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Review Article

Management of non-compressible torso hemorrhage: An update

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ABSTRACT

With the widespread adoption of advanced tourniquets, the mortality rate of limb wound hemorrhage has decreased significantly, and non-compressible torso hemorrhage has gradually occupied the leading position of potentially preventable death, both in military and civilian circumstances. With the emergence of novel hemostatic devices and materials, strategies for the management of non-compressible torso hemorrhage have changed significantly. This review summarizes the current treatment strategies and types of equipment for non-compressible torso hemorrhage and suggests future research directions, hoping to provide a comprehensive review for the medical personnel and researchers engaging in this field.

Introduction

Hemostasis and resuscitation are the eternal themes of trauma care on the battlefield. The race between hemostasis and bleeding is a significant determinant of survival in the wounded. Hemorrhage usually progresses quickly and offers only a narrow time window for intervention, traditionally termed as the “golden hour”.[1] With the widespread application of tourniquets, the mortality rate of limb wound hemorrhage has decreased significantly, but non-compressible torso hemorrhage (NCTH) has emerged as the leading cause of potentially preventable death on the battlefield.[2–5] With the development of the modern concepts of surgery and the emergence of novel hemostatic devices and materials, the management of NCTH has been significantly transformed. This review summarizes the tools and adjuncts for NCTH and suggests future research directions hoping to provide a comprehensive review for medical personnel and researchers engaging in trauma care.

The evolution of NCTH

The definition of NCTH has not been fully standardized and has mostly been driven by military experience.[6] This entity, which unifies many different torso injuries, gained recognition with the increasing number of deaths in Iraq and Afghanistan. Prior to this, most studies on torso injuries focused on specific organs, such as the liver, spleen, or substantial vessel injuries, which may only be recognized after surgery or advanced radiology. However, the effective treatment measures for these injuries are typically not applied in the early stage of assessment and care. Developing a standardized definition of NCTH is critical to promoting targeted treatments, focusing research, and gaining a better grasp of risk factors and efficacy of treatments.[7] The current definitions of NCTH have originated from an intuitive concept. The involuntary action for hemorrhage control is to compress the bleeding site by pressure dressings, tourniquets, or by bare manual application of pressure. If the given pressure is high enough, the bleeding will cease, thus termed as compressible hemorrhage and often found in accessible sites, such as the extremities. If there is a hemorrhagic focus that is inaccessible to a tourniquet or pressure dressing, such bleeding is termed as non-compressible hemorrhage; being more difficult to break the cycle of bleeding and organ dysfunction.[7] The inaccessible sites include the head, neck, torso, and junctional areas. Because of the high mortality rate and nonsurvivable nature, severe

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hemorrhage from the head and cardiac trauma are not included in the definition of NCTH.[7,8] An additional exception is the neck area, in which hemorrhage may be associated with airway obstruction as the cause of death as opposed to hemorrhagic shock. Thus, the neck is also not omitted from the classification of non-compressible hemorrhage. Because it is not amenable to tourniquet application or direct pressure, junctional hemorrhage from the vessels in the groin or axilla can also be classified as non-compressible. With the development of new junctional tourniquets, however, junctional hemorrhage has also become compressible. Hemorrhage of the torso (Fig. 1) exemplifies the hurdles of non-compressible hemorrhage therapy, where in general, surgical intervention is essential for bleeding control.[6]

The terminology of "Non-compressible truncal hemorrhage" was first used by Holcomb et al.[8] They retrospectively studied the autopsy results of special operation forces team members who were killed in the Afghanistan and Iraq wars from 2001 to 2004. In their study, 82 fatalities were judged as nonsurvivable (e.g., fatal cranial or cardiac trauma) or potentially salvageable, and 50% of the potentially survivable injuries were found to be associated with "non-compressible truncal hemorrhage". In early studies from the Iraq and Afghanistan wars, NCTH is not clearly defined but includes any trunk-related vascular structure or physical destruction. After the wars in Afghanistan and Iraq, a unifying classification of this injury pattern was proposed in the reports from the US Military's Joint Trauma System as well as some selected civilian institutions based on the anatomical site, which includes severe pelvic fracture, major vascular, solid organ, and pulmonary injury associated with bleeding and abbreviated injury scale (AIS)$\geq$4.[9] In order to rule out injuries of high-risk anatomical types without active bleeding, Morrison et al.[7] added the hemodynamic and procedural criteria (systolic blood pressure <90 mmHg; or need immediate operation). To achieve early recognition of the patients in a compensating shock state with relatively normal physiology, a metabolic metric (lactate>4 mmol/L) was included.[6] The epidemiological character of NCTH also evolved along with definition. With the development of new techniques, the evolution NCTH's definition will continue.

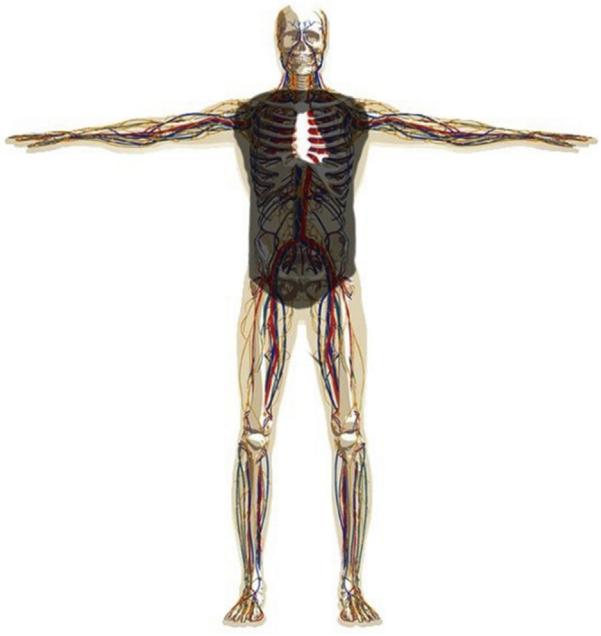

Fig. 1. Hemorrhage area of non-compressible torso hemorrhage. The shaded area marks the anatomic area defined as non-compressible torso hemorrhage.

Hemostatic devices and agents

Pelvic binder

There is no suitable external hemostatic device for the injury of vessels and organs in the chest and abdominal cavity. Nevertheless, for pelvic injuries, the pelvic binder is a good choice. Open pelvic fracture was thought to have the highest risk in bleeding due to the disruption of the vasculature and increased volume in the pelvis. The primary source of bleeding of pelvic fractures originates from the venous system. Pelvic binders were thought to be an effective way to control excessive bleeding by limiting pelvic volume. Cadaveric studies have shown that using a pelvic binder can significantly reduce the pelvic volume and increase the pressure in the pelvic cavity.[10]

To date, pelvic binder is the only external hemostatic device recommended for combat injuries with NCTH in the pre-hospital setting.[11–13] The latest Tactical Combat Casualty Care (TCCC) guidelines also emphasize the positive effects of early use of pelvic binders on hemorrhagic patients. Whenever pelvic fracture or unknown source of bleeding is suspected, a pelvic binder should be applied.[14]

In civilian settings, the pelvic binder was also proven effective. According to the research of Croce et al.,[15] those who received pre-transfer pelvic binders required less blood transfusion and had a shorter length of stay (LOS). However, the results of several recent studies challenged this view. Ghaemmaghami et al.[16] found that early use of the pelvic binders did not reduce pelvic hemorrhage when evaluating the use of an external mechanical compression device on pelvic fractures. In a multi-center retrospective study of open pelvic fractures performed by Cannada et al.,[17] it was found that patients with open pelvic fractures presenting in shock had a mortality rate of 33%. For those patients on whom a binder was placed, the mortality rate was 32%. To determine whether using a pelvic binder could decrease the mortality of open pelvic fractures needs further higher-level clinical evidence. Thus, seizing the time to conduct damage control operations to stop bleeding is still a priority.

Abdominal aortic and junctional tourniquet (AAJT)

External compression devices for vascular control can be traced back to the Crimean War in 1851. Staff surgeon George Russell Dartnell used a self-made device to treat aneurysms in the British army, but due to poor effect, the device did not continue to be used.[18] However, this device's design concept was proposed again due to the increasing demands for combat injuries. AAJT is the first device designed for the purpose of blocking the blood flow of the aorta. However, the evidence for this adjuvant is limited to animal experiments and case reports. Nevertheless it represents a promising solution for bleeding controlling in a pre-hospital environment. The practical use of AAJT was reported in Afghanistan.[19] A soldier with bilateral traumatic amputations of his lower extremities was evacuated via helicopter with an AAJT in place and survived without bowel injury or renal failure 48 h post-operation. Croushourn et al.[20,21] reported two successful civilian applications in gunshot wounds, one in the axilla and another in the groin. The AAJT was applied in the emergency department in both cases and maintained until surgical management was available. Both of the patients survived, and no complication related to the AAJT was observed.

Complications due to long time compression are the main concern of using such a device. The maximum time of flow blocking still needed to be settled to prevent further complications. According to the existing animal data, AAJT does not cause irreversible damage within 1 h.[22] However, small intestine and liver ischemia

were observed 240 min after AAJT release.[22] Compression induced pain may be another issue. Studies on healthy volunteers proved that application to the umbilical region achieves the intended result of blocking blood flow but pain was severe. Groin placement was more comfortable than umbilical application.[23,24] This fact indicates that the pain may be linked with different anatomical structures. However, this may not be troubling for hypotensive and nonresponsive patients, for they are expected to tolerate the pain.

Based on current research and practical experience, AAJT proved to be efficient in the early stage of NCTH management. Although it may cause some complications, in the absence of superior tools, AAJT is still an option. Based on the research of Kheirabadi and colleagues,[25] the US Food and Drug Administration (FDA) recommend the abdominal application of the AAJT for less than 1 h.

iTClamp

The iTClamp is a temporary bleeding control device. Like a big-sized Raney clip with needles on the edges, this device can self-locked when applied on bleeding wounds, providing extra pressure and promoting hematoma generation to stop the bleeding. The device was produced by Innovative Trauma Care Inc. (Canada) and has acquired the approval of the FDA in 2013. During these years, iTClamp has been proved to be useful in hemorrhage management, and it is reported that the overall use of iTClamp has surpassed 245 cases, with the most frequently applied areas being the scalp (37%), arm (20%), and leg (19%).[26] However, for NCTH injury, it still stands as an option. Experiments on swine model showed that it is reliable to control bleeding in the specific regions of NCTH, and that applying iTClamp improves the survival rate in a preclinical junctional hemorrhage model, and meanwhile performing better if used with other modalities, such as packing and compression.[27,28] The TCCC guideline has recommended iTClamp use as a primary treatment modality along with direct pressure and hemostatic dressing.[29] The shortages of iTClamp are obvious. It can only be applied in superficial areas, meaning that patients with deep tissue injury, it is no better than hemostatic forceps.

XStat

XStat (RevMedx Inc., USA) is composed of a syringe and rapidly expanding mini-cellulose sponges that fill the syringe. Once in contact with bodily fluids, the sponge will rapidly expand, creating packing and stopping the bleeding. Recommended by the TCCC guideline as well,[30] it has been used in level I trauma centers. A review of trauma admissions showed the effectiveness of XStat, with a total number of 362 cases, 90% of hemorrhage can be stopped at the first application of XStat, and almost half of cases were junctional injuries. After removal from the wound, no complications were observed. However, sponge retentions was found in two patients.[31] Compared with other devices, a junctional hemorrhage swine model showed that XStat can be applied faster than others, and the blood loss during the application process is similar.[32,33] Because it can evenly oppress the bleeding blood vessels and surrounding tissues, XStat performs very well in trauma that produces a cavity. The disadvantages of this device include the need for additional removal, limited retention time, and tendency to remain in the wound.

ResQFoam

Although “close the tap” is the ideal method in hemorrhage control, mechanical packing may be another choice. One method being explored is self-expanding polyurethane foam or ResQFoam. After percutaneous injection into the abdominal cavity, the foam can expand to nearly 30 times from the original volume, and provide volume-filling to slow or stop bleeding. In addition, ResQFoam binds to the fluid in the peritoneal cavity then turns to a solid-state, providing more effective pressure for bleeding vessels during laparotomy and simplifying foreign body extraction. Portal and iliac vein bleeding models confirm the efficiency of ResQFoam compared to resuscitation alone. However, potential risks also need to be addressed. Complications such as abdominal compartment syndrome, bowel injuries, thermal injuries, and long-term impact of foreign body retention warrant further investigation.[34] Future research should focus on long-term safety and the determination of safe doses for humans. If these problems can be solved, ResQFoam may become a reliable tool in pre-hospital and in-hospital emergency treatment.

Antifibrinolytic tranexamic acid (TXA)

Early use of tranexamic acid is beneficial in preventing trauma patients from dying due to bleeding in both military and civilian settings. A meta-analysis of orthopedic trauma patients showed that all 12 studies (1333 patients) confirmed a significantly lower risk of blood transfusion and blood loss after treatment by TXA than that in the control group. No difference in the risk of thromboembolism was observed.[35] Roberts et al.[36] demonstrated that using TXA in trauma patients within 3 h after injury is beneficial, but using TXA after 3 h may increase the risk of death from bleeding.

Regarding the method of administration, Wright et al.[37] suggested that 1 g TXA should be incorporated as an intramuscular auto-injector and distributed to combat forces for self- or buddy-administration in the event of enduing serious injury. In a recent review,[38] more evidence demonstrates that TXA administration in pre-hospital trauma patients is clinically and economically achievable. This literature recommends intravenous use of a loading dose of 1 g of TXA, followed by 1 g infusion over 8 h within 3 h after injury.

Resuscitation

Whole blood program

The basis of the modern blood bank system was developed in the early 20th century. The United States adopted its blood program during World War II due to the observation-based evidence of the lower death rate of injured British soldiers after receiving whole blood (WB) transfusions.[39] However, once the preferred blood product for trauma resuscitation was applied, the use of WB nearly ceased by the 1970s as component therapy replaced its use. Trauma resuscitation protocols were radically changed and WB was scarcely used.[40] With the recent revision of fluid resuscitation guidelines of Committee on Tactical Combat Casualty Care (CoTCCC), which encouraged the use of WB for the treatment of hemorrhagic shock victims, WB implementation is back at the forefront.[41] Table 1 summarizes the recommended order for massive blood loss resuscitation by the TCCC guideline.

Table 1
Tactical Combat Casualty Care recommendation order for massive blood loss resuscitation.[42]

No.	Type of resuscitation fluid
1	Whole blood
2	1:1:1 plasma: RBC: platelet
3	1:1 plasma: RBC;
4	Plasma (liquid, thawed, dried) or red blood cells alone
5	Hydroxyethyl starch
6	Ringer's lactate or plasma-lyte A

In patients with NCTH, WB can help improve tissue oxygenation and blood coagulation, which cannot be provided by crystalloid resuscitation. WB provides all blood components (RBCs, platelets, and plasma) in a nearly physiological ratio and achieves balanced resuscitation. Fresh WB is the best choice when using for resuscitation.[42] Blood donors without infectious diseases should be picked out in advance to prevent blood shortage. Low antibody titer of type O WB is a good choice for storing due to its wide application. The targets of resuscitation include an improved state of consciousness (if no central nervous system damage is present) and a normal radial pulse (approximately 80 mmHg systolic blood pressure). For NCTH, excessive resuscitation should be avoided, which may cause the fall of the clot at the internal bleeding site, making the bleeding more serious.

Freeze-dried plasma

Plasma replenishes blood volume and protects cells and organs. Freeze-dried plasma is a blood component product, which is separated from WB donated by healthy people (or collected by a blood component collection machine), with the characteristics of being in solid powdered form after undergoing viral inactivation and freeze-drying. Dried plasma is more convenient for damage control resuscitation, and has a broad application prospect in war injuries due to its stable properties, shelf-life and efficiency. During World War II, dried plasma was widely used in the US military for hemorrhagic shock resuscitation.[43] In the 1950s, the Chinese military also studied and produced freeze-dried plasma to meet the shortage of blood in the Korean War. However, it was then been banned because of the multiplicity of its sources and potential risks for infectious disease transmission such as hepatitis and human immunodeficiency viruses.[44] With the development of virus inactivation technology, dried plasma has regained attention. The FDA approved the use of French-produced plasma products in by the US army in 2011, which was accredited by the French army in 1994.[45] Also, dried plasma products have been introduced to clinical practice in Europe and the North Atlantic Treaty Organization (NATO) for war injuries.

Surgical and endovascular measures

Open surgery

Before the invention of endovascular technology, open surgery to control hemorrhage was the definitive method for NCTH. The main task for trauma surgeons includes opening the chest or abdomen to achieve rapid bleeding control. Today, in institutions not equipped with endovascular imaging equipment and specialized staff, open surgeries are still the mainstay for trauma hemorrhage control. The surgical approaches for hemorrhage control in these anatomic regions include packing, vascular ligation, the removal of solid organs, non-anatomical organ resections and temporary shunting, but proximal and distal control is a common principle for all of these maneuvers.

Resuscitative thoracotomy is used to control hemorrhage within the thoracic cavity, to decompress cardiac tamponade and resolve aortic occlusion as well as to control infra-diaphragmatic hemorrhage.[46] The anterolateral approach is preferable for thoracotomy. Patients should be in the supine position and hold a lateral flexion that increases the intercostal space of the injury side. The incision needs to through the fourth intercostal space, which facilitates the extension of this incision across the sternum into the right hemithorax or the clam-shell incision. It also permits access to either mediastinum or contralateral thoracic cavity if required. However, with the wide application of resuscitative endovascular balloon occlusion of the aorta (REBOA), resuscitative thoracotomy is applied only in limited cases, such as pericardial tamponade and gradual loss of its position in NCTH.[47]

Laparotomy is used to control hemorrhage stemming from solid abdominal organs and repair damaged vessels. When there is an extensive injury to the abdominal organs, persistent bleeding in the abdominal cavity, or long-distance evacuation before a further operation, a damage-controlled laparotomy is warranted. A midline incision from the xiphoid to the pubic symphysis is preferable in order to access all four quadrants. The approaches to deal with hemorrhage from the different abdominal organs differ, and thus needs to be handled by a professional and experienced surgeon. Packing remains the best method for damage control, as it permits time for resuscitation and specialized operations.

For pelvic injury, preperitoneal pelvic packing (PPP) should be adapted as a damage control measure when patients are actively bleeding or still hemodynamic unstable after transfusion of two units of RBC. The incision of PPP is a median incision starting from the pubic symphysis, extending 6–8 cm superiorly. It is worth noting that if laparotomy is needed, the two incisions should be separated; otherwise, it is difficult to achieve effective packing. Once the pelvis is filled, the bleeding slows down, allowing the patient to receive a CT scan or other hemorrhage control measures. Angiography helps to locate the bleeding site and embolize the injured vessels. The packing material needs to be removed after 24 h if the patient becomes stable; otherwise, it may increase the risk of infection. With the innovative tools and methods such as AAJT (mentioned above) and preperitoneal balloon tamponade being adopted clinically, the technical threshold for early control of bleeding is also gradually lowered. Experiments on animal models of pelvic injury have shown no difference between PPP and these two novel techniques.[48,49]

Resuscitative endovascular balloon occlusion of the aorta (REBOA)

REBOA was first used to treat aortic arch and pelvic bleeding in the Korean War. With the improvement of the endovascular technique, its clinical application has expanded. REBOA can increase the perfusion of vital organs as well as cardiac afterload and aortic pressure by blocking distal blood flow and bleeding with a balloon. Compared with traditional methods, such as resuscitative thoracotomy, REBOA has the dual effect of significantly improving the survival rate and reducing complication incidence.[50] The routine approach for vascular intervention is the femoral artery (via femoral artery incision, ultrasound-guided or percutaneous puncture). After inserting and expanding the balloon, various imaging methods such as fluoroscopy, ultrasound and radiographs can be used to determine whether the appropriate position is attained. If imaging assistance is not available, blind insertion can be performed according to anatomical surface landmarks. The elevated systolic pressure can be used as an indicator of proper placement. In a recent multi-center study, REBOA demonstrated the ability to allow more patients to maintain hemodynamic stability when compared to an open aortic occlusion technique.[50] The tolerance limits for occlusion depends on the aortic placement sites. The time limit for zone I occlusion is 30–45 min, whereas zone III is up to 120 min.[51] Since the operative aspect of REBOA is not overly complicated, non-surgeons can also be trained to perform the operation successfully. In the future, mastering the REBOA strategy is an essential skill for the mobile surgical teams confronted with hemorrhage casualties. Subsequent improvements may include "targeted regional perfusion optimization" realized by a novel intermittent REBOA strategy. Alternatively, development of innovative equipment allowing for improved for distal perfusion, and simultaneously managing to overcome the issue of ischemia-

Table 2
Summary of current management of non-compressible torso hemorrhage.

Classification	Approach	Advantages	Disadvantages
Hemostatic devices and agents	Pelvic binder	Simple to use, portable, stable effect	Auxiliary, not reducing mortality
	Abdominal aortic and junctional tourniquet	Suitable for axilla, groin and trunk, the abdominal aorta being blocked	Fragile, umbilical cord application causing pain and ischemic injury, cannot be used in trunk penetrating injury
	ResQFoam™	Simple to use, minimally invasion, no professionals needed	Insufficient on arterial hemorrhage control, potential complication
	Antifibrinolytic tranexamic acid	Improving survival rate, reducing blood products use	An application time window within 3 h after injury, use after 3 h increasing the risk of bleeding
	XStat-30™	Simple to use, suitable for deep penetrating wound or wound cavity	Only for junctional injury, need to remove after 4 h
	Trauma clamp iTC™	Simple to use, used for any wound	Only seal the surface, apt to form hematoma, assemble needed
Resuscitation	Whole blood program	Improve oxygenation and coagulation, balanced resuscitation	Difficulty in production, storage and transportation
	Dried plasma	Easy to store and transport	Simple ingredient, potential risk of transmitting diseases
Surgical and endovascular measures	Open surgery	Intuitive, specific damage repair	Professional surgical teams needed
	Resuscitative aortic occlusion	Proximal control, raising central arterial pressure	Invasive, risk of infection, professionals needed
	Resuscitative endovascular balloon occlusion of the aorta (REBOA)	Minimally invasion, raising central arterial pressure	Professionals needed, risk of spinal ischemia, imaging support required
	ER-REBOA™	Minimally invasion, raising central arterial pressure, visualization	professionals needed, risk of spinal ischemia, risk of spinal ischemia
Other measures	Non-steroid anti-inflammatory drugs	Non-steroid anti-inflammatory drugs should not be used for pain relief in non-compressible torso hemorrhage due to the interruption of coagulation	
	Hypothermia prevention	Reducing temperature loss, help to avoid coagulation disorder	
	Valproate	Reducing mortality, similar survival effect with WB resuscitation	Mechanism, usage and dosage need further study

reperfusion injury, may extend the allotted operating time-window and increase survival rate.

Additional measures

Avoid using non-steroid anti-inflammatory drugs (NSAIDs) interfering coagulation

NSAIDs such as aspirin, ibuprofen, ketorolac that interfere with coagulation should be avoided in combat settings. Besides, NSAIDs are not recommended for pain relief when NCTH occurs, and acetaminophen or meloxicamare is optional when necessary, which do not hinder platelet function.[52] In a 2012 survey, 75% of soldiers reported using NSAIDs more than twice a week.[53] For soldiers who are prescribed NSAIDs for other conditions should be administered alternative agents prior to entering combat.

Hypothermia prevention

The onset of hypothermia in NCTH patients is often overlooked. Most patients lose temperature at the point of injury and during the evacuation. Heat loss is more rapid in helicopter evacuation, with an average decrease of 1.7 °C/h.[54] The most immediate impact of hypothermia is the resulting caogulopathy. Even a slight drop in body temperature can interfere with blood clotting and increase the risk of death from excessive bleeding. Studies have shown that for every degree drop in body temperature below 36.0°, RBC infusion is increased by 10% within 24 h of admission.[55] With reasonable precautions, hypothermia can be mitigated. Removing wet clothing, covering casualties and utilizing hypothermia prevention equipment may in large part prevent hypothermia. Therefore, thermal insulation must be initiated early in the clinical course.

Valproic acid (VPA) and pharmacologic resuscitation

NCTH patients not exhibiting progressive and rapid deterioration during evacuation have a greater chance of survival. In order to improve patients' tolerance to trauma and bridge the time to surgery, researchers explored the promotion of a "pro-survival phenotype", that is, pharmacologic resuscitation. Studies have found that severe trauma can lead to the deacetylation of cell proteins, resulting in a decrease in cell metabolism, growth, proliferation, differentiation and signal transduction.[56] Studies of histone deacetylase inhibitors (HDACIs) have revealed that HDACIs can induce post-translational modification of a variety of proteins and cell transcription in hemorrhagic shock and has the effect of reducing mortality.[57] Hemorrhagic shock is the central denominator of early death in patients with NCTH. The favorable performance of VPA in the study of hemorrhagic shock brings good news to NCTH patients. At least 18 human HDACIs subtypes have been identified and classified into four functional categories (I, IIa/IIb, III, and IV),[58] VPA as a non-selective classI/IIa inhibitor has the best effect of promoting survival rate among other HDACIs.[59] Using VPA alone without blood products had a similar survival effect as with active WB resuscitation.[60] In a rat hemorrhagic shock model[61] and swine model of severe multitrauma,[62] the use of VPA increased the survival rate. VPA also reduced the physiological ramifications of ischemia-reperfusion injury in fatal shock animals.[63] In addition, acidosis, coagulation disorders, and the use of vasopressor drugs were also reduced during resuscitation.[64] However, in the current trauma treatment experiments, the dosage of VPA exceeds the maximum dose recommended by FDA (60 mg/kg/day). A phase I clinical trial (clinical trials govNCT01951560) showed that the maximum tolerable dose for healthy adults was 140 mg/kg intravenously within 1 h. With excessive adverse reactions, including nausea and headaches,[65] VPA is still in the experimental stage, and more safety assessment is needed for its widespread clinical use.

Conclusion

NCTH is defined as a combination of anatomical torso injury, hemodynamic instability and requirement for immediate hemorrhage control. The management strategies of NCTH consist of the following three parts: (1) hemostatic measures to control the source of bleeding ("close the tap"); (2) appropriate resuscitation to maintain the volume and vital organ perfusion ("fill the tank"); (3)

increase of body's tolerance to ischemia ("upgrade the armor"). The current management of NCTH is summarized in Table 2. The future directions of NCTH prevention and treatment embrace iterative upgrade of body armor (scope expanded, flexibility enhanced or combat suit embedded), optimal design of external hemostatic devices (integration, light-weighted, miniaturization, repeatability), novel hemostatic dressings (nontoxic, highly-effective), innovations of drugs and materials in vivo (hazard-free, design for hemorrhagic sites, simple application) and integration of advanced comprehensive treatment strategies.

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Ethical statement

Not applicable.

Declaration of competing interest

All authors report no conflicts of interest.

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