific outcomes.

Section 4: Discussion

The concept of accelerated fracture healing after TBI is biologically plausible and has been described predominantly in closed fractures. Systemic osteogenic stimulation after brain injury may contribute to increased callus formation and faster radiological progression of healing. However, open fractures are biologically distinct from closed injuries.
In open injuries, fracture union depends heavily on the local biological environment. Soft-tissue loss, contamination, periosteal stripping, devascularisation, infection, bone loss, fracture instability, repeated debridement, and delayed soft-tissue coverage are important determinants of delayed union and nonunion. These factors may override any potential systemic osteogenic stimulus associated with TBI.

Perumal et al. is the only directly relevant study that analyzed open fractures separately. It found no acceleration of union in open fractures with TBI. The other included articles support a general association between TBI and enhanced callus formation, but did not clearly classify fractures as open or closed or provide open-fracture-specific outcomes. Therefore, the presence of TBI should not be considered protective against delayed union or nonunion in open injuries. Standard principles of open fracture care remain the key determinants of successful union.

Section 5: Risk of Bias of Included Studies

Study	Risk of Bias
Perumal et al., 2018	Moderate to high: Retrospective comparative design, single-centre study, limited sample size, heterogeneity in TBI severity and fracture characteristics, and possible confounding from open fracture severity, fixation method, infection, soft-tissue injury, timing of coverage, and rehabilitation protocol.
Newman et al., 1987	High: Small observational study, limited sample size, no robust control group, older methodology, and no clear open/closed fracture reporting.
Perkins and Skirving, 1987	Moderate to high: Comparative study but older methodology, limited adjustment for confounders, and unclear open/closed fracture distribution.
Spencer, 1987	Moderate to high: Quantitative assessment but older methodology and no separate open-fracture analysis.
Giannoudis et al., 2006	Moderate: Review/observational evidence mainly focused on femoral fractures with head injury; not open-fracture specific.
Shim et al., 2022	Moderate: Case-control study with useful tibial fracture data, but severe open fractures were excluded; applicability to open injuries remains indirect.

Section 6: Response / Recommendation

Recommendation: In patients with open fractures, concomitant traumatic brain injury should not be assumed to accelerate fracture union. Current evidence does not show a significant healing difference between open-fracture patients with and without TBI, so treatment should not be altered solely on that basis.

Consensus statement: No. Current evidence does not support the conclusion that concomitant traumatic brain injury significantly accelerates fracture union in open fractures. Therefore, standard principles of open fracture management, including timely debridement, antibiotic therapy, skeletal stabilization, infection prevention, and soft-tissue reconstruction, should be followed irrespective of the presence of TBI.

Final answer: No, concomitant traumatic brain injury does not significantly accelerate fracture union in open injuries based on currently available evidence.

Section 7: Level / Strength of Evidence

Level / strength of evidence: LOW

Justification: Several studies have reported increased callus formation and accelerated fracture healing in patients with traumatic brain injury (TBI); however, these findings are derived primarily from mixed or closed-fracture populations. Only one study specifically evaluated open fractures and found no evidence that TBI accelerated fracture union. Therefore, current evidence is insufficient to conclude that TBI improves healing in open injuries, and standard principles of open fracture management should be followed irrespective of the presence of TBI.

Strength of recommendation: Moderate.

References

1. Perumal R, Sivakumar SP, Vijay Shankar CBS, Gaddam SR, Jayaramaraju D, Rajasekaran S. Does accelerated bone healing associated with traumatic brain injury (TBI) occur in open fractures? International Journal of Orthopedics Sciences. 2018;4(2j):677-681.
2. Newman RJ, Stone MH, Mukherjee SK. Accelerated fracture union in association with severe head injury. Injury. 1987;18(4):241-246.
3. Perkins R, Skirving AP. Callus formation and the rate of healing of femoral fractures in patients with head injuries. Journal of Bone and Joint Surgery British Volume. 1987;69(4):521-524.
4. Spencer RF. The effect of head injury on fracture healing. A quantitative assessment. Journal of Bone and Joint Surgery British Volume. 1987;69(4):525-528.
5. Giannoudis PV, Mushtaq S, Harwood P, et al. Accelerated bone healing and excessive callus formation in patients with femoral fracture and head injury. Injury. 2006;37 Suppl 3:S18-S24.
6. Shim DW, Chung YH, Kim H, et al. Accelerated tibia fracture healing in traumatic brain injury in accordance with increased hematoma formation: case-control study. BMC Musculoskeletal Disorders. 2022;23:1068.