Consensus Statement on the Pre-Hospital Management of Crush Injury

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Introduction

Guidance is required for UK pre-hospital care providers managing patients with suspected crush injury to minimise preventable morbidity and mortality. This consensus statement gives relevant and practicable recommendations following a structured evidence review and a consensus process. Differences between this and previous guidance reflect, in part, the context for which these recommendations are intended. The role of aggressive fluid administration and concerns regarding hyperkalaemia are de-emphasised. This consensus statement may also be relevant for providers working in other developed healthcare systems.

Background

The incidence of crush injury, which may result in crush syndrome, is unknown in the UK. Despite encountering cases infrequently, pre-hospital and hospital care providers must have a strategy to manage patients at risk of these conditions in order to minimise preventable morbidity and mortality. The previous FPHC statement[1] on this topic was published in 2003 and relevant international guidelines focus on the management of multiple patients in the context of natural disasters. There is therefore a need to provide evidence-based recommendations relevant to UK providers.

Crush injury is a direct injury resulting from compression. While any part of the body may be injured by a compressing force, injuries to the head, chest and abdomen should be managed in line with established trauma protocols and were not a focus of this evidence review and consensus process. Unless otherwise specified, this document mainly refers to crush injury of the limbs and areas of muscle bulk such as the gluteal region.

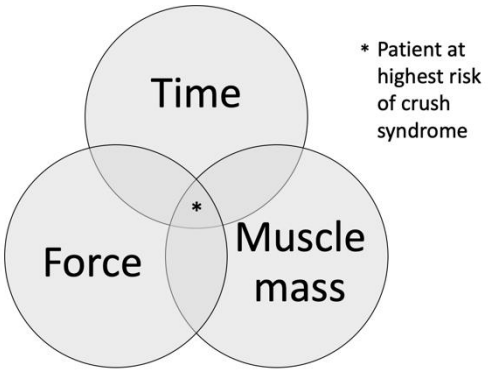
Crush syndrome is the systemic manifestation of ischaemia and muscle cell damage following crush injury. Increasingly recognised in the first half of the 20th century[2], in 1999 the mortality rate of patients with crush syndrome was estimated at 20% [3]. Potential clinical issues associated with crush syndrome can be categorised into early manifestations and later complications. It is hypothesised that, immediately following release of a compressing force and on subsequent reperfusion of an ischaemic area, there may be significant fluid redistribution and release of lactic acid and potassium[4]. Later complications include Acute Kidney Injury following renal deposition of myoglobin[2].

Risk factors

Factors increasing the risk of developing crush syndrome include a greater mass of injured muscle as well as the degree and duration of compression[5,6] (Figure 1). Other risk factors also need to be considered such as co-morbid conditions (e.g. pre-existing Chronic Kidney Disease) and hydration status (e.g. prolonged entrapment). Due to the difficulties inherent in assessing patients with potential

crush injury (e.g. an injured limb may be hidden from view), the risk of crush syndrome developing can be difficult to predict.

Figure 1. Risk factors for developing crush syndrome. Of these, time is the only modifiable risk factor.



Patient specific examples

Patients are at risk of crush syndrome in the following illustrative scenarios:

- Prolonged period lying on a hard surface following a medical event resulting in incapacitation: the force is low, but duration is high.

- Pedestrian's lower limbs rolled over by a heavy vehicle. Muscle mass affected is large and compressive force is large, even if the duration of compression is shorter.

- Limb crushed in building collapse. Muscle mass affected, force and duration may all be high.

It is not possible to define specific criteria to accurately predict whether crush syndrome will occur.

Consensus Recommendations

1. **The earliest possible safe release of the compressing force should be a treatment priority. [Grade: C]**

The duration of compression is a key modifiable risk factor. As such, early release should be prioritised. This will likely require close multi-agency working. By its nature, crush injury may occur in hazardous settings. Safety protocols are paramount to prevent further injury to casualties or rescuers.

2. **Not all entrapped patients will have suffered significant crush injury, although the risk should be considered. [Grade: C]**

It must be recognised that physical entrapment is not the same as crush injury. While entrapped patients may be at risk, the degree of crush injury and development of crush syndrome will depend on the factors above (Figure 1).

3. **Concerns regarding potential crush injury should not impede trauma care, including the management of bleeding. The administration of blood products, if available, should be considered in line with local protocols following trauma. [Grade: D]**

“Patients who are physically entrapped [in a vehicle] as a result of intrusion have a high likelihood of significant injuries”[7], as will those with other mechanisms putting them at risk of crush injury such as industrial accidents or building collapse. In the context of expected UK response times, managing these injuries in line with standard trauma protocols (using a <C>ABCDE approach) initially is likely to bring most benefit.

4. **The over-arching aim should be the rapid evacuation of patients with suspected crush injury to definitive care carrying out essential life-saving interventions en route. Patients with significant suspected crush injuries should usually be conveyed to a Major Trauma Centre. [Grade: C]**

Given the potential injury burden requiring orthoplastic surgical input and specialist critical care interventions, patients with significant suspected crush injuries should usually be conveyed to a Major Trauma Centre. Patients will benefit from having access to the specialist assessment and care in a timely manner.

5. **In the context of a large-scale incident with multiple crush-injured patients, regional plans for casualty distribution should be enacted. If regional resources are overwhelmed, destination decisions should be based on the availability of trauma expertise and renal replacement therapy and supported by national coordination. [Grade: C]**

If local Major Trauma Centre capacity is overwhelmed, then casualties should be distributed in a coordinated manner to match care needs with capability and capacity.

6. **Analgesia should be given early within the rescuers' scope of practice [Grade: D].**

Crush injuries may be extremely painful and this may worsen as the compressing force is removed. Analgesia is crucial for symptomatic relief and to facilitate evacuation. Multiple options are now available in UK pre-hospital care and the choice of analgesic will be governed by patient factors, availability, practitioner skillset and potential side-effects.

7. **While planning safe and timely extrication, intravenous (IV) or intraosseous (IO) access should be established in the trapped patient, if practicable, and fluids (ideally warmed 0.9% sodium chloride) should be available in case of deterioration. These interventions should not delay extrication. [Grade: C]**

In addition to hypovolaemic shock following haemorrhage, crush injured patients may be at risk of distributive shock following release of a compressive force[4]. Theoretically, a sudden increase in perfusion could lead to reactive hyperaemia in previously ischaemic tissues. This may lead to systemic vasodilation from toxic metabolites and third space losses due to inflammatory processes and damaged capillaries. There is uncertainty as to how frequently this may occur due to only isolated case reports in the literature. In the experience of the panel, concerns about precipitating shock may significantly delay extrication and evacuation to definitive care.

8. **Fluid administration for patients with suspected crush injury should be individualised. Practitioners should consider the likely other injuries present, the muscle mass crushed, the degree and duration of compression and patient factors such as comorbidity and hydration status. Isotonic crystalloid solutions without potassium (e.g. 0.9% sodium chloride) should be used initially. These should be warmed, if possible. [Grade: C]**

Significant attention is given in international crush injury guidance to the potential benefits of liberal fluid administration in reducing the risk of clinically significant acute kidney injury (AKI). Table 2 Retrospective observational evidence suggests that early, aggressive fluid resuscitation and ongoing administration following significant crush injury (e.g. >6L per day in adults) is associated with a reduced risk of AKI requiring renal replacement therapy [8]. BestBET- A However, what little evidence exists is based on populations injured in natural disasters. Frequently, they have endured days under the rubble before extrication and those with significant traumatic injuries, for example causing haemorrhage, may have died before help arrives. Following rescue, access to advanced resources (e.g. haemofiltration) may be limited.

Box 1. Case example illustrating potential 'pre-loading' with IV fluid.

Acknowledging the lack of evidence relevant to this context but seeking to give some pragmatic figures for the pre-hospital care provider, the panel considered the following example:

An 80 kg, normally fit and well adult is trapped by the wheel of a lorry across one thigh. No external haemorrhage is seen but there is suspicion of a pelvic injury. While a plan is made to move the lorry, a cannula is inserted and analgesia administered. Following this the patient is normotensive with a heart rate of 90 bpm. The compressing force will be removed approximately 90 minutes after the patient became trapped.

The consensus view was that it would be reasonable to administer 500ml of warmed 0.9% sodium chloride over 10 minutes prior to release with a further bolus prepared in case of deterioration. This must not delay removal of the compressing force.

In the UK context, most patients suffering from crush injury will be accessed and extricated in a timely manner, although there will be exceptions to this. Assuming timely arrival of pre-hospital care resources, it is necessary to focus on the standard management of traumatic injuries (e.g. controlling bleeding) before addressing specific crush injury management. In this context, administration of large volumes of crystalloid fluid may worsen trauma-induced coagulopathy with more immediate adverse consequences for the patient. Liberal fluid administration may also worsen subsequent compartment syndrome.

Early urine output monitoring may be considered to guide ongoing fluid administration, particularly if a delay is anticipated to arrival at definitive care, although this will not always be practicable or necessary.

Guidance from the Renal Disaster Relief Task Force advocates more generous fluid administration[9]. In austere settings with delayed extrication and limited access to advanced hospital treatments, its use may be considered in patients where crush injury is felt to be the predominant pathology.

9. **The application of tourniquets in patients with crush injury should be reserved for the management of catastrophic haemorrhage. [Grade: C]**

Loose pre-positioning of tourniquets as distally as possible prior to removal of a compressive force is a sensible precaution so they can be rapidly applied in the event of catastrophic haemorrhage. If not required they should be removed after release to avoid confusion. Pre-hospital amputation should be a last resort to facilitate urgent evacuation where patient safety is imminently threatened. BestBET- B

10. **During entrapment and evacuation, interval cardiac monitoring may be appropriate. If dynamic ECG changes are seen consistent with hyperkalaemia, then temporising treatment should be considered. Pre-hospital point of care testing, if available, may provide more definitive information or reassurance. [Grade: D]**

Considerable concern has been expressed by pre-hospital practitioners about the potential for life threatening hyperkalaemia due to muscle cell damage, particularly following removal of the crushing force. Despite this plausible concern, the limited available evidence[10] suggests that clinically significant hyperkalaemia is uncommon, even following severe injury and prolonged entrapment. BestBET- C Continuous cardiac monitoring, as has previously been advocated, may be neither sensitive nor specific to detect hyperkalaemia[11] and has the potential to hamper rescue efforts.

In the presence of proven hyperkalaemia with an abnormal ECG or dynamic ECG changes, IV calcium should be administered with the aim of stabilising the myocardium[12] (10mL 10% calcium chloride or 30mL 10% calcium gluconate by slow IV injection[13]). To temporarily reduce plasma potassium levels, administering 10mg nebulised salbutamol is a widely available option[12] in the pre-hospital setting. IV bicarbonate (in the presence of co-existing hyperkalaemia and acidosis) may be considered with expert support but co-administration of insulin and glucose is unlikely to be practicable.

11. Prophylactic treatment based on the presumed presence of hyperkalaemia following crush injury is not supported. [Grade: C]

Given the limited likelihood of clinically significant hyperkalaemia in patients with suspected crush injury, prophylactic treatment is not supported. However, it is sensible to avoid fluids containing potassium and drugs (e.g. suxamethonium) which may increase potassium levels.

12. The use of bicarbonate administration, targeted urinary alkalinisation or forced diuresis is not routinely recommended. [Grade: C]

Despite theoretical benefits, no convincing evidence was found to support the view that bicarbonate administration, targeted urinary alkalinisation or forced diuresis reduce morbidity or mortality following crush injury in humans. The panel does not recommend their use in the early management of patients with suspected crush injury in routine UK practice. BestBET- D BestBET- E

13. Patients with crush syndrome may develop acute kidney injury requiring access to renal replacement therapy. [Grade: C]

Although no evidence was found to support prophylactic renal replacement therapy in cases of crush syndrome, patients are certainly at risk of developing renal failure. BestBET- F This should be considered in destination decisions to minimise the need for secondary transfers. Renal replacement therapy in crush syndrome should be initiated according to standard indications (oliguria/anuria, volume overload or severe uraemia/hyperkalaemia/acidosis).

14. Fasciotomies, if required, should be performed according to standard indications and are not recommended in the pre-hospital setting. [Grade: C]

A crushed limb is at risk of developing compartment syndrome. In hospital, there may be a role for intravenous mannitol in the conservative management of compartment syndrome (contraindicated in anuria) and fasciotomies may be required for surgical management according to local practice guidelines.

Prophylactic fasciotomies outside of standard indications are not supported.

BestBET- G

15. Better data are needed to guide future recommendations. Consideration should be given to retrospectively reviewing patients diagnosed with crush injury in trauma registries and a pre-approved study protocol could be considered to be instituted in the context of a mass casualty event. [Grade: D]

Patients with crush injury and crush syndrome are heterogenous and present infrequently to developed healthcare systems. Gathering data and conducting controlled trials during large-scale incidents or natural disasters is challenging. As such, the paucity of evidence to guide management decisions is anticipated. This is borne out by the fact that all recommendations are made with a low level of certainty.

Alternative hypothesised treatment strategies

There is insufficient evidence to support the following treatment strategies that have been hypothesised to be of potential benefit following crush injury. Hyperbaric oxygen therapy has been used as an adjunct in wound healing following crush injury, its use is not widespread in the UK. Gastric Pentadecapeptide BPC 157 has shown promise in animal models to potentially aid wound healing. Data in rats shows potential benefits of localised cooling following crush injury. Other possible therapeutic interventions may aim to reduce mitochondrial dysfunction and oxidative stress or to modulate the inflammatory response and apoptosis.

Conclusion

This consensus statement has been formed after an expert panel reviewed the latest available evidence relevant to the management of patients with crush injury and crush syndrome in the United Kingdom. We acknowledge there is a lack of high-quality evidence to guide these consensus recommendations, but it is hoped this document will enable a consistent standard of care for patients.

There are differences between this and other previous guidance, particularly the de-emphasising of aggressive fluid administration and of concerns regarding hyperkalaemia. These differences are summarised in Table 2 and reflect, in part, the different context for which this guidance is intended. This consensus statement may have relevance to others working in developed healthcare systems.

Appendix A - References

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Appendix B - Methods

The FPHC convened a panel of clinicians including expertise in Pre-Hospital and Emergency Medicine, Anaesthesia, UK Urban Search and Rescue (USAR), mass casualty events and evidence review. After surveying other published guidance and establishing potentially contentious issues, relevant clinical questions relating to the management of crush injury and crush syndrome were agreed at a virtual panel meeting and resultant correspondence. These questions are summarised in Table 1.

Table 1. The following questions were used to guide the BestBET evidence reviews.

- What is the optimum fluid resuscitation strategy in suspected crush injury?
- Is there a role for tourniquets or amputation to mitigate the risk of crush syndrome in patients with crush injury?
- What is the optimum strategy to manage potential hyperkalaemia associated with crush injury?
- Is there a role for IV bicarbonate in suspected crush injury?
- Does solute-alkaline diuresis reduce morbidity or mortality in patients with crush injury?
- Does early haemofiltration reduce morbidity or mortality in patients with crush injury?
- What is the optimum strategy for managing compartment syndrome in the context of crush injury?
- What are the remaining unanswered questions/areas to watch for the future based on the search results?

A literature search, performed in December 2022, yielded 367 potential sources. Appendix E A team of volunteers was recruited from current UK paramedics and doctors to screen articles and generate evidence summaries. Title and abstract screening was carried out by two blinded investigators, with any discrepancies adjudicated by a third. This identified relevant articles and classified them into broad clinical areas. Each question was allocated to two investigators who reviewed the full text of the articles identified and summarised the most relevant evidence in a BestBET format[14]. This multi-BestBET method was chosen due to the heterogeneity of evidence anticipated.

BestBET results were reviewed by the panel and the resulting guidance agreed by consensus following written and verbal discussion. As in other FPHC consensus statements, the GRADE classification system[15] was used to classify recommendations. Prior to submission, internal peer review was carried out by

expert clinicians not involved in the original process and recommendations updated as necessary by the panel.

An updated literature search was performed in November 2024. Appendix E The 84 articles identified included observational studies following two earthquakes on 06 February 2023 in Turkey and Northern Syria. One new position statement was found from the National Association of EMS Physicians regarding management of the entrapped patient, which aligned with previous guidance for managing those at risk of crush syndrome in the humanitarian setting. No RCTs were identified. No evidence was identified that challenged the outcome of BestBETs completed using the earlier literature search.

The FPHC wish to acknowledge and thank the authors and many contributors below:

Lead author and panel/evidence review co-ordinator: Felix Wood[1,2]

Expert panel:
Phil Cowburn[3,4,5,6], Jason Smith[1,2], Lauren Weekes[2,7,8], Tim Godfrey[4,5,9]
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Internal peer review:
Richard Lyon, Tim Nutbeam, Ian Greaves

FPHC review:
Charlotte Haldane, Fionna Moore, Chris Boyle, Matthew Newport

The FPHC wish to express thanks for reviewing and endorsing this consensus statement to:

Joint Royal Colleges Ambulance Liaison Committee (JRCALC)

Appendix C - Summary of differences from other relevant guidance

Table 2. Summary of differences from other relevant guidance.

	Fluid management	Hyperkalaemia	Bicarbonate administration	Urinary alkalinisation	Mannitol administration
2024 FPHC consensus statement	Tailored	POC / intermittent ECG	Not routinely	Not recommended	Not recommended
2003 FPHC consensus statement[1]	Liberal administration	No recommendation	Identified as an unknown	Recommended	Recommended
2009 ACEP[16]	Liberal	Consider pre-emptive treatment	For urinary alkalisation	Recommended	Recommended
2012 US CDC[17]	Liberal	Consider pre-emptive treatment	Recommended	Recommended	Recommended
2012 Renal Disaster Relief Task Force[18]	Tailored	Measure ASAP in hospital	Consider in hospital for hyperkalaemia or acidosis	Not recommended	May consider
2023 Scottish Ambulance Service[19]	Early administration	ECG	In hyperkalaemia	Not recommended	Not recommended
2023 INSARAG[5]	Initial bolus, re-evaluate	Treat if suspected	Bolus	Consider	Not recommended

Appendix D - Hierarchy of evidence & grading of recommendations

Hierarchy of Evidence

Level of evidence	Type of evidence
Ia	Evidence from systematic reviews or meta-analysis of randomised controlled trials
Ib	Evidence from at least one randomised controlled trial
IIa	Evidence from at least one controlled study without randomisation
IIb	Evidence from at least one other type of quasi experimental study
III	Evidence from non-experimental descriptive studies such as comparative studies, correlation studies and case-control studies
IV	Evidence from expert committee reports or opinions and/or clinical experience of respected authorities

Grade of recommendation	Type of evidence
A	Based on hierarchy I evidence
B	Based on hierarchy II evidence or extrapolated from hierarchy I evidence
C	Based on hierarchy III evidence or extrapolated from hierarchy I or II evidence
D	Directly based on hierarchy IV evidence or extrapolated from hierarchy I, II or III evidence

Shekelle PG, Woolf SH, Eccles M, et al. (1999). Clinical guidelines: developing guidelines. BMJ: British Medical Journal. Feb 27;318(7183):593.

Appendix E – Literature searches

On **02 and 06 December 2022**, the following databases were searched:

Medline on EBSCO platform

CINAHL on EBSCO platform

EMBASE on Ovid platform

Limiters:

English language

Last 10 years

Conference abstracts excluded

Medline

Search ID#	Search Terms	Search Options	Results
S14	S11 OR S12	Limiters - Scholarly (Peer Reviewed) Journals; Date of Publication: 20000101-20221231; English Language	336
S13	S5 AND S9	Limiters - Scholarly (Peer Reviewed) Journals; Date of Publication: 20100101-20221231; English Language	721
S12	S3 AND S7		140
S11	S6 AND S9	Limiters - Scholarly (Peer Reviewed) Journals; English Language	435
S10	S5 AND S9		1,504
S9	S7 OR S8		6,110,372
S8	AB management OR treatment		5,343,341
S7	TI management OR treatment		1,719,727
S6	S1 OR S2 OR S3		1,709
S5	S1 OR S2 OR S3 OR S4		4,262
S4	AB "Crush injur*" OR "crush syndrome"		3,367
S3	TI "Crush injur*" OR "crush syndrome"		1,302
S2	(MM "Crush Syndrome")		789
S1	(MM "Crush Injuries+")		1,037

CINAHL

Search ID#	Search Terms	Search Options	Results
S11	S6 OR S10	Limiters - English Language; Peer Reviewed	380
S10	S5 AND S9		150
S9	S7 OR S8		731,914
S8	AB management OR treatment		357,126
S7	TI management OR treatment		468,984
S6	S1 OR S2 OR S3		346
S5	S1 OR S2 OR S3 OR S4		769
S4	AB "Crush injur*" OR "crush syndrome"		589
S3	TI "Crush injur*" OR "crush syndrome"		271
S2	(MM "Crush Syndrome")		155
S1	(MM "Crush Injuries")		48

EMBASE

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1 exp *crush trauma/ (1823)
2 *crush syndrome/ (879)
3 ("Crush injur*" or "crush syndrome").ti. (1278)
4 ("Crush injur*" or "crush syndrome").ab. (4263)
5 1 or 2 or 3 or 4 (5364)
6 1 or 2 or 3 (2218)
7 (management or treatment).ti. (2041513)
8 (management or treatment).ab. (7334872)
9 7 or 8 (8069432)
10 5 and 9 (1961)
11 6 and 9 (772)
12 1 and 9 (635)
13 3 and 9 (499)
14 limit 13 to conference abstracts (68)
15 13 not 14 (431)
16 limit 15 to (english language and yr="2000 -Current") (277)
17 from 16 keep (203)

Number of articles retrieved

Database	Total retrieved	Total included
Medline	336	223
CINAHL	380	173
EMBASE	277	203

Total retrieved from all databases	993
Total included from all databases	599
Total duplicates	232
Total included in the results	367

Articles identified for identified and categorised by title/abstract screening for consideration by BestBET authors:

Fluid resuscitation	Renal failure	Hyperkalaemia	Tourniquets/amputation	Surgical management
44	63	40	33	40

A survey of the grey literature was also conducted aiming to identify previously published international guidance.

On **19 November 2024** an updated literature search was conducted as follows:

Limiters
English language
Publication year – December 2022 – November 2024
Conference abstracts excluded

Medline

Search ID#	Search Terms	Search Options	Results
S12	S6 OR S10	Limiters - Publication Date: 20221201-20241131; English Language	338
S11	S6 OR S10		2,883
S10	S5 AND S9		1,633
S9	S7 OR S8		6,899,382
S8	AB (management OR treatment)		6,093,490
S7	TI (management OR treatment)		1,883,105
S6	S1 OR S2 OR S3		1,933
S5	S1 OR S2 OR S3 OR S4		4,477
S4	AB ("Crush injur*" OR TI "crush syndrome")		3,733
S3	TI ("Crush injur*" OR TI "crush syndrome")		1,423
S2	(MM "Crush Syndrome")		827
S1	(MM "Crush Injuries+")		1,204

CINAHL

Search ID#	Search Terms	Search Options	Results
S12	S6 OR S10	Limiters - Publication Date: 20221201-20241131; English Language	79
S11	S6 OR S10		616
S10	S5 AND S9		355
S9	S7 OR S8		1,436,541
S8	AB (management OR treatment)		1,156,786
S7	TI (management OR treatment)		521,070
S6	S1 OR S2 OR S3		403
S5	S1 OR S2 OR S3 OR S4		834
S4	AB ("Crush injur*" OR "crush syndrome")		605
S3	TI ("Crush injur*" OR "crush syndrome")		306
S2	(MM "Crush Syndrome")		159
S1	(MM "Crush Injuries")		76

EMBASE

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1 exp *crush trauma/ (2112)
2 exp *crush syndrome/ (1051)
3 ("Crush injur*" or "crush syndrome").ti. (1417)
4 ("Crush injur*" or "crush syndrome").ab. (4703)
5 1 or 2 or 3 or 4 (5997)
6 1 or 2 or 3 (2540)
7 (management or treatment).ti. (2268554)
8 (management or treatment).ab. (8379265)
9 7 or 8 (9166178)
10 5 and 9 (2296)
11 6 or 10 (3898)
12 limit 11 to english language (3290)
13 limit 12 to conference abstracts (610)
14 12 not 13 (2680)
15 limit 14 to dd=20221130-20241119 (53)
16 from 15 keep (9)

Number of articles retrieved

Database	**Total retrieved**	**Total included**
Medline	338	82
CINAHL	79	31
EMBASE	53	9

Total retrieved from all databases	470
Total included from all databases	122
Total duplicates	38
Total included in the results	84

Appendix F – BestBET Evidence Summaries

Best Evidence Topic Report A	
Title	What is the optimum fluid resuscitation strategy in suspected crush injury?
Report by	Rhiannon Wilkinson
Checked by	Felix Wood
Clinical question	**In patients with suspected crush injury, what fluid resuscitation strategies demonstrate improved morbidity and mortality?**
Search outcome	• 44 abstracts identified for review • No systematic reviews or clinical trials were found comparing fluid strategies in crush injury. • Thirteen articles were identified for full article screening • Five are summarised below

Author, date and country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Altintepe et el., 2007, Turkey[1]	Seven rhabdomyolysis patients rescued from Zümrüt apartment collapse	Case Series	Requirement for haemodialysis	Of 29 individuals rescued from the rubble 9 were hospitalised for crush syndrome and 7 followed up in this study (remaining 2 were excluded due to transfer to centres where records were inaccessible) Entrapped for approximately 11.1 +/- 7.3 hours. Highest CPK of the patients was 79049. Intervention: Primary intervention - prophylactic mannitol-bicarbonate solution (40mEq Sodium Bicarbonate, 50ml of 50%	Small number of patients Loss of 2 to follow up – extracted on day 6&7 (those included extracted within 24hr) Authors attribute the recovery of 5 individuals not requiring haemodialysis to mannitol-bicarbonate without consideration of other factors

				mannitol into 1000ml 0.45%NaCl and 5% Dextrose). Between 4-8L of fluid daily, on average 5580 +/- 3300ml of fluid within first 24 hr. Bicarbonate was adjusted to urinary pH. Other - CVP monitoring, Result: ● 2 of 7 developed acute renal failure and required haemodialysis for hyperkalaemia (one required 69 units of blood & plasma and the other 35 units of blood & plasma due to bleeding from fasciotomy wounds) ● 5 of 7 required fasciotomies (8 fasciotomies total) ● No cases of permanent renal failure or death	
Ensari et al., 2002, Turkey[2]	38 individuals diagnosed as Crush Injury Marmara Earthquake	Case Series	Trapped time, time spent between event and beginning treatment (admission time), site and extent of injury, systolic blood pressure, heart rate, central venous pressure, blood studies and number of fasciotomies.	Of 38 individuals presenting with Crush Injury 27 developed Crush Syndrome (ARF). Of these 27, 10 required dialysis and 17 did not. These two groups were compared to see if delayed fluid therapy had contributed to risk of dialysis. Intervention: IVF, mannitol, diuretics, alkalization to target urine pH >6.5. No	Study does not detail how much fluid the individuals received Small study

				intravenous fluids given pre-hospital due to scale of incident. Result ● 17 recovered with the above regime while 10 proceeded to dialysis. ● All 27 had Crush Injury in at least a lower limb. In the dialysis group a significantly higher number had Crush Injury in more than one extremity (80% vs 29%) ● The dialysis group had a significantly lower SBP and CVP at time of admission, and higher creatinine, BUN, CK, CRP and fibrinogen. No significant difference in K+ ● Between the two groups there was no significant difference in age, trapped time, admission time (time to treatment commencing). Author concludes therefore that even delayed fluid therapy can prevent development of ARF	

Najafi et al, 2011, America[3]	Individuals >15 years old with rhabdomyolysis in the aftermath of the BAM earthquake. No history of CKD or other causes for ARF	Multicentre cohort	Effect of DFT (delayed fluid therapy), TUR (time under rubble), level of CPK and VFR (volume of IVF received per day) on the formation of AKI and need for dialysis	638 individuals included, 134 of which had AKI and 110 of these requiring dialysis Results ● DFT in AKI group was significantly longer when compared to rhabdomyolysis group (2.8 days vs 1.2, P<0.001) ● TUR in AKI group was significantly longer when compared to rhabdomyolysis group (6.3 hours vs 2.4. P<0.001). ● VFR in AKI group was significantly less when compared to rhabdomyolysis group (2.8 vs 4L per day for first 5 days, P<0.001). It was noted in the Univariate analysis that as the VFR in first 5 days increases from <3L to >6L the need for dialysis and incidence of AKI significantly decreases (P<0.001 and P<0.05). This can be broken down further ● An increase in VFR from <1L to </=3L causes a 19.2%ARR and 48.9%RRR of AKI.	Appears a strong study. Data was collected contemporaneously. Questionnaire designed on day of earthquake, and there was a designated individual at each site to ensure data collection. Limitations Data on oral intake was not collected due to lack of precise records. No data on type of fluids used. Multicentre study with different hospitals using different fluid protocols

				• There is a smaller decrement in VFRs of 3-5L • Multivariate analysis - In individuals with a CPK >15000 and TUR>5 hours a VFR<3L had no significant effect, and VFR>6L had a preventative role. • Multivariate analysis – DFT lost its significance but CPK, TUR and VFR affected the occurrence of AKI and need for dialysis Conclusion: In severely traumatized patient a VFR>6L are required whereas VFR3-6L may be satisfactory in less traumatised patients.	
Sagheb et el., 2009, Iran[4]	Twenty individuals who developed acute renal failure following BAM earthquake	Cohort	Duration of acute renal failure, requirement for dialysis	• Of 20 individuals who developed acute renal failure 7 received standard fluid therapy and 13 received variable hydration and volume treatment. • Fluid therapy was 0.9% saline, as well as bicarbonate 50mmol/L, and mannitol in those with UO>20ml/hr to target 300ml/h – unclear if this is the standard or variable protocol • 15 required dialysis	Small numbers Attributes lower rates of renal failure to standard fluid therapy but no comment on the differences between the standard fluid and the variable fluid groups. The latter had longer under the rubble, and there is no comment on the injury profile across the two groups No indication as to what the variable fluid therapy was

				• Individuals received standard treatment had a significantly shorted duration of ARF (7 vs 19d, P0.008) and less need for dialysis (1 vs 6, p0.007) • Mortality = 3 individuals	No indication as to what the volume of the standard therapy was
Mardones et al 2016, Chile5	40 year old with crush injury	Case Report	AKI	• Landslide victim buried for 19 hours • Pre-hospital care commenced two hours after landslide • Victim administered 1.0L/hr 0.9% saline for 3 hours, and 0.5L/h thereafter • Victim diagnosed with compartment syndrome in left leg requiring fasciotomy, and CK 118,700 U/L • No observed increase in plasma electrolytes and no requirement for haemodialysis Comments made by the authors • Potassium containing fluids should be avoided • With the lack of RCTs aggressive early fluid therapy holds the consensus – 0.9% Saline at 1.0L/h for two hours,	• Case-Report

				followed by 0.5-1.0L/h thereafter. ● In the case of this individual AKI was prevented despite high CK scores	

Comment	Najafi et al[3] was the only identified study to quantify the relationship between volume of fluid resuscitation and acute kidney injury as an outcome. Their univariate analysis demonstrated a 19.2%ARR and 48.9%RRR of AKI when 1-3L of intravenous fluid is given per day for treatment of crush injury, when compared to less than 1L. They demonstrated a further though less dramatic decline with fluid resuscitation between 3-5L per day. However, in their multivariate analysis they did identify that individuals with markers for greater severity of injury, a CPK >15000 and TUR>5 hours, had no significant benefit when volume of resuscitation was less than or equal to 3L/day, but volumes of greater than 6L per day were preventative. This would support the suggestion that volume resuscitation needs to be tailored to the severity of injury. Current guidelines[6] recommend the use of 0.9% Saline for the treatment of crush injury at a rate of 1.0L/h for the first two hours, followed by a rate of up to 0.5L/h thereafter. This should be started in the prehospital environment if possible. Overall, it is recommended that 3-6L should be administered and further fluid should be guided by the urine output, risk of overload and the ability to provide close monitoring. Isotonic solutions are generally preferred due to the theoretical risk of contributing to hyperkalaemia with the use of potassium-containing solutions. Three of the studies above used a saline/bicarbonate/mannitol solution but the use of bicarbonate and mannitol will not be discussed further here.
Clinical bottom line	The evidence would suggest an improvement in morbidity when at least 1-6L of intravenous fluid is given per day, with higher volumes being indicated in individuals suspected of having more severe injuries and prolonged extractions.
References	1. Altintepe L, Guney I, Tonbul Z, Turk S, Mazi M, Agca E, et al. Early and Intensive Fluid Replacement Prevents Acute Renal Failure in the Crush Cases Associated with Spontaneous Collapse of an Apartment in Konya. 2007;(29:6):737–41. 2. Ensari C, Tufekcioglu O, Ayli D, Gumus T, Izdes S, Turanli S. Response to Delayed Fluid Therapy in Crush Syndrome. Nephron. 2002 May 15; 3. Najafi I, Safari S, Hosseini M, Sanadgol H, Sharifa A, Rashid FF, et al. Prophylactic fluid therapy in crushed victims of BAM earthquake. Am J Emerg Med. 2011;29. 4. Sagheb MM, Sharifian M, Roozbeh J, Moini M, Gholami K, Sadeghi H. Effect of Fluid Therapy on Prevention of Acute Renal Failure in Bam Earthquake Crush Victims. Ren Fail. 2009 Jul 7; 5. Mardones A, Arellano P, Rojas C, Gutierrez R, Oliver N, Borgna V. Prevention of Crush Syndrome through Aggressive Early Resuscitation: Clinical Case in a Buried Worker. Prehospital Disaster Med. 2016 Mar 28;31(3). 6. Sever, Mehmet S, Vanholder R. Management of Crush Victims in Mass Disasters. Clin J Am Soc Nephrol CJASN. 2013 Feb;8(2):328–35.

Best Evidence Topic Report B	
Title	Is there a role for tourniquets or amputation to mitigate the risk of crush syndrome in patients with crush injury?
Report by	Sam Wilkins, Paramedic (WMAS), Hereford
Checked by	Leo Wood
Three part question	**In [adults with suspected crush injury], does [the use of tourniquets or amputation] improve [morbidity and mortality]?**
Search outcome	• 33 articles identified for review • No studies identified comparing treatments • 3 case reports summarised below

Author, date and country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Anderson, J.L. et al., 2022, USA	Single case study of Special Operations Force Sniper who sustained crush injury.	Retrospective case review and proposed assessment and management.	No specific outcome mentioned however guidelines discussed are to improve casualty survival to and beyond definitive care.	A single case study of a special forces sniper who sustained a crush injury. A general discussion of management strategies proposed use of arterial tourniquets for pinned limbs prior to extrication to prevent reperfusion and systemic insult due to hyperkalaemia and release of myoglobin. The authors propose these secondary effects would be better managed in a hospital setting.	Single case study of 1 person, in an extreme environment. Limited generalisability to civilian population. Did not follow case through, only proposed management options.
Dhir, K., et al., 2018, USA	Single case study of a 76yr old woman who sustained a crush injury following a fall.	Retrospective case review and proposed management strategies.	Patient died in hospital on day of admission.	A single case study of a patient who developed crush syndrome from a trapped upper limb following a fall and trapping her arm in a handrail. Upon release by EMS, she suffered a hyperkalaemic cardiac arrest. No tourniquet was used. The article hypothesised as to the value of tourniquet prior to release of the mechanism in containment of toxins, until the patient reaches definitive care where these secondary effects may be managed. This raised the question as to whether a tourniquet could have prevented this patient's cardiac arrest in the pre-hospital setting.	Single case study No tourniquet actually used, authors just speculating retrospectively as to possible management options.

Badar, J. et al., 2015, USA	Single case study of a 30yr old male crushed by heavy machinery.	Retrospective case review and review of literature.	Patient made full recovery following discharge. No specific outcome measures discussed.	Case study of a patient crushed by heavy machinery. Bilateral tourniquets applied to legs to prevent reperfusion, which authors hypothesis facilitated safe extrication to hospital. Upon release of tourniquets in hospital patient experienced sudden cardiac dysrhythmia, which was successfully in the higher care centre. Patient made full recovery, with full function of both lower limbs. The authors propose the ensuing dysrhythmia would have been less well managed in the pre-hospital setting. Article proposes that, due to limited resources in the pre-hospital setting, the containment of toxins in ischaemic limbs, improves haemodynamic and cardiac membrane stability until definitive care. Any risks associated with tourniquet application such as necrosis and nerve palsies are unfounded and outweighed by benefits.	Singular case study No control Difficult to assess degree of injury, given patient made full recovery

Comment	Research into the use of arterial tourniquets for the management of crush syndrome is limited to just a handful of individual case studies as discussed above. Despite evidence being predominantly anecdotal, it would seem from these limited cases that patients have the potential to rapidly deteriorate upon release due to hyperkalaemia associated with toxic reperfusion. Therefore, it would make hypothetical sense to contain said toxins within the crushed limb, until the secondary effects of the release of these toxins into the systemic circulation can be better managed in a hospital setting. There is some additional supporting evidence from Popov and Yakirevich, (2018) who conducted a retrospective case series on 38 casualties who suffered crush syndrome through large earthquakes. All 38 casualties had the same preventive treatment including tourniquet application prior to release to maintain stable haemodynamics. All patients survived with good outcomes; however, the study was not directly looking at tourniquets but a whole package of interventions, so it is impossible to establish cause and effect of multiple variables. Nevertheless, tourniquets are being used in this manner with minimal deleterious effects. The side effects associated with tourniquet use are likely a significant factor as to why this course of management is not routine in practice today. For example, Sever and Vanholder (2012) state that tourniquets should only be used for catastrophic haemorrhage control and not as an adjunct to crush syndrome due to risk of nerve palsies and necrosis. The above articles propose that these side effects are based on old evidence and that the side effect profile of tourniquet use may be overstated. A patient who has suffered a crush injury with prolonged extrication will already have some degree of ischaemia and the potential benefits of reducing adverse outcome risks, including cardiac arrest upon release are outweighed by any potential threat to limb. Authors of the above studies propose the use of tourniquets may be of value in the prehospital management of crush injuries to limbs as part of wider management strategy especially in areas with prolonged transfer and extrication times. Further research, ideally in the form of randomised control trials, is required to fully evaluate the risk-benefit of tourniquet use in this setting. However, due to the small incidence of crush injuries and crush syndrome particularly in developed countries, the feasibility of such studies would be challenging. No studies investigated amputation as a prophylactic measure to prevent reperfusion and subsequent systemic toxin release in the pre-hospital setting. Sever and Vanholder (2012) stated that that amputations should not be performed to prevent crush syndrome, only as a last resort if the limb is not salvageable or is required for a rapid extrication if the patient's safety is at imminent risk. Nevertheless, they state that should amputation be indicated, it is best performed as soon as possible following injury. There is an array of literature discussing amputations in association with crush syndrome in the hospital phase, but this is usually secondary to infection or severe necrosis. While again there is a hypothetical benefit to removing the limb with toxins contained to prevent reperfusion, this effect could be similarly achieved with use of a tourniquet, and the limb remains salvageable, as demonstrated in the case above.

Clinical bottom line	The are no published articles collecting objective data to support or confute the use of tourniquets to delay reperfusion and the subsequent adverse effects of this. The only available data are individual case reports. As such, the use of tourniquets in the prehospital management of patients suffering a crush injury cannot be routinely recommended. The collection of objective data is required to facilitate further understanding of the risk-benefit of tourniquets in the crush injury patient and subsequently discussion of their potential use.
References	1. Anderson, J.L., Cole, M. and Pannell, D. (2022) 'Management of Severe Crush Injuries in Austere Environments: A Special Operations Perspective', *Journal of Special Operations Medicine*, 22(2), pp. 43-47. 2. Badar, J., Schwartz, D.S. and Weisner, Z. (2015) 'Immediate Lower Extremity Tourniquet Application to Delay Onset of Reperfusion Injury after Prolonged Crush Injury', *Prehospital Emergency Care*, 19(4), pp. 544-547. 3. Dhir, K., Ferguson, J.D., Spangler, J.D., Whiffin, A.N.H. and Zhang, R. (2018) 'Bathroom Entrapment Leading to Cardiac Arrest From Crush Syndrome', *Prehospital Emergency Care*, 23(1), pp. 90-93. 4. Popov, A. and Yakirevich, I. (2018) *Complex Treatment of Crush Syndrome in Field Hospital in Emergency Area.* Available at: https://military-medicine.com/article/3465-complex-treatment-of-crush-syndrome-in-field-hospital-in-emergency-area.html (Accessed: 19 July 2023). 5. Sever, M.S. and Vanholder, R. (2012) 'Recommendations for the management of crush victims in mass disasters', *Nephrology Dialysis Transplantation*, 27(1), pp. 11-27.

Best Evidence Topic Report C	
Title	What is the optimum strategy to manage potential hyperkalaemia associated with crush injury?
Report by	Owen Williams
Checked by	Oliver Brown
Clinical scenario	A 23 year old farmer presents to the Emergency Department having trapped his legs by a piece of falling machinery. He is diagnosed with a crush injury of the lower limbs. Initial blood gas results show a potassium of 7mmol/L. You want to provide the optimum strategy for managing the hyperkalaemia.
Three part question	**In [patients with crush injury] what is [the optimum strategy] to [manage hyperkalaemia]?**
Search outcome	• 40 articles identified for review • 0 articles identified comparing treatments • Relevant findings summarised below

Comment	No papers were found which describe a treatment regime for the management of hyperkalaemia related to crush injury. Although this literature search did not identify and treatment regimes for the management of hyperkalaemia secondary to crush injury, important information relating to hyperkalaemia in crush injury was found. Multiple studies present the incidence of hyperkalaemia following crush injury. Despite heterogeneity in the definition of hyperkalaemia between studies, incidence is low nonetheless. In a study of 595 patients who presented with crush syndrome following the Maramara earthquake disaster in 1999, admission serum potassium was 5.3+/- 1.3 (range 2.4-13.3) mEq/L1. 176/595 were admitted with levels ≥6 mEq/L. Median serum potassium was higher in those requiring dialysis and in non-survivors, but no cut off point was identified to predict those who would require renal replacement therapy. A study of 9 patients presenting with crush syndrome following limb compression longer than 24 hours from the Sichuan earthquake of 2008 identified 5 patients with hyperkalaemia2. 3/9 patients underwent haemodialysis and alkalinisation. 2/9 patients had potassium levels >6 mEq/L Potassium levels were corrected to normal within days of ICU care. A retrospective study of 49 patients with crush injury found only one patient with a serum potassium of greater than 6mmol/L3. A further study of 135 patients with crush syndrome following the Bam earthquake in 2003 found a mean potassium concentration of 5.6 mEq/L +/- 1.3, with no patients having a potassium level greater than 6 mEq/L4. It can be seen, therefore, that although a potentially fatal complication of crush injury, hyperkalaemia is rare. Definitions of hyperkalaemia differ, but as the Resuscitation Council UK states, "hyperkalaemia is a continuum" and as the potassium concentration increases, so does the risk of adverse events and requirement for treatment5. The most common definition of hyperkalaemia amongst studies, including the Resuscitation Council's guidelines, is of a serum potassium concentration greater than 5.5mmol/L. Given no study of hyperkalaemia in crush injury provides an evidence-based treatment regime, it would be prudent to follow the hyperkalaemia management guidance provided by the Resuscitation Council.
Clinical bottom line	The are no published articles collecting objective data to support or confute the use of tourniquets to delay reperfusion and the subsequent adverse effects of this. The only available data are individual case reports. As such, the use of tourniquets in the prehospital management of patients suffering a crush injury cannot be routinely recommended. The collection of objective data is required to facilitate further understanding of the risk-benefit of tourniquets in the crush injury patient and subsequently discussion of their potential use.

References	1. Sever, M. et al. 2003. Serum potassium in the crush syndrome victims of the Marmara disaster. Clinical Nephrology; 59(5); pp.326-333. 2. Chunguang, Z. et al. 2010. Characteristics of crush syndrome caused by prolonged limb compression longer than 24h in the Sichuan earthquake. Emergency Medicine Journal; 27; pp. 627-630. 3. Motilall, S. et al. 2014. The incidence of an elevated admission serum potassium in crush injury patients at Dr George Mukhari academic hospital. Anaesthesiology Intensive Therapy; Supplement 2; pp. 104-105. 4. Safari, S. et al. 2017. 20-Day Trend of Serum Potassium Changes in Bam Earthquake Victims with Crush Syndrome; a Cross-sectional Study. Emergency; 5(1); pp. e5. 5. The Resuscitation Council (UK) 2021. Advanced Life Support: Cardiac Arrest in special circumstances pp.113-115. Available at: https://lms.resus.org.uk/modules/m10-v2-cardiac-arrest/10346/resources/chapter_12.pdf&ved=2ahUKEwjLl7-Iq7uAAxXFgv0HHW7AA0EQFnoECA8QAQ&usg=AOvVaw25BawfiocmILuH7-dQzVFQ [Accessed 01 August 2023].

Best Evidence Topic Report D	
Title	*Does sodium bicarbonate improve outcomes in crush injury?*
Report by	Peter Gimson
Checked by	Felix Wood
Three part question	In patients with suspected crush injury, does sodium bicarbonate improve morbidity and mortality?
Search outcome	68 articles were identified for review. - No systematic review was identified comparing sodium bicarbonate treatment vs placebo or vs alternative treatment. - Five literature reviews relating to the management of crush injury discussed the use of sodium bicarbonate. Three of these advocated the use of sodium bicarbonate in reducing renal failure through urinary alkalization. One argued there was no benefit vs active fluid resuscitation. One argued the evidence was unclear - Two cases reports were included. Administration of sodium bicarbonate did not prevent renal failure. - One RTC involving animal testing was included. - A consensus statement and a review of guidance both advocate the use of sodium bicarbonate in preventing renal failure. The relevant articles are summarised below:

Author, date and country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Greaves et al. 2003. UK.	Crush injury patients.	Consensus Statement	ARF	Urine pH should be kept above 6.5 by administration of 50mls 8.4% sodium bicarbonate to fluid regime. Thought to decrease metabolic acidosis and decrease precipitation of myoglobin in the renal tubules. Currently no evidence on pre-hospital administration / administration immediately post extraction. This should be explored further.	No data - consensus statement

Jagodzinski et al. 2010.Trauam. United Kingdom	Crush injury in disaster settings	Literature review	ARF. Hyperkalaemia.	Intervention with sodium bicarbonate can prevent the need for dialysis if used for urine alkalinisation by preventing pigment nephropathy. Urine pH should be kept above 6.5. 50 mEq l sodium bicarbonate to each 2nd and 3rd litre after admission to hospital. Sodium bicarbonate can also counteract hyperkalaemia. Acetazolamide can be used to manage metabolic alkalosis. Post-traumatic rhabdomyolysis patients in a single study (Brown et al.) found that bicarbonate and mannitol did not prevent ARF, the need for dialysis or mortality when CK > 530,000.	Data from rhabdomyolysis from different aetiologies. Treatment included mannitol as well as sodium bicarbonate for some patients.
Gibney et al. 2013, kidney international	Crush injury in disaster settings	Literature review	No specific measures	Current evidence does not suggest benefit from alkalinization over active fluid resuscitation. May worsen hypocalcaemia associated with crush injury.	No data provided.
Malinoski et al. 2004, Crit Care Clin, USA	Patients with crush injury and rhabdomyolysis	Literature review	ARF	Relative benefits of early fluid resuscitation versus forced solute diuresis are unclear. Acetazolamide required to prevent alkalaemia. Bicarbonate may be useful but lack of class 1 evidence. Not assessing pre-hospital use.	No data provided to support bicarbonate use.

Sever and Vanholder. 2013. USA	Crush injury patients in disaster settings	Review of current guidelines.	ARF, hyperkalaemia	Bicarbonate added to half-isotonic saline precent tubular deposition of myoglobin and uric acid, correct metabolic acidosis, reduces hyperkalaemia.	No data provided to support bicarbonate use.
Altintepe et al. 2007. Turkey	Earthquake related crush injuries	Case report	ARF	Mannitol-bicarbonate administered to all 9 hospitalised patients with crush syndrome. 2 developed ARF.	No comparison group. ARF still occurred. Patients were also treated with energetic fluid replacement.
Sever et al. 2006. United States.	Earthquake related crush injuries	Literature review	ARF	Addition of 50 mEq of sodium bicarbonate to each second or third litre of saline will maintain urinary pH above 6.5 and prevent intratubular deposition of myoglobin. This will reduce ARF.	Statement - no linked evidence. No comparison of fluids alone vs fluids with bicarbonate.
Yokota. 2005. Japan.	Disaster victims with crush syndrome.	Review article	No specific outcome	44mEq/l Sodium bicarbonate should be added to every other 500 ml. Adjust to maintain urinary pH above 6.5. Improves hyperkalaemia and metabolic acidosis, prevent myoglobin and uric acid deposition in the renal tubules. Requires correction with acetazolamide if urinary pH goes above 7.5.	Statement - no comparison with other treatments or linked evidence.
Arango-Granados et al. 2020. Colombia.	29 year old patient trapped in landslide.	Case report	ARF	The patient received sodium bicarbonate, but this did not prevent renal failure from developing. Consideration of the adverse effects of sodium bicarbonate should be given.	Single patient. No details on timing of administration of intervention. No comparison.

Murata et al. 2017. Japan.	Animal study	Randomised control trial.	Survival at 48 hours. Pathological changes to the nephron at 3hrs, 24hrs and 48hrs.	Anaesthetised rats underwent hind limb compression using a tourniquet for 5 hours. One of the six groups received normal saline plus 25mEq/l sodium bicarbonate. This was compared with no treatment, normal saline, and normal saline plus differing doses of NaNO2. The sodium bicarbonate group showed reduced pathological dilation of distal convoluted tubules at 24 hours compared to the control group and saline only group. The sodium bicarbonate group had a higher survival rate than the control and saline only group. Survival was higher in the NaNO2 group.	Small sample sizes (60 rats split between different groups). Animal study in laboratory conditions.
Gonzalez. 2005. Critical Care Medicine.	Patients with crush injuries, mixed aetiologies.	Literature review	ARF	Use of 40 mEq / l sodium bicarbonate added to intravenous fluids. Aim for pH >6.5. This diminishes myoglobin renal toxicity by increasing solubility of heme pigments. Acetazolamide may be required if urinary pH is >7.5.	Discussion rather than any evidence to support treatment. No comparison with alternative treatments e.g. saline alone.

Comment	The literature on the use of sodium bicarbonate is broadly in agreement. Sodium bicarbonate should be added to intravenous fluids to facilitate urinary alkalisation, keeping urine above a pH of 6.5. This is done to help prevent renal failure from developing. There is theoretical evidence to support this, as it will help to prevent cast formation, improve heme pigmentation solubility, and prevent myoglobin deposition. It is also suggested that sodium bicarbonate will help address other complications of crush injury, such as hyperkalaemia and metabolic acidosis. There is a general consensus that treatment should be delivered following admission to hospital. There is very limited evidence to support this intervention. There is no tier one evidence demonstrating that sodium bicarbonate improves outcomes, such as ARF, or improves overall mortality. There is some discussion as to whether sodium bicarbonate provides additional benefit to aggressive, early fluid resuscitation. Comment is also made regarding potential side effects of sodium bicarbonate, as well as the need to use acetazolamide if urinary pH rises above 7.5. Further research would be required to assess whether sodium bicarbonate improves outcomes. This could also be explored with mannitol, which is frequently referred to as a treatment given in combination with sodium bicarbonate. Currently, there is no hard evidence that sodium bicarbonate improves outcomes.
Clinical bottom line	There is a clear consensus that sodium bicarbonate reduces the likelihood of developing acute renal failure. There is no tier one evidence to support this view.
References	1. Greaves et al. Consensus Statement On The Early Management Of Crush Injury And Prevention Of Crush Syndrome. From Here, Health. 2003. 2. Jagodzinski et al. Crush injuries and crush syndrome – a review. Trauma. 2010. 12:69-88 3. Gibney et al. Disaster nephrology: crush injury and beyond. Kidney international. 2014. 85:1049-57 4. Malinoski et al. Crush injury and rhabdomyolysis. Crit Care Clin. 2004. 20:171-192 5. Sever and Vanholder. Management of Crush Victims in Mass Disasters: Highlights from Recently Published Recommendations. Clin J Am Soc Nephrol. 2013. 8:328-335 6. Altintepe et al. Early and Intensive Fluid Replacement Prevents Acute Renal Failure in Crush Cases Associated with Spontaneous Collapse of Apartment in Konya. Renal Failure. 2007. 29:737-741 7. Sever et al. Management of Crush-Related Injuries after Disasters. N Eng J Med. 2006. 354:1052-63 8. Yokota. Crush Syndrome in Disaster. Japan Medical Association Journal. 2005. 48(7):341-52 9. Arango-Granados et al. Amputation in crush syndrome: a case report. International Journal of Surgical Case Reports. 2020. 72:346-50 10. Murata et al. Low-dose sodium nitrate fluid resuscitation prevents lethality from crush syndrome by improving nitric oxide consumption and preventing myoglobin cytotoxicity in kidney in a rat model. Shock. 2017. 48(1):112-8 11. Gonzalez. Crush Syndrome. Crit Care Med. 2005. 33(1):S34-41

Best Evidence Topic Report E	
Title	*Does solute-alkaline diuresis reduce morbidity or mortality in patients with crush injury?*
Report by	*Dr Benjamin James Earle-Wright*
Checked by	Dr Lizzie Freeman
Clinical scenario	*You are the A&E registrar on night shift. There has been a major incident involving a stadium collapse and your department has received 25 patients with various crush injuries. The level 3 patients have been moved to intensive care, but you are to provide ongoing care to 5 patients overnight due to bed pressures. All the patients have a CK of > 5000 and you know they all are likely to have rhabdomyolysis. You wonder if alkaline diuresis (using sodium bicarbonate infusion fluid alongside a diuretic e.g. mannitol or furosemide), will improve their chances of not developing acute renal failure, requiring haemodialysis or survival?*
Three part question	**In adult patients with suspected crush injury does solute alkaline diuresis improve morbidity and mortality?**
Search outcome	88 abstracts were screened and 28 full text papers reviewed: - No systematic review, clinical trial or observational study was found evaluating the use of solute alkaline diuresis vs normal fluid therapy in crush injury - One systematic review encompassing 6 studies with variable patients numbers, definitions and outcomes (rows 1-4) - Two additional case series not identified by the above systematic review are also included and summarised below.

Author, date and country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Scharman & Troutman, USA. 2013	Total of 461 patients across 6 different trails with varying definitions of rhabdomyolysis	Systematic Review	Development of acute renal failure, requirement of haemodialysis	6 Studies included: - 1 x retrospective cohort with 382 patients with CK >5000, 40% received sodium bicarbonate + mannitol. No difference in renal failure or mortality - 2 x retrospective cohort with 24 + 10 patients respectively with CK >500 - no benefit of sodium bicarbonate + mannitol over standard fluid therapy - 3 case series (2 included below - Gunal + Altintepe) with various numbers of patients (small) and treatment regimes - 2 suggesting benefit of sodium bicarbonate + mannitol, 1 suggesting no difference	No Level 1-3 evidence identified. No direct comparison could be made between papers due to different definitions of rhabdomyolysis, urine output and AKI. Different causes of rhabdomyolysis (some trauma, some drug induced). Small numbers of patients throughout. Different background fluid regimes use

Brown et al. 2004, USA	382 intensive care patients with CK > 5000	Retrospective cohort study	Primary: Development of acute renal failure Secondary - Need for dialysis, length of stay in ITU, mortality	40% of patients received sodium bicarbonate + mannitol. No difference in retail failure (p = 0.27), dialysis (p = 0.57) or mortality (p = 0.37)	Only patients with CK > 5000 evaluated. Sodium B / mannitol given and discontinued on treating clinicians' discretion
Altintepe L, Guney I, et al. 2009, Turkey	7 survivors from a 10-floor apartment collapse with crush injury	Case series	Development of acute renal failure	All 7 patients received a sodium bicarbonate / mannitol infusion (when urine output >20ml/h) alongside normal fluid resuscitation. Only 2 patients (28.6%) developed ARF requiring haemodialysis despite all having clinical rhabdomyolysis.	Very small number of patients. No control group.
Gunal, Celiker et al. 2004, Turkey	16 survivors of the 2003 Bingol earthquake in Turkey all with crush injuries	Case series	Requirement for RRT	All patients received combination of early fluid resuscitation, sodium bicarbonate and mannitol (as long as urinary output >20ml/h). Only 4 patients required RRT.	Small sample size. No control group.
Bartal, Zeller et al. 2011. Israel	8 survivors of the 2010 Haiti earthquake	Case series	Recovery from ARF within 48 hours	All 8 patients received sodium bicarbonate / furosemide infusion alongside normal fluid resuscitation. 2 patients recovered within 48 hours, 6 died. No RRT was available for 10 days in this disaster.	Very small number of patients. No control group. Very wide range of patient injuries and time under rubble (2h - 72h)
Sagheb, Roozbeh et al. 2008 Iran	20 survivors of the Bam earthquake with acute renal failure	Case series	Duration of acute renal failure. Requirement of dialysis	7 patients who received standard fluid therapy (NaCl + Sodium bicarbonate + Mannitol (As long as urine output >20ml/h) vs 13 who received variable fluid therapy (details not recorded) The standard therapy group had a reduced duration of acute renal failure (7 vs 19 days) and lower requirement for haemodialysis (1 vs 6 sessions)	Small sample size. Control group but no details about variable fluid therapy. In general, the variable fluid therapy group had spent more time under the rubble (6.3 vs 3.2 hours)

Comment	*Overall, the evidence base for the use of solute alkaline diuresis in crush syndrome is poor. There have been no studies since 2013 identified in this literature search on the topic. Research into crush injuries is inherently difficult as large numbers of crush victims are usually only seen in major incidents or disasters when there is likely to be reduced access to healthcare (4). This is compounded by poor access to healthcare data and ethical approval resulting in poor quality evidence. The one systemic review highlighted above had to draw on multiple case reports and retrospective cohort studies (5) with differing definitions and concluded that the efficacy of solute-alkaline diuresis was still not known.* *The theory behind the use of sodium bicarbonate is that alkalising the urine >6.5 prevents the renal deposition of myoglobin and uric acid hence improving metabolic acidosis and reducing hyperkalaemia (1). The addition of mannitol is thought to decrease blood viscosity and dilate glomerular capillaries and hence increase filtration rate (2). However, whilst the theoretical support for this therapy clearly exists the lack of any randomised studies or even comparative studies between this treatment and standard fluid resuscitation remains. In the few case reports identified above which advocate use of solute alkaline diuresis there were no control groups.* *The differences in definitions between acute kidney injury, rhabdomyolysis also make it difficult to draw definitive conclusions. A large scale prospective study is needed comparing a standard fluid regime vs fluid regime + sodium bicarbonate + mannitol with established international definitions of rhabdomyolysis and AKI in order to answer the question.*
Clinical bottom line	*The current evidence does not support the use of solute-alkaline diuresis in the treatment for crush injury, it is, at best non inferior to standard fluid therapy and carries additional risks (i.e. the overuse of mannitol in anuric patients). The combination should be avoided until better evidence if available.*
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Best Evidence Topic Report F	
Title	Does early renal replacement therapy reduce morbidity or mortality in patients with crush injury?
Report by	Lizzie Freeman
Checked by	Benjamin Earle-Wright
Three part question	**In patients with suspected crush injury, does early renal replacement therapy improve morbidity and mortality?**
Search outcome	71 abstracts screened, with 26 identified for full article screening. No systematic review, clinical trial, or prospective cohort study was found comparing the effect of early vs delayed renal replacement therapy on morbidity and mortality in suspected crush injury. Results from 2 retrospective cohort studies and 5 case series deemed to be of most relevance are summarised below.

Author, date and country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Erek E *et al*, 2002, Turkey	639 patients admitted with acute renal failure to 35 hospitals after the Marmara earthquake in 1999.	Retrospective cohort analysis	Clinical and laboratory findings, surgical interventions, frequency and duration of RRT.	477 (74.6%) of patients received renal replacement therapy (RRT), 147 recovered without RRT and 15 died before RRT was started (factors linked to acute renal failure such as hyperkalaemia and circulatory overload reported not to have played a major role in this group). Overall mortality was 15.2% (17.2% in the RRT group, 9.3% in the non RRT group). On multivariate analysis, only DIC and ARDS/respiratory failure showed a significant association with mortality.	Criteria for starting RRT not reported. Time to initiation of RRT not reported.
Huang K *et al*, 2002, Taiwan	95 patients with crush syndrome (defined as peak CK >1000 u/L), admitted to 8 major hospitals in the area surrounding the Chi-Chi earthquake in 1999, within the first two weeks.	Retrospective cohort analysis	Laboratory data, time trapped, time to hospital, injury sites, total fluid volume in first 48 hours, oliguria, dialysis, fasciotomy, morbidity, mortality, discharge, transfer.	44 of the 95 patients were reported to have acute renal failure, and 30 of these received dialysis. All 30 regained normal renal function. Incidence of acute oligoanuria, renal failure and need for haemodialysis were increased significantly in the group with peak CK >50,000. 8 patients (8.4%) died.	Mortality in the acute renal failure group not reported. Time to initiation of dialysis not reported.
Kazancioğlu R *et al*, 2001, Turkey	60 patients admitted to units of the Istanbul School of Medicine following the Marmara	Case series	Laboratory parameters, trauma sites, fasciotomies, requirement for RRT, type of RRT, complications, cause of mortality.	40 patients required RRT (peritoneal dialysis in 1, haemodialysis in 37, haemofiltration in 2). The clinical and laboratory data of those who required RRT (n=40) and those who did not (n=20) were compared. Time spent under the rubble, admission blood pressure, serum potassium, phosphate, uric acid creatinine phosphokinase and	Criteria for starting RRT not reported or discussed. Time to initiation of RRT not reported.

	earthquake (1999), fitting criteria for diagnosis of crush syndrome.			haematocrit differed between the two groups (p<0.05). Of note, the RRT group had shorter mean time under the rubble and higher mean admission BP. Mortality in the RRT group was 23%, and in the non RRT group 20%. Overall mortality was 21.6%, with all remaining patients reported to regain normal renal function.	
Ersoy A *et al*, 2003, Turkey	60 patients admitted to Uladag University Medical School hospital following the Marmara earthquake (1999) who underwent RRT.	Case series	Mortality (time point not specified).	Patients divided into survivors (Group A, n=39) and non-survivors (Group B, n=21). Dialysis was started in group A at a mean time of 2.8 +/- 0.2 days (range 1-8) and in group B at 3.7 +/- 0.6 days (range 1-12) post earthquake, with a p value >0.05. The parameters found to be statistically significant predictors of mortality were female gender, multiple trauma, serum peak CK >20,000 U/l and systolic hypotension on admission. Overall mortality rate in dialysed patients was 35%.	No analysis of data from patients who did not undergo RRT.
Bartal C *et al*, 2011, Israel	8 patients with acute oligoanuric renal failure treated at the Israel Defence Forces medical Corps Field Hospital in Haiti, 2010 (RRT not available).	Case series	Mortality following 48 hours of conservative treatment.	8 patients were admitted with oligoanuric renal failure having had no early prophylactic treatment. RRT was not available. Of these, 2 recovered within 48 hours, 4 patients (50%) died, and 2 were transferred to another hospital for palliative care with signs of pulmonary oedema. Clinical characteristics and laboratory parameters were compared between the two groups, but statistical analysis was not performed.	Small case series. No statistical analysis performed.
Chunguang Z *et al*, 2010, China	9 patients with severe crush syndrome admitted to the Intensive Care Unit at the West China Hospital of Sichuan University following the Sichuan earthquake (2008).	Case series	Laboratory findings, interventions, complications, mortality (time point not specified).	All 9 patients whose data was analysed survived. All patients received unspecified volumes of intravenous fluid prior to transfer to the hospital studied. Duration of burial, time to administration of fluid and time from injury to ICU admission were reported for each case but not analysed with respect to other parameters/outcome measures.	Small case series. Time to RRT not reported. No statistical analysis performed.
Demirkiran O *et al*, 2003, Turkey	18 patients admitted to the intensive care unit of a University Hospital following the Marmara earthquake in 1999.	Case series	Patient characteristics (age, sex, APACHE II score, time to rescue, time to admission, length of stay, mortality), laboratory findings, interventions.	The mean time to rescue was 24.1 hours (range 8-45) and time from first hospital admission to transfer to ICU was 16.35 days (range 45 minutes – 72 hours). 13 patients developed renal failure, 6 underwent continuous renal replacement therapy (CRRT) and 7 underwent haemodialysis. 7 patients of the 25 admitted to ICU died, not all of whom received RRT.	Small case series. Multiple missing data points. Time to initiation of RRT not reported. Requirement for RRT not correlated with time to admission to ICU.

Comment	No study has specifically looked at whether the timing of initiation of RRT affects morbidity and mortality in crush injury. All existing studies are retrospective analyses of data from disparate groups of patients with acute renal failure following crush injury. Most of these are patients evacuated after earthquakes, where timing of evacuation and access to initial treatment and resuscitation varies significantly. Access to RRT is also variable, often requiring further evacuation and inter-hospital transfer. Data is often incomplete and the timing of initiation of RRT is infrequently reported. The clinical thresholds for starting RRT in these patient populations are not specified and are also likely to be variable and resource dependant. In the existing studies that include data on incidence of acute renal failure, use of RRT and mortality, conclusions on causality cannot be drawn due to presence of multiple confounding factors. Existing review articles are based on expert opinion. It has been recommended that RRT in crush injury is initiated according to standard indications (oliguria/anuria, volume overload or severe uraemia/hyperkalaemia/acidosis), with consideration of prophylactic RRT in those at high risk of hyperkalaemia [3]. The existing literature does suggest that not all patients who develop acute renal failure secondary to crush injury require RRT, and early, individualised intravenous fluid therapy can prevent AKI and avoid the need for RRT [4]. Given the risks associated with starting RRT (e.g. large bore access, coagulopathy, haemodynamic instability) and the challenges around resource management in mass casualty incidents associated with crush injury, early RRT is unlikely to be clinically justifiable without evidence of benefit. Of note, early initiation of RRT in critically ill patients with acute kidney injury (non-crush specific) has not demonstrated a survival benefit and remains controversial [1][2]. A well-designed randomised trial examining the effect of pre-defined 'early' and 'standard' initiation of RRT on morbidity and mortality is required in both crush and non-crush related acute kidney injury.
Clinical bottom line	There is inadequate evidence to address the question of whether early RRT reduces morbidity and mortality in patients with crush injury. Current guidelines are based on expert opinion and suggest initiating RRT according to standard indications.
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Best Evidence Topic Report G	
Title	What is the optimum strategy for managing compartment syndrome in the context of crush injury?
Report by	Hannah Clancy
Checked by	*Leo Wood*
Three part question	*As close as possible to PICO version of research question. Some won't fit neatly. No dramas if not.* **In [patients with suspected crush injury], does [conservative management vs early / late fasciotomy vs amputation] improve [morbidity and mortality]?**
Search outcome	40 articles screened identifying: One systematic review comparing conservative management vs fasciotomy vs amputation in the management of crush injury. Two retrospective observational studies.

Author, date and country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Gerdin, M.; Wladis, A.; Schreeb J. v., 2012, Sweden	14 review articles.	Systematic review	Conservative management	3 reviews favour conservative management over surgical, 1 considers conservative and surgical equally beneficial. Early fluid resuscitation, preferably prior to extrication, is recommended with the primary aim of limiting renal injury. Mannitol can be used to lower compartment pressures but should not be used in oliguric/anuric patients or those with acute renal failure. Limbs should be splinted to limit movement. Hyperbaric oxygen may play a role in limb salvage. Conservative treatment should be prioritised when patient presents 48-72hrs following onset of symptoms.	Based on narrative reviews, limited statistical analysis. Basic search strategy Only articles written in English are included. Much experience of crush injuries is from earthquake prone regions where English is not the native language.
			Fasciotomy	Increased infection risk when closed compartment syndrome turned into an open wound.	

				Complications of fasciotomy include sepsis and death. 9 reviews recommended fasciotomy after closed crush-induced compartment syndrome. 5 of these reviews recommended early over late fasciotomy (late being 6-12 hours post admission). Muscle and nerve damage is felt irreversible by late fasciotomy. One review suggested no role for fasciotomy due to the difference in pathophysiology from ischaemia induced compartment syndrome.	
			Amputation	Discussed in 3 reviews to be used as a last resort as a lifesaving strategy to facilitate extrication.	
Oda, J. et al. 1997, Japan	372 victims of the 1995 Hanshin-Awaji earthquake.	Retrospective observational study of patients in hospital.	Fasciotomy performed	Statistically significant differences in persistent muscle weakness between fasciotomy and non-fasciotomy patients in the lower leg but not in the thigh: Anterior tibial ($p = 0.0009$), toe extensor ($p < 0.0001$), toe flexor ($p = 0.0004$), superficial peroneal ($p = 0.003$), deep peroneal ($p = 0.03$), tibial nerve ($p = 0.01$). Delayed rescue, fasciotomy and radical debridement may worsen physical prognosis and recovery.	Loss to follow up: 42 out of 372 patients attended long term follow up. Only 17 of these had fasciotomies. Time to rescue was a confounding variable and was and independent predictor of outcome.
			Fasciotomy not performed.	Persistent muscle weakness is more commonly associated with sensory disturbance ($p = 0.04$).	
Duman, H.; Kulahci, Y.; Senegezer, M.; Turkey, 2003	35 victims of the 2002 Turkey earthquake.	Retrospective observational study		16 patients had an urgent fasciotomy performed 8-21 hours post extrication. Four patients required subsequent amputation due to sepsis. The most common complication was crush syndrome and the most severe was sepsis. The mean time to admission was higher in those who required amputation than those who didn't. 8 patients who had fasciotomy regained normal function while four required further rehab or had ongoing functional / sensory loss. Fasciotomy wounds need careful monitoring and early antibiotics / debridement if signs of infection due to their propensity for infection.	Small numbers. Limited statistical analysis. Does not directly compare outcomes of different treatments.

Comment	The evidence available does not suggest one method of treatment is clearly superior and is not of high enough quality to produce clinical guidelines. It would appear the benefit of different treatment types depends on time from the injury being sustained but this has been not objectively investigated. Conservative management with the administration of mannitol was felt to be beneficial whenever the patient presented but must be used with caution in patients with or at risk of renal injury. Fasciotomy is of greatest benefit when performed 0-6 hours post extraction, should be used with caution at 6-12 hours and not be used post 12 hours due to lack of benefit. Amputation should be a last resort.
Clinical bottom line	Optimum surgical management of crush induced compartment syndrome is likely to be dependent on time from injury to treatment, resources and expertise available. Further research is required.
References	1. Gerdin M, Wladis A, von Schreeb J. Surgical management of closed crush injury-induced compartment syndrome after earthquakes in resource-scarce settings. J TRAUMA ACUTE CARE SURG 2012 09;73(3):758-764. 2. Matsuoka T, Yoshioka T, Tanaka H, Ninomiya N, Oda J, Sugimoto H, et al. Long-term physical outcome of patients who suffered crush syndrome after the 1995 Hanshin-Awaji earthquake: prognostic indicators in retrospect. J.Trauma 2002 2002;52(1):33-39. 3. Duman H, Kulahci Y, Sengezer M, Duman H, Kulahci Y, Sengezer M. Fasciotomy in crush injury resulting from prolonged pressure in an earthquake in Turkey. Emerg.Med.J. 2003 05:251-252.

Quick Reference Guide

Summary of Recommendations

1. The earliest possible safe release of the compressing force should be a treatment priority [Grade: C]

2. Not all entrapped patients will have suffered significant crush injury, although the risk should be considered [Grade: C]

3. Concerns regarding potential crush injury should not impede trauma care, including the management of bleeding. The administration of blood products, if available, should be considered in line with local protocols following trauma. [Grade: D]

4. The over-arching aim should be the rapid evacuation of patients with suspected crush injury to definitive care carrying out essential life-saving interventions en route. Patients with significant suspected crush injuries should usually be conveyed to a Major Trauma Centre. [Grade: C]

5. In the context of a large-scale incident with multiple crush-injured patients, regional plans for casualty distribution should be enacted. If regional resources are overwhelmed, destination decisions should be based on the availability of trauma expertise and renal replacement therapy and supported by national coordination. [Grade: C]

6. Analgesia should be given early within the rescuers' scope of practice [Grade: D].

7. While planning safe and timely extrication, intravenous (IV) or intraosseous (IO) access should be established in the trapped patient, if practicable, and fluids (ideally warmed 0.9% sodium chloride) should be available in case of deterioration. These interventions should not delay extrication. [Grade: C]

8. Fluid administration for patients with suspected crush injury should be individualised. Practitioners should consider the likely other injuries present, the muscle mass crushed, the degree and duration of compression and patient factors such as comorbidity and hydration status. Isotonic crystalloid solutions without potassium (e.g. 0.9% sodium chloride) should be used initially. These should be warmed, if possible. [Grade: C]

9. The application of tourniquets in patients with crush injury should be reserved for the management of catastrophic haemorrhage. [Grade: C]

10. During entrapment and evacuation, interval cardiac monitoring may be appropriate. If dynamic ECG changes are seen consistent with hyperkalaemia, then temporising treatment should be considered. Pre-hospital point of care testing, if available, may provide more definitive information or reassurance. [Grade: D]

11. Prophylactic treatment based on the presumed presence of hyperkalaemia following crush injury is not supported. [Grade: C]

12. The use of bicarbonate administration, targeted urinary alkalinisation or forced diuresis is not routinely recommended. [Grade: C]

13. Patients with crush syndrome may develop acute kidney injury requiring access to renal replacement therapy. [Grade: C]

14. Fasciotomies, if required, should be performed according to standard indications and are not recommended in the pre-hospital setting. [Grade: C]

15. Better data are needed to guide future recommendations. Consideration should be given to retrospectively reviewing patients diagnosed with crush in injury in trauma registries and a pre-approved study protocol could be considered to be instituted in the context of a mass casualty event. [Grade: D]