Journal of High Threat & Austere Medicine

Literature review

Timeline effects of tourniquets used in trauma care

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Keywords tourniquet, trauma, timeline, effects, health

For referencing. Pascoe B, Weinrauch P. Timeline effects of tourniquets used in trauma care. JHTAM. 2024;6(2):26-32.

DOI https://doi.org/10.33235/JHTAM.6.2.26-32

Submitted 9 April 2024, Accepted 17 June 2024

Abstract

This literature review describes the time-dependent effects of tourniquet application in trauma care. Tourniquet application is discussed from both clinical and pathophysiologic perspectives as a graduated spectrum of injury starting from the time of initial tourniquet application through to terminal cellular death. Research was conducted utilising existing case studies and reviews of combat application tourniquet use and outcomes. This review also offers a discussion on the application of this information and a suggested two hour protocol to be introduced to any working environment where extended combat application tourniquet use may be encountered.

Introduction

Combat Application Tourniquets are used in emergency trauma situations – most commonly by the military – specifically for cases of traumatic amputations or catastrophic arterial haemorrhage. Their use has passed into and out of common use and protocols through the years as clinical professionals have considered their advantages and their disadvantages. In the right situation, tourniquets have been proven to be a life-saving intervention[1] as their purpose is to put enough pressure on arteries to stop the flow of blood out of the body.

In cases of extreme catastrophic haemorrhage, without the early application of an effective arterial tourniquet, catastrophic limb haemorrhage may result in life threatening exsanguination within five minutes.[2] However, the tourniquet has been known to have its own side effects over time — such as nerve paralysis and the requirement for amputation.[3] It can be difficult to understand how long tourniquets are able to be in place as direct clinical research on these devices is scarce to find and arterial tourniquet ischaemia itself is ethically problematic to perform studies on and are dominated by indirect evidence.

This article aims to evaluate research of broad context to create a practical timeline of what happens when tourniquets are implemented in trauma cases. This timeline should be understood as a framework of clinical guidance, as there are a myriad of factors which effect the impact of ischaemia on limb injury and how an individual will react to an intervention.

Methodology

A review of the academic literature regarding historical tourniquet use was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology[4,5] to systematically, transparently, and objectively select and include articles. To collate publications that were relevant to the research questions posed by our study, the authors began by identifying the keywords and search terms from a preliminary review of literature on the history of tourniquet use. Keyword search strings were then created by combining the terms for "tourniquet", "history", "timeline", "physiology", "application", and "haemorrhage". Databases used included PubMed, Embase, Scopus, ScienceDirect, and Wiley Online Library. The search yielded 6030 results.

Inclusion and exclusion criteria

The inclusion criteria included studies evaluating tourniquet application in traumatic situations, including randomised controlled trials, cohort studies, case-control studies, and systematic reviews. No publication date restrictions were applied.

The animal studies, studies that were not translatable into English, and studies on amputations and tourniquet use that did not include data on patient outcomes while the tourniquet was applied or that included patient data but did not include times of tourniquet application were excluded. Exclusion criteria also involved the use of intraoperative tourniquets and pneumatic tourniquets.

Process of analysis

Authors screened titles and abstracts based on inclusion and exclusion criteria which resulted in 52 articles. Those 52 articles were then read in entirety and their reference lists were then examined for other articles that may be applicable resulting in a further 268 articles to be examined. Inclusion and exclusion criteria was again applied to the references where another 12

full articles were added to the list and screened for inclusion and exclusion criteria. This process resulted in 26 articles being added to the full review.

The final 64 articles that were read in their entirety were also screened for bias, however after the search criteria had been applied again, in the final 26 articles that were included in the review did not contain any obvious or reported bias. Due to the small area of research in this subject, no further screening was conducted based on sample size, heterogeneity, or data presentation.

Results

Some articles originally appeared to fit the inclusion criteria, but on reading the full article they were found to be unsuitable for inclusion due to insufficient detail or applicability to arterial tourniquet use in trauma. For example; Tantry et al's 2013 study[6] had great information on hot and cold ischaemia times which the authors would have liked to include in the final document, however the article contained no information on patient outcomes or how the amputated stump was treated, cared for, if a tourniquet was even used, or information on the state of the tissue before the limb was reattached and healed – therefore on an article focusing on tourniquet use, it was not acceptable.

In the 26 papers that were included, some had information that ended up being used in the discussion that on first glance would have been ruled out due to the exclusion criteria. For example, while it provided no information on tourniquet pathophysiology, Odinsson A, Finsen V. Tourniquet use and its complications in Norway. J Bone Joint Surg Br. 2006 Aug;88(8):1090–1092[7] provided useful information on the practical results of implementing guidelines such as are suggested in the discussion of evidence in this review.

Discussion of evidence

When used effectively, tourniquets save lives by preventing mass haemorrhage. To be effective clinically, practitioners must know the dangers of all interventions they utilise. Tourniquets specifically come with complications and dangers that clinicians must be aware of to ensure optimal outcomes for the patient.

Limitations of current research

Tourniquet ischaemia in trauma applications still requires more research. Randomised clinical trials in the use and effectiveness of tourniquets would be invaluable as this could give researchers more detailed understanding into how the body responds to tourniquets, however this is difficult to obtain for ethical reasons.

Tourniquet complications

In 2006, a seven month study of battlefield use of tourniquets was conducted by Kragh et al,[8] who highlighted that even with evacuation to a surgical unit within one hour and effective tourniquet use, sometimes the limb will still develop further morbidities. Tourniquets, while being a life-saving intervention do not work effectively without risk. Morbidities in this study

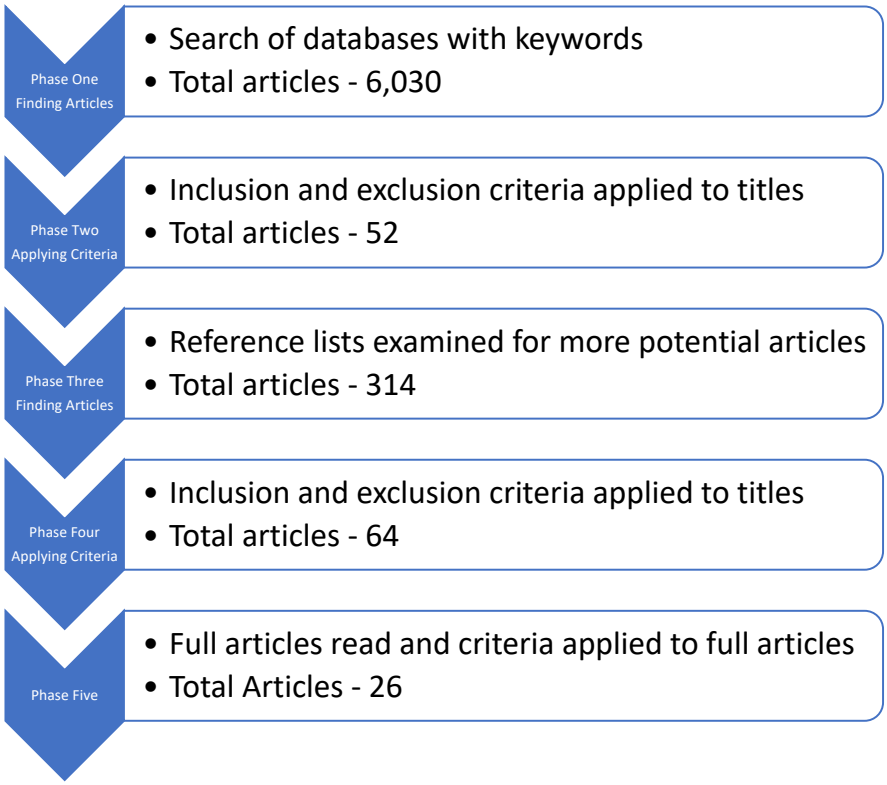

Figure 1. Process of article selection and review

included; amputation or stump shortening, palsy, myonecrosis, significant pain, embolus, fasciotomy, acute renal failure, rigor, abscess, blisters, abrasions, contusions, and pinching sensations.

The results of this study (Table. 1), concludes that the longer the tourniquet is in place for, the longer the limb is at risk of developing secondary latrogenic injury. The second pertinent conclusion of this study was that even when tourniquets are in place for less than an hour, they are still at risk.

Even though this timeline only extends to eight hours past tourniquet application, there have been cases of tourniquets which have been applied for longer periods of time with still positive outcomes for the patient and successful limb preservation.[1] However, these cases are rare and must be viewed as the exception, not the rule.

While most studies indicate the length of time that the tourniquet is applied has the most significant impact on limb injury, there are other factors which also should be taken into account by clinicians.

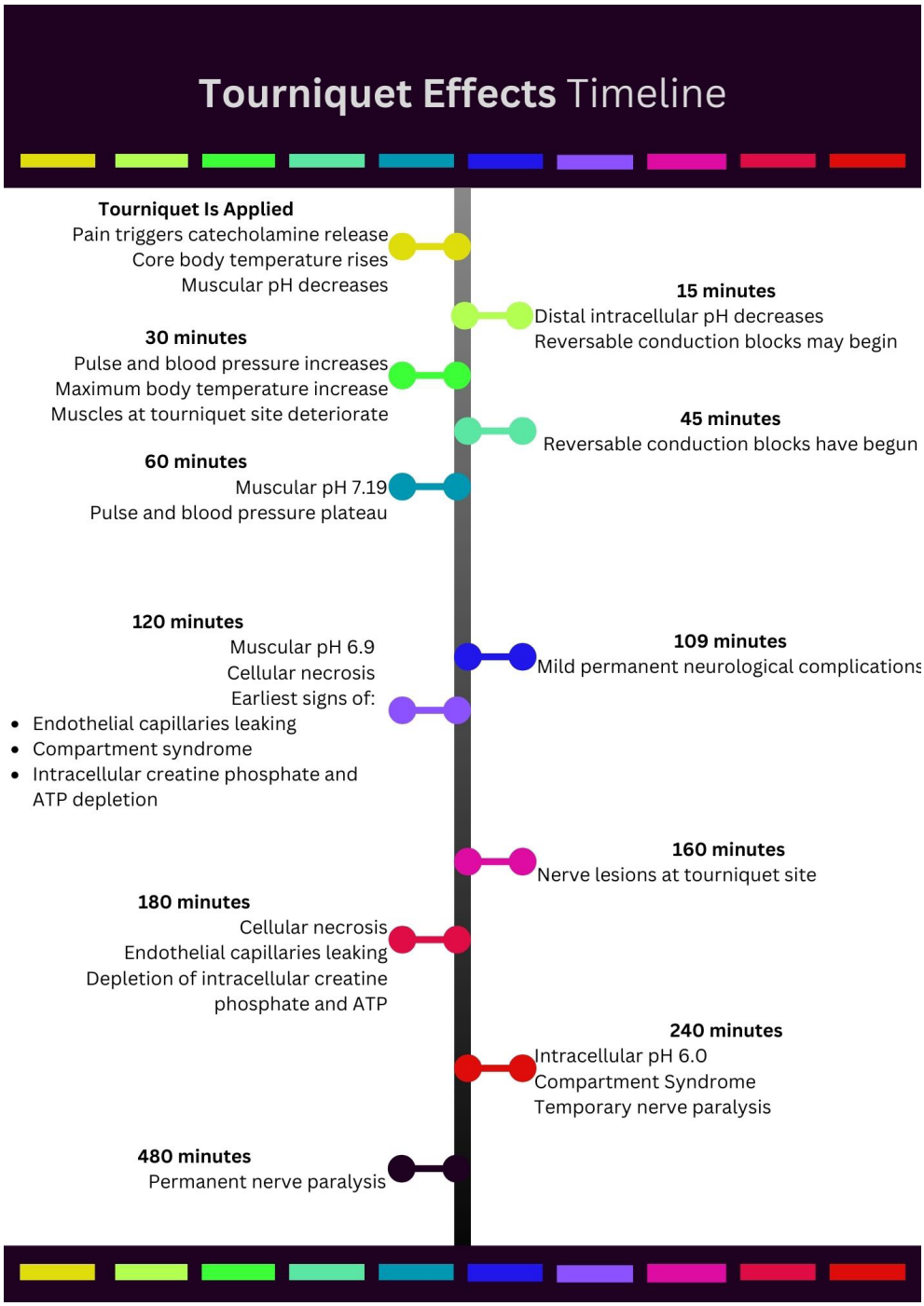

Figure 2. A collated timeline of tourniquet effects.

Placement of the tourniquet can have a significant impact on the side effects caused by the device. As per the 2008 study on fibre-type composition recovery by Thomas J Walters et al,[9] muscles comprised of various types of muscle fibres will react differently to tourniquet ischaemia and will recover differently. Distal extremities which have fewer myocytes will tolerate ischemia the best, while larger proximal muscle groups will tolerate ischaemia differently depending on the structural makeup of those myocytes.

Under the tourniquet itself, the nerve most susceptible to pressure damage is the peripheral nerve under the proximal edge of the tourniquet, while the distal edge is the least likely to be injured. When looking at the pressure gradient under the tourniquet, these results coincide with the pressure distribution.[10]

Finally, arterial occlusion is essential to tourniquet effectiveness. Without arterial occlusion the patient is instead given a venous tourniquet. Venous tourniquets involve incomplete occlusion of the artery allowing for arterial blood flow in and restricting venous return which creates complications specific to venous tourniquets. These complications have been previously mistaken for a complications affecting all tourniquet use which falsely inflated perception of risks associated with tourniquet use.[11]

Other factors that can affect limb recovery include, but are not limited to age, race, gender, weight, co-morbidities, stress levels, placement of tourniquet, hydration levels, and nutrition at time of injury.[3] These factors are outside of the scope of this manuscript.

At the moment of tourniquet application

Tourniquets applied in prehospital settings are painful devices.[12] If used effectively, a tourniquet will often be more painful than the injury — which in itself is a powerful statement when one also considers the injury requiring a tourniquet is most likely a traumatic in origin. Pain, regardless of the cause, presents distinct physiological manifestations. In the case of intense pain, such as the tourniquet causes, the body will release catecholamines which in turn create an effect of hypercoagulopathy.[13] This can be a useful side effect as hypercoagulopathy, in this instance, is assisting the body to stop the bleeding internally. However, this hypercoagulopathy over time can become a problem as the catecholamines also stimulate tPA to cleave plasminogen and form plasmin, responsible for the degradation of fibrin mesh. This over time results in a 10% symptomatic incidence of thromboembolic events which are major postoperative complications and are associated with increased morbidity and mortality.[14] These catecholamines also cause tachycardia and vasoconstriction, causing a steady rise in both pulse and blood pressure.

A large part of the body's homeostatic cooling process occurs by utilising the blood vessels close to the surface of the skin, allowing the heat to dissipate through the skin.[15] Although this process is most visible in cases of heat injuries (such as a heat stroke) when the skin becomes flushed, this process occurs constantly in the body. When a tourniquet is applied, the body is no longer able to shunt the heat from the core out through the limb as it normally would. This, combined with the heart working faster than at rest, ensures that in isolation the body temperature theoretically begins rising.[16] However, in practical application, due to the host of external factors that contribute to hypothermic concerns in patients with traumatic injury, hyperthermia due to tourniquet use is not something that needs to be included in the clinical decision making process.

Simultaneously, the cellular processes are still occurring, which means that the cells are using up oxygen and expelling carbon dioxide at a standard rate. However, the blood that would normally take up that carbon dioxide and carry it away is now blocked from reaching the lungs. This causes the cells and muscles begin to become more acidic due to the build-up of carbon dioxide.[12] On application of a tourniquet, this does not result in immediate clinical manifestations, but will continue to build up in the background. This is not the only time muscles can be subjected to a build-up of residual acidic substances, as this is a common practice when working out, however, muscles can only tolerate a certain amount before becoming damaged.

15 minutes

At the 15 minute point, the build-up of acidic carbon dioxide is now becoming noticeable as the distal (to the tourniquet) intramuscular pH begins to drop.[17] At this time, there would be no ill effects of this pH drop, however this process will continue and could lead to further complications later.

Reversible conduction blocks are now beginning to form under the tourniquet site due to a lack of oxygen to the tissues causing mild ischemia.[12] These lesions start small and at this point are not permanent. They cause some neurological type sensations beyond the tourniquet — tingling and numbness — which will

Table 1. Tourniquet duration vs morbidity percentage[3]

Total tourniquet duration	0-1h	>1-2h	>2-3h	>3-4h	>4h
Limbs with morbidity (%)	64	71	94	100	100
Limbs with morbidity (n)	98	84	16	3	5
Limbs without morbidity (n)	56	34	1	0	0

linger after the tourniquet is removed and potentially through rehabilitation, however they will heal over time.

If the tourniquet can be released at this point or earlier, most patients will have experienced no ill effects of having it applied.[18]

30 minutes

After half an hour, pulse and blood pressure will have markedly risen,[17] body temperature increases solely due to the tourniquet use now reaches a plateau with an increase of temperature varying from 1˚ to 1.7°[16] and muscles under direct pressure from the tourniquet are becoming injured. At this point, the injuries to the muscles are reversible. There are a variety of tourniquets in use around the world, with varying amounts of pressure over varying widths, which then affects how much damage the muscles directly under the tourniquet are experiencing. For an ideal tourniquet in place, the pressure is spread out over an inch or more,[3] which does less damage than some improvised tourniquets which may be significantly more narrow. No matter which version is used though, after half an hour, some damage is to be expected.

60 minutes (1 hour)

After an hour, muscular pH will now have dropped from its' initial average of 7.4 to 7.19. This is not yet damaging to the tissues, however the pH will continue to drop from this point.[17] Pulse and blood pressure have now plateaued out and any increase in these vital signs is no longer being caused by the identified injury and should be explored further.

Distal to tourniquet application, tissues become necrotic, releasing intracellular components into extracellular and intravascular spaces. Known commonly as Crush Injury, this will continue to build up from this point. While not harmful at this time, if the tourniquet is released after this point, they will move through the venous system and can contribute to the adverse metabolic consequences observed after extended duration tourniquet release. This damage is reversible if the tourniquet is released <2 hours post tourniquet application.[19]

109 minutes (1 hour, 49 minutes)

Beyond this point, the limb will develop permanent neurological morbidities. Neurological damage can manifest itself as tingling, numbness, palsy or even paralysis.[18] As with most health-related issues, these symptoms will start off as mild and slowly increase in severity as the tourniquet is left on for longer periods of time. While upper limbs are more prone to nerve injury than lower limbs, both have their weak spots with the radial nerve being the most vulnerable in the upper limbs and the sciatic nerve in lower limbs.[20] It has been suggested that palsy is twice as likely in the brachium as opposed to the quadriceps as the brachium has smaller limb girth which transmits higher tourniquet pressures.[3]

120 minutes (2 hours)

Mostly due to a build-up of carbonic acid, intramuscular pH has at this point dropped to around 6.9 (known as the muscular fatigue point).[21] From here, the muscles can tolerate the build-up of carbon dioxide less and will begin to weaken. If the tourniquet was not in place, an acidic environment like this in the muscles would have them feeling sore and tired. However, with the tourniquet in place, muscular weakness and mild soreness can be difficult to measure as the patient would already be in significant amounts of pain and with the tourniquet restricting tendons, the muscles are already feeling significantly weaker (those that have not been torn by the initial injury). Along with this muscular fatigue, the cells themselves will be suffering from the ill effects of the build-up of carbonic acid, constant pressure, and a lack of fresh oxygen and will begin dying off — causing cellular necrosis.[22]

At this time, we also start to see an effect occurring in the endothelium. This layer around blood vessels works in conjunction with leukocytes to create tears or holes in itself in order to ensure that leukocytes are able to pass through the blood vessels' walls and enter the intercellular space, thereby gaining access to areas of potential infection.[23] This intrinsic part of the inflammation process works against the limb around the two hour post tourniquet application as the endothelium shunts large amounts of leukocytes into the intercellular space in an attempt to heal the injury being caused by the tourniquet. This, in conjunction with the tiny amount of blood probably still coming in through the artery — and with no blood coming out through the veins — will increase the pressure in the inter-compartmental space resulting in the beginnings of compartment syndrome. This effect is worsened by an incorrectly tensioned CAT resulting in a slightly less occlusive effect, in which case, the effects are seen much earlier. This is due to the partially constricting effects of a loosely applied tourniquet and is referred to as a venous tourniquet. The venous and lymphatic systems are closer to the surface and tend to be more delicately formed than the deeper and thicker formed arterial structures. If a tourniquet is not applied tight enough it is in danger of restricting the outer structures, but allowing the artery to continue to pump blood into the limb. Compartment syndrome is potentially exacerbated as the lymphatic and venous system are in place to drain fluid out of the limbs.

The last affect noticeable at the two hour mark is the depletion of intracellular creatine phosphate and ATP.[17] Both of these chemicals are used as energy by all metabolically active cells and by this point, without a new supply of nutrients and oxygen the cells are noticeably depleted, which collates affects with muscular fatigue.

160 minutes (2 hours, 40 minutes)

The exact time it takes for nerve lesions to form under a tourniquet is unclear. However, regardless of how long it has

taken them to form, by the 160 minute mark in all cases studied, lesions have definitely begun appearing. These lesions are able to heal in <6 months, causing neurological deficits such as palsy or paralysis and only rarely are any of these symptoms permanent.[16]

180 minutes (3 hours)

Most studies into tourniquet application write about times of co-morbidities occurring as a scale, not as a definitive mark. As such, three hours is the upper limit for the onset of cellular necrosis, endothelial capillaries to be leaking into the intercellular space, and for the depletion of energy substances such as creatine phosphate and ATP.

240 minutes (4 hours)

At this time, intracellular pH of the distal limb, has now reached around 6.0 steadily dropping due to the increase of carbon dioxide.[24] This is not only affecting the intramuscular strength, it is also going to affect how well the muscles are able to regain function after the tourniquet has been removed. By now, the cellular necrosis has firmly set in and the increase of carbon dioxide is leaving the muscles in a poor state of myopathy. By now, healing will take longer and muscles will require extreme work to regain their previous level of health, if they do at all. On top of this, the risk of developing compartment syndrome is significantly higher after tourniquet release.

480 minutes (8 hours)

At eight hours, permanent limb paralysis begins to occur.[25] After this point it is rare to regain function in the limb and the chances of clinically advised limb amputation is significantly more likely.

Implementing guidelines

In World War II, medical personnel were encouraged to allow for reperfusion of the limb by loosening the tourniquet every 30 minutes. It then followed that patients on the battlefield would die from cumulative blood loss, leading to a complete policy reversal later on in the war.[26] When examining the effects of tourniquets, it is apparent that a reperfusion time frame less than two hours is not required as the cumulative effects of the tourniquet will likely not result in permanent disability before this point.

After reviewing current evidence, for any patient where the limb may be considered viable below the site of injury, a maximum time of two hours would be a safe guideline to work with and has been mentioned by other professionals.[17] This timeframe of two hours lessens the chances of severe co-morbidities which are seen to appear later, such as nerve necrosis/paralysis, and compartment syndrome. This two hour guideline also allows for a greater chance of full recovery by avoiding a dangerous depletion of intracellular creatinine phosphate and ATP.

If the tourniquet must be kept on longer due to difficulties in transportation or other extenuating circumstances, it would hardly be appropriate to remove it entirely. Therefore it is suggested for clinicians with access to whole blood products to consider adopting the reperfusion guidelines as stated by Jai Sharma and Rashmi Salhotra in 2012.[27] They concluded that the pressure of the tourniquet be released every two hours for the lower limbs and 1.5 hours for upper limbs for a duration of at least 10 minutes. Removing the tourniquet after 2 hours also gives the wound time to begin clotting and re-assessing the bleeding may show the tourniquet is no longer needed and can be replaced by a pressure bandage.[28]

When following similar guidelines, a Norwegian study found rates of tourniquet related complications were around one in 2442 cases, while only one in 31,742 cases were not able to be resolved in under six months.[7] In pre-hospital trauma management, however, it is recognised that the greatest cause of reversible battlefield death remains catastrophic blood loss. The benefit of intermittent tourniquet release, therefore, needs to be carefully balanced against the risk.

Another important factor to consider in this evidence is the importance of correct application of the combat application tourniquet. Incorrect application, such as the application of a venous instead of arterial tourniquet, can cause a worsening of co-morbidities and can lead to deteriorated patient outcomes.[11] If a tourniquet has not successfully occluded arterial bleeding, evidence shows placing another tourniquet side-by-side to the ineffective tourniquet increases the efficacy of the tourniquet at stopping the arterial bleed when compared to increasing pressure in a lone tourniquet.[3] Better education before the point of injury on the correct use, application, and side-effects of the tourniquet would positively affect patient outcomes.

Conclusion

After reviewing current evidence, having evacuation protocols which ensure tourniquets are only required to be applied for an upper window of two hours would be a safe guideline to work with. Prioritising the evacuation of patients to ensure they are moved to a facility where tourniquets are able to be removed within the upper limit of two hours, would minimise the risk of serious co-morbidities and maximise the chance for full recovery. In addition to this, improving education on the correct use and application of the tourniquet would also improve patient outcomes.

Acknowledgements

I would like to thank MAJ Stewart Holmes-Brown, WO2 Jayden Pyper, Adam Nothdurft, Paul Hemans, and David Bell for their valuable assistance with language, medical jargon and article structure. I would also like to thank Brett Pascoe for his patience and constant encouragement.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

No funding was received for the conduct of this research.

Disclosures

The material in this article is solely the opinion of the authors and does not reflect ADF policy.

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