AZ Draft proposal

RQ [1]: In major crush injuries of the upper limb, should limb salvage be prioritized due to the limited availability of prosthesis?

Section 1: Background (<300 words):

- Mangled upper limb injuries result from high-energy trauma — motor vehicle accidents, industrial/farm machinery, crush injuries, and blast wounds — and are defined by severe damage to at least 3 of the 5 tissue components: skin, soft tissue, bone, artery, and nerve. Their incidence is rising globally with industrialization and increasing road traffic.
- The upper extremity is anatomically and physiologically distinct from the lower limb: it has richer collateral vascularity, a smaller muscle mass (reducing crush syndrome risk), and a longer warm ischaemia tolerance (8–10 hours for the arm; up to 24 hours for digits cold ischaemia vs 6 hours for lower limb), making direct extrapolation of lower-limb scoring systems anatomically unjustified.
- All existing injury severity scoring systems — MESS, MESI, GHOISS, NISSSA, HFS-97 — were developed and validated exclusively for lower extremity trauma. None are validated for the upper limb. MESS specificity for predicting upper extremity amputation has been reported as low as 27.5%; successful limb salvage has been documented in patients with MESS ≥7 in multiple independent series.
- Upper limb prostheses are costly, technically demanding, and significantly less tolerated than lower limb alternatives. Up to 30% of upper limb amputees abandon their devices entirely. Access to functional prostheses — particularly myoelectric devices — is severely limited in low- and middle-income countries, where device cost may far exceed annual household income.
- Loss of the upper limb — especially the dominant hand — produces disproportionate functional, psychological, and socioeconomic disability due to the irreplaceable role of the hand in prehension, sensory feedback, fine motor control, and activities of daily living. International consensus (Milan ICC 2017, GoR 2B) explicitly recommends that reconstructive efforts be prioritized for complex upper limb injuries.

Section 2: Data extraction table

For each included study: Author/Year, Study Design, Sample Size, Population, Groups Compared, and Key Results.

S.no	Author, Year, Country	Study Design	Sample Size	Study Population (Inclusion & Exclusion Criteria)	Groups Compared	Results
1	Kumar RS, Singhi PK, Chidambaram M. India, 2017 J Orthop Case Rep	Prospective case series	N=10 (8M/2F) Mean age 35.8y (range 6–58y) Follow-up: 1 year	Mangled UE injuries (≥3 of 5 components: skin, soft tissue, bone, artery, nerve). Excluded: life-threatening polytrauma.	Salvage (n=7) vs Amputation (n=3); MESS and MESI scoring applied at presentation and in theatre	Mean MESS 7.7 (range 7–9); MESI 18.1 (range 16–22). 7 salvaged, 3 amputated (1 primary, 2 delayed for crush syndrome/sepsis). MESI more reliable than MESS for UE. Functional outcomes satisfactory at 1y (SF-36, VAS). Prosthesis expensive and poorly tolerated; 'woody limb' well accepted. Mean 4.4 procedures/patient.

S.no	Author, Year, Country	Study Design	Sample Size	Study Population (Inclusion & Exclusion Criteria)	Groups Compared	Results
2	Miller EA, Iannuzzi NP, Kennedy SA. USA, 2018 JBJS Reviews	Critical analysis review	N/A (literature review) Up to 2017	Mangled UE — all etiologies (falls, MVA, industrial machinery, firearms, explosions). Heterogeneous population.	Salvage vs amputation; multiple management strategies reviewed across evidence hierarchy (Tables I–VI)	MESS not effective predictor for UE salvage (Grade B). No published scoring system proven valid for UE. Salvage of even partial hand function frequently outperforms prosthetics. Debridement within 24h = <8h (Grade A). Coverage 3–21 days (Grade B). PTSD/depression prevalent; multidisciplinary team including prosthetist essential.
3	Bumbasirevic M, Stevanovic M, Lesic A, Atkinson HDE. Serbia/USA/UK, 2012 Int Orthop (SICOT)	Narrative review	N/A (literature review)	Mangled UE (cutting, tearing, or crushing; ≥3 tissue types affected). Includes complete and incomplete amputations.	Salvage vs amputation; reconstruction techniques and outcomes reviewed comprehensively	Limb salvage preferred wherever possible. 30% of UE amputees abandon prostheses entirely. 'Bad hand still functionally better than good UE prosthesis.' Scoring systems unreliable for UE; surgical judgment primary. Warm ischaemia: muscle ≤4–6h; digits up to 24h cold ischaemia. Early complete reconstruction (within 72h) superior to delayed. Phantom pain 30–79% of amputees.
4	Heim M, Oppenheim U, Arazi Margalit D, Azaria M. Israel, 1998 Disabil Rehabil	Case report / ethical discussion	N=1 (58-year-old woman) Follow-up: 25 years post-injury	25-year history of infected open distal radius/ulna fracture with non-union; completely anaesthetic, non-functional, deformed left hand; no active infection at assessment	Amputation + functional/cosmetic prosthesis offered (medical recommendation) vs patient refusal (no surgery)	Patient refused amputation despite loss of function, medical recommendation, and confirmed financial neutrality (no loss of benefits). Body image (Schilder's theory) deeply psychologically integrated and stable over time, even with dysfunctional limb. Cultural/geographical variation in prosthesis acceptance significant. Even deformed, anaesthetic UE preferred over amputation and prosthetics.
5	Levin LS, Goldner RD, Urbaniak JR, Nunley JA, Hardaker WT Jr. USA, 1990 J Orthop Trauma	Retrospecti ve case series	N=25 (20M/5F) Mean age 34y (range 16–73y) Follow-up mean 21mo (range 6–48mo)	Grade III open UE fractures (IIIA n=6, IIIB n=8, IIIC n=11). MVA 48%, industrial/farm 36%, GSW 16%. >50% had polytrauma.	Salvage attempted in all 25 (staged reconstruction protocol); functional outcome graded Excellent/Good/Fair/Poor at final follow-up	Salvage achieved in all 25. Outcomes: Excellent 12%, Good 20%, Fair 52%, Poor 16%. Mean 4 additional procedures; mean soft tissue coverage at 10 days; bone union at mean 10 months. Complications: nonunion 4, osteomyelitis 3, pin tract infections 5. Severe crush/blast/traction mechanism consistently associated with poor functional outcomes despite successful salvage.
6	Bumbaširević M, Matić S, Palibrk T et al. Serbia, 2021 Injury	Narrative review with updated treatment protocols	N/A (literature review) Up to 2021	All mangled extremities (civil and war); special focus on UE prosthetics limitations and emerging bionic technology	Salvage vs amputation; conventional prostheses vs bionic prostheses (TMR, direct muscle/nerve interfacing) compared	30% abandon conventional prostheses. Bionic prosthetics (targeted muscle reinnervation, direct muscle/nerve interfacing) emerging but still inferior to biological limb. Amputation rate declined from ~60% (WWII) to ~10% modern era. Economic model supports salvage as lower cost and higher utility than amputation. MESS ≥7 decision-making should be re-evaluated with modern techniques. Indications for amputation now limited to: haemodynamic instability, unreconstructable nerves, ischaemia >6h.
7	Mascia B, Mazzocchi M, Passador D et al. Italy, 2024 Reg Anesth Pain	Conference abstract / single case report	N=1 (34-year-old man) Follow-up: 42 days to	Severe mangled UE with marked tissue loss, multiple open comminuted fractures, muscular	Novel adjunct protocol: daily ozone autohemotherapy + supraclavicular regional	Significant tissue improvement after first ozone session; reduced putrescent tissue, improved limb perfusion. Progressive recovery led to definitive osteosynthesis and flap grafting at day 42. Limb salvage achieved. Ozone therapy +

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	Med (Abstract P179, ESRA)		definitive surgery	necrosis → septic shock, rhabdomyolysis, multi-organ failure. High disarticulation risk.	anaesthesia + VAC therapy + surgical curettages vs conventional management	regional anaesthesia proposed as synergistic to reduce inflammation and recruit microcirculation. Preliminary, unvalidated, LOE V evidence.
8	Darabos N, Cesarec M, Grgurovic D et al. Croatia/USA, 2010 Mil Med	Case report with staged protocol description	N=1 (60-year-old man, left dominant) Follow-up: 12 months	Low-energy shotgun wound left arm (Gustilo IIIB); ~10cm humeral bone defect; radial nerve defect (1cm gap); MESS=7; patient refused amputation.	Salvage (staged): debridement + external fixation + epineural nerve suture → serial I&D → IM nailing + autogenous bone graft + muscle flap + STSG	Successful salvage despite MESS=7. Bone union at 12 months; no infection. Near-full radial motor reinnervation; functional shoulder, elbow, and wrist ROM restored; returned to military duty. Explicitly demonstrates MESS score of 7 should not mandate amputation — individualized approach essential.
9	Lovero S, Ruocco G, Delle Femmine P et al. Italy, 2022 Eur J Plast Surg	Systematic review (PubMed; 53 studies, 1976–2020; 66 included after screening)	66 studies (1976–2020) All study designs	Open fractures and complex limb injuries (UE and LE); all published classification and scoring systems evaluated for reliability and surgical guidance	Scoring/classification systems compared: Gustilo-Anderson, OTA-OFC, MESS, NISSSA, GHOISS, HFS-8, PSI, LSI	No ideal classification for complex UE injuries. MESS specificity for UE: 27.5% (Elsharawy et al.). MESS ≥7 salvage achieved in multiple series. UE prosthetics less efficient than LE prosthetics. Preganglionic brachial plexus lesion = contraindication to reimplant. Limb reconstruction yields better psychological outcomes than amputation (meta-analysis cited). Multidisciplinary management essential.
10	Cimbanassi S, O'Toole R, Maegele M et al. Italy/International, 2019 J Trauma Acute Care Surg (Milan ICC, Dec 2017; 14 scientific societies; 200 delegates)	International Consensus Conference + systematic review (PRISMA, GRADE)	124 papers reviewed (2000–2017) 20 papers for mangled extremity Level of Evidence: II overall	Adult multi-trauma patients with mangled extremities (GA type IIIB/IIIC); endorsed by AAST, ESTES, WSES, SIOT, AO Italy and others	Salvage vs amputation; DCO vs ETC strategies; scoring systems evaluated by international expert panel	Consensus: 'Reconstructive efforts should be encouraged for complex UE injuries' (GoR 2B). Scores cannot be sole criterion for amputation (GoR 1B). ~30% abandon UE prostheses. Replantation superior to prosthetics: MHQ 47.2 vs 35.1 ($p<0.001$) and lower DASH score (Pet et al., n=31). MESS sensitivity 46% for all limbs. Salvage considered unless life-threatening (GoR 1C).
11	Nayar SK, Alcock HMF, Edwards DS. UK, 2022 Eur J Orthop Surg Traumatol (PRISMA; PROSPERO-registered; ROBINS-I bias tool)	Systematic review (MEDLINE, EMBASE, Cochrane)	15 studies N=6,113 total (141 amputation; 5,972 salvage)	Upper limb major trauma; all study types; English language; all levels of UE injury from hand to proximal arm	Primary amputation (n=141) vs limb salvage (n=5,972); scoring system performance evaluated	Amputation indicated when ≥2 of: haemodynamic instability, extensive concurrent tissue/vascular/nerve injuries, prolonged ischaemia, blunt arterial or crush injury. MESS alone insufficient predictor; MESI may be more precise. MESS <7 and/or MESI <20 → salvage plausible. Comparable functional/psychological outcomes between modalities in matched groups. Multidisciplinary team and patient choice essential. LOE predominantly IV.
12	Yoneda H, Takeda S, Saeki M, Iwatsuki K, Yamamoto M, Tatebe M, Hirata H. Japan.	Systematic review and meta-analysis	10 studies N=338 (MESS analysis; upper	Mangled upper extremity; studies reporting scoring system used and individual treatment	MESS performance for predicting amputation vs limb salvage in UE injuries;	Pooled MESS sensitivity 0.95 (95% CI 0.69–0.99); specificity 0.81 (0.65–0.91); AUROC 0.95 (0.93–0.97). Limb salvage achieved in ≥20% of patients with MESS above amputation threshold. Lower specificity in isolated vascular injury

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	Injury. 2024 Apr;55(4):111447. PMID: 38417237	(English + Japanese literature; 3 databases; 1985–Jan 2022; QUADAS-2 quality assessment)	extremity only)	outcome (salvage or amputation) as primary endpoint	subgroup analysis for isolated vascular injuries	subgroup. Scoring systems poorly predict UE salvageability and should NOT be used to justify amputation. Limb salvage preferred given prosthetic functional limitations.
13	Graham B, Adkins P, Tsai TM, Firrell J, Breidenbach WC. Canada, 1998 J Hand Surg Am (Carroll test functional evaluation)	Retrospective comparative study	N=44 (22 replants; 22 amputees) Matched by amputation level	UE traumatic amputation at or proximal to the wrist; replantation vs revision amputation with prosthetic fitting; adults and children	Replantation (n=22) vs revision amputation + prosthetic rehabilitation (n=22); subgroup analysis: below-elbow adults	Replantation: 36% excellent/good outcomes vs 0% in prosthetic group. Below-elbow adult subgroup: 50% excellent/good replantation vs 0% prosthetics. Younger patients + more distal injuries = best replantation outcomes (ANCOVA, $p<0.05$). Replantation statistically superior to amputation + prosthesis. Landmark study directly demonstrating functional superiority of biological limb over prosthetic fitting.

Section 3: Results summary write-up (up to 500 words)

Across 13 studies — comprising prospective and retrospective case series, case reports, narrative reviews, systematic reviews, one quantitative meta-analysis, and an international consensus conference — the evidence consistently supports limb salvage as the primary goal in major upper limb crush injuries, with prosthetic alternatives consistently inferior in function, tolerability, and availability.

Evidence on scoring systems: The only quantitative meta-analysis on this topic (Paper 12, 2024, N=338, 10 studies) reported a pooled MESS specificity of 0.81 (95% CI 0.65–0.91) for upper extremity injuries, meaning limb salvage was achieved in at least 20% of patients above the amputation threshold. The largest systematic review (Paper 11, Nayar 2022, N=6,113) confirms MESS alone is insufficient and identifies MESI as a more precise tool; MESI <20 supports salvage as a plausible option. Kumar et al. (Paper 1) demonstrated MESI to be more reliable than MESS in a prospective upper limb series. The Milan ICC (Paper 10) found MESS sensitivity of only 46% for all mangled extremities. Multiple studies (Papers 2, 9, 10, 11, 12) uniformly conclude that no scoring system should be used as the sole criterion for upper extremity amputation.

Evidence on prosthesis limitations and functional outcomes: Five papers (Papers 3, 6, 9, 10, 11) consistently report that up to 30% of upper limb amputees abandon their prostheses. Graham et al. (Paper 13) — the landmark comparative study — demonstrated replantation produced excellent or good outcomes in 36% of cases versus 0% in the prosthetic group using the Carroll functional test; for matched below-elbow adults this was 50% vs 0%. Pet et al. (cited in Paper 10) reported significantly higher MHQ scores for replantation versus prosthetic rehabilitation (47.2 vs 35.1, $p<0.001$) alongside lower DASH disability scores. Even modern bionic prostheses cannot replicate biological sensory feedback and fine motor control (Paper 6).

Evidence on salvage feasibility: Levin et al. (Paper 5) achieved salvage in all 25 patients with Grade III upper extremity open fractures, though outcomes were often fair/poor in severe crush/blast mechanisms — reinforcing that salvage feasibility and functional recovery are distinct outcomes. Bumbasirevic 2012 (Paper 3) confirms early complete reconstruction within 72 hours produces superior results to delayed procedures. The global amputation rate has declined from approximately 60% in World War II to approximately 10% in modern trauma care (Paper 6), reflecting the expanding reach of microsurgical reconstruction.

Evidence on prosthesis availability in resource-limited settings: No published formal health-economic analyses of upper extremity prosthetics in low- and middle-income countries were identified. However, the consistent narrative across multiple papers (Papers 1, 3, 4, 6) is that upper limb prostheses are prohibitively expensive, technically demanding, and largely inaccessible. Kumar et al. (Paper 1) note explicitly that even a non-functional 'woody' upper limb is well accepted in their Indian patient population because prosthetic alternatives are financially and practically unreachable. Heim et al. (Paper 4) demonstrate that even in a setting where prosthetics were financially accessible, psychological body image integration drove a patient to retain a 25-year-old anaesthetic, functionless limb — underscoring that the argument for salvage extends beyond economics.

The available case reports further demonstrated that even highly contaminated or apparently unsalvageable injuries may occasionally be reconstructed successfully through staged multidisciplinary management. Finally, Heim et al. (Paper 4) highlighted the importance of patient values, demonstrating that even severely impaired limbs may retain considerable psychological significance.

Section 4: Discussion (<1000 words)

The convergent evidence from three decades of literature — spanning case series, systematic reviews, and international consensus — consistently supports prioritizing limb salvage in major upper limb crush injuries. Four principal domains inform this recommendation.

Inadequacy of current scoring systems for the upper extremity: The MESS, originally designed for lower extremity injuries, has been widely applied to upper limb trauma without adequate validation. The only quantitative meta-analysis available (Paper 12, N=338) reports a pooled specificity of 0.81, confirming that approximately 1 in 5 patients above the conventional amputation threshold can achieve successful salvage. Lovero et al. (Paper 9) cite a MESS specificity as low as 27.5% when applied to combined upper and lower extremity injuries. The Nayar systematic review (Paper 11) — the largest in this field at 6,113 patients — concludes that MESS alone is insufficient for upper limb decision-making, and both the Milan ICC (Paper 10, GoR 1B) and the 2024 meta-analysis (Paper 12) explicitly state that scoring systems should not be used as the sole criterion for amputation. The MESI may offer greater precision for upper extremity cases (Papers 1, 11), though it equally lacks prospective upper-limb-specific validation. In the absence of a validated upper extremity scoring system, clinical judgment informed by a structured multidisciplinary assessment remains paramount.

Unique anatomy of the upper extremity justifying a salvage-first approach: The upper limb's anatomical characteristics support a more persistent salvage strategy than the lower limb. Its richer collateral arterial network means that isolated major vessel occlusion is less likely to result in irreversible ischaemia. The smaller muscle mass reduces the risk of reperfusion injury and crush syndrome. The extended warm ischaemia tolerance — 8–10 hours for the arm and up to 24 hours of cold ischaemia for the hand and digits (Papers 2, 3, 6) — allows more time for complex reconstruction without the urgency imposed by lower limb physiology. These distinct properties explain why scores calibrated for lower extremity physiology systematically overestimate amputation risk in upper limb injuries.

Functional superiority of salvage over prosthetic rehabilitation: The evidence consistently demonstrates that biological limb preservation outperforms prosthetic rehabilitation when salvage is technically achievable. Graham et al. (Paper 13) provide the most direct comparison: using the Carroll functional test in matched groups, replantation produced excellent or good outcomes in 36% of cases versus 0% in the prosthetic group — rising to 50% versus 0% for below-elbow injuries. Pet et al. (cited in Paper 10) corroborated this with validated patient-reported measures (MHQ 47.2 vs 35.1, $p<0.001$; lower DASH scores), confirming superior overall function, activities of daily living performance, and patient satisfaction with replantation. Miller et al. (Paper 2) emphasise that salvage of even a portion of the hand's prehensile and sensory function frequently markedly improves quality of life and outperforms prosthetics — particularly for the thumb and index finger, which together account for the majority of hand function.

Prosthesis limitations and the role of resource availability: Unlike lower extremity prosthetics, where functional ambulation is broadly achievable, upper limb prostheses cannot replicate sensory richness, dexterity, proprioception, or fine motor control. Up to 30% of upper limb amputees abandon their devices entirely (Papers 3, 6, 10, 11), and phantom limb pain affects 30–79% of amputees (Paper 3). Bionic prostheses incorporating targeted muscle reinnervation and direct nerve interfacing represent a promising frontier (Paper 6), but remain expensive, technically specialized, and largely unavailable outside high-income healthcare systems. In resource-limited settings — which represent a significant portion of the global trauma burden — functional upper limb prostheses are even less accessible, reinforcing the argument for salvage-first in these contexts. The research question directly addresses this disparity: when prosthetic rehabilitation is neither functionally equivalent nor practically accessible, the threshold for limb salvage should be set as low as safely possible.

When primary amputation remains appropriate: Despite the evidence favouring salvage, primary amputation remains indicated in specific circumstances: uncontrollable haemodynamic instability where the mangled extremity constitutes a life-threatening burden, irreversible ischaemia beyond safe reconstruction windows, extensive multi-level destruction with no viable tissue for reconstruction, or preganglionic brachial plexus avulsion rendering meaningful nerve recovery impossible (Papers 10, 11). The decision must remain individualized, multidisciplinary, and — where patient capacity allows — incorporate informed patient preference (Papers 2, 11). Primary amputation should be regarded as a deliberate treatment choice rather than a failure, enabling earlier rehabilitation when salvage is genuinely not feasible.

The above rationale extends beyond simple anatomical preservation and includes restoration of sensibility, positioning, dexterity, body image and psychological wellbeing.

Section 5: Risk of bias of included studies

MODERATE

The evidence base is heterogeneous in quality. The highest-quality evidence comes from one quantitative systematic review and meta-analysis (Paper 12, LOE I) and two PRISMA-compliant systematic reviews (Papers 11 and 9, LOE II–III). One international consensus conference with systematic literature review contributes Level II evidence (Paper 10). The remaining studies comprise narrative expert reviews (Papers 2, 3, 6, LOE V), retrospective case series (Papers 1, 5, 13, LOE III–IV), and case reports (Papers 4, 7, 8, LOE V). No randomised controlled trials exist. The overall risk of bias is therefore MODERATE, with the consistent direction of findings across heterogeneous study designs providing substantive reassurance regarding the validity of the conclusions.

Section 5: Response/Recommendation (1-2 lines as a conclusion and recommendation statement for the question)

In major crush injuries of the upper limb, limb salvage should be prioritized when the patient's life is not threatened, given the functional superiority of biological limb preservation over prosthetic alternatives, the poor tolerability and limited global availability of upper limb prostheses — particularly in resource-limited settings — the absence of any validated scoring system that reliably justifies primary amputation in the upper extremity, and the consistent recommendation of international expert consensus in favour of reconstructive efforts for complex upper limb injuries.

Section 6: Level/strength of Evidence:

MODERATE with justification.

The evidence base comprises: one systematic review and meta-analysis (LOE I, Paper 12); two PRISMA-compliant systematic reviews (LOE II–III, Papers 11, 9); one international consensus conference with systematic literature review (LOE II, Paper 10); one critical analysis review (LOE II, Paper 2); two narrative expert reviews (LOE V, Papers 3, 6); two retrospective case series (LOE IV, Papers 1, 5); one retrospective comparative study (LOE III, Paper 13); and three case reports/abstracts (LOE V, Papers 4, 7, 8). No randomised controlled trials exist on this specific topic, and large prospective cohort studies specifically addressing upper limb mangled injuries are absent. These limitations restrict the overall evidence strength to MODERATE. However, the consistent direction of evidence across all study designs — uniformly favouring salvage and highlighting the functional inferiority and limited availability of upper limb prosthetics — provides a sufficient basis for a strong clinical recommendation in the context of this research question.

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