



Review Article

Military training-related abdominal injuries and diseases: Common types, prevention and treatment

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ABSTRACT

Military training is intense, difficult and often dangerous, so all kinds of injuries or diseases frequently occur during training. Most of the previous studies and reviews on military training-related injuries focused on musculoskeletal system, whereas there are no reviews of abdominal injuries and diseases. Although the incidence of military training-related abdominal injuries and diseases is relatively low, the patients' condition is often critical especially in the presence of abdominal organ injury, leading to multi-organ dysfunction syndrome and even death. This paper elaborates on common types of military training-related abdominal injuries and diseases as well as the prevention and treatment measures, which provides some basis for scientific and reasonable training and improvement of medical security.

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Introduction

Military training is the essential way to grow and reinforce warfare capability and plays a strategic role in promoting military development. During military training, injuries have a serious impact on trainee's health as well as training efficiency and effect, and cause unnecessary non-combat attrition as well as gain military and national burden. Studies reported that the overall incidence of military training-related injuries in China ranges from 7.43%–60.7%, with a concentration of 10%–20%, and the incidence varies among different services and arms, different subjects and different times.^{1–9} Thereinto, the incidence of military training-related injuries in recruits is up to 50%–60%,^{6–8,10} and obstacle training, physical training and tactical training are the most injury-inducing subjects,^{4,9} with the highest number of injuries during the fatigue period 6–8 weeks after the training.¹¹

About 90% of military training-related injuries occur in skeletal and muscular systems,^{12–14} while 4.74%–15.77% occur in the abdomen or trunk, and its risk factors include low level of physical fitness, previous abdominal diseases history, improper eating habits, etc.^{15–18} Once military training-related abdominal injury appears, it will seriously harm soldier's health. Particularly, in the presence of abdominal organ injury, it often contributes to

disastrous consequences and even life-threatening. Previous studies or reviews mainly have explored the extremities or spinal column and other areas with high incidence of training-related injuries, but ignored abdominal injuries. The paper aims to summarize and analyse the relevant research reports of military training-related abdominal injuries and conclude the types, causes, prevention and treatment managements to supply a certain basis for scientific training, reducing training-related injuries and improving the quality of medical care.

Common types of military training-related abdominal injuries and diseases

Training-related functional gastrointestinal disorders

Gastrointestinal symptoms are highly prevalent during military training, such as abdominal pain, nausea, vomiting, fullness or diarrhea, but many trainees have no organic explanation for these symptoms. Most of these trainees are labelled as having a functional gastrointestinal disorder (FGID). FGIDs have a complex pathophysiology and are not completely understood to date.¹⁹ Training-related FGIDs are commonly induced by improper diet, overeating, insufficient warming-ups, substantial air input during strenuous exercise, etc. These symptoms frequently overlap and lack specificity, making it important to exclude other organic abdominal diseases with caution.

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Given the lack of understanding of the mechanism of training-related FGIDs, the following prevention and treatment measures are mostly experience-based and symptom-controlling.

Prevention measures: (1) No strenuous exercise 1–2 h after meals; (2) Rehydration after strenuous exercise should be in a small amount but multiple times, so as to avoid gastrointestinal discomfort; (3) Adjust breathing rhythm during exercise and try to avoid gulping, and breathe through your nose or place your tongue against the palate to slow down the inhaled airflow.

Treatment measures:^{20,21} (1) Once abdominal symptoms appear, trainees should stop exercise and have a rest; (2) If the symptoms persist, anti-spasmodic drugs (such as anisodamine and scopolamine) can be taken orally or be injected, along with use of acid suppression drugs (such as omeprazole) to protect the gastric mucosa; (3) If the abdominal pain is severe and intolerable, pain killers like ibuprofen, can be properly used under the exclusion of other acute abdominal diseases.

Abdominal muscle spasm

Muscle spasm, commonly known as “cramps”, is a sort of tonic involuntary contraction of muscle. Sometimes the outbreak of abdominal muscle spasm is along with gastrointestinal spasm.^{22–24} Abdominal spasms are common in training subjects involving abdominal movements, such as sit-ups and swimming. When they outbreak, partial muscle stiffness and movement restriction occur accompanied by severe pain, which sometimes put trainees in danger. Statistics show that 84.7% of drowning accidents during swimming training in Navy are because of muscle spasms.²⁵ It is easy to diagnose but muscle strain should be considered when the pain persists.

Main causes: (1) Inadequate warming-ups; (2) Overexercise, week physical quality, sudden high-intensity muscle training, or muscle fatigue and training without adequate rest; (3) Non-standard and uncoordinated training movement, or too much force on partial muscle; (4) Overlook of relaxation training after exercise; (5) Excessive temperature difference, like sudden diving into the water or training from warm indoors into cold outdoor; (6) Neurovascular pressure, mainly at non-standard training movement, large movement range, or long-term bad sitting posture and sleeping posture.

Prevention measures:^{22–25} (1) Trainees should have adequate warming-ups before training; (2) The training intensity should be gradual and combine work and rest. The weak trainees should start from low intensity training to gradually strengthen the core muscle strength; (3) The key points of training movements should be standardized, and non-standard and uncoordinated movements should be guided to correct; (4) After training, trainees should relax, such as static muscle stretching to gradually relax the muscle.

Treatment measures:^{22–25} (1) Relaxation: once abdominal spasm occurs, immediately exercise should stop and take a break. It can be combined with partial patting and massage. Most of the injured can relieve themselves after a break; (2) Stretching: abdominal muscle stretching can be implemented assisted by the team doctor or partners to relieve muscle spasm; (3) Physiotherapy: the use of hot compress, infrared and other physical therapy can relieve the symptoms like muscle soreness after abdominal spasm.

Abdominal muscle strain

Muscle strain is a kind of common sport injury, accounting for 10%–55% in all acute sport injuries. It is caused by the rapid and intense muscle contraction or excessive muscle stretch, which is beyond the capacity of the muscle tissue leading to a partial or

complete break of the muscle tissue.²⁶ Theoretically, any strain that can cause the muscle to exceed its elastic range can result in a muscle strain. The types of stress can be divided into passive strain of the muscle, such as the strain of weight or training equipment, and active contraction of the muscle, such as the strain of sit-ups.²⁷ Abdominal muscle strain is mainly presented as pain and swelling of the abdominal muscle, limited muscle movement, and skin bruising or discoloration. Mild cases may merely have partly muscle soreness and stiffness.

Although the diagnosis for muscle strain is usually clinical, imaging tools such as ultrasound, CT and MRI are often useful to identify the extent and site of lesion. A new classification distinguishes muscle injuries as injuries after direct and indirect trauma. The latter is classified as non-structural and structural injuries.²⁶ According to the degree of muscle fiber injury, muscle strain can be divided into three levels²⁷: Level I, mild injury – no more than 5% continuity damage of muscle structure, no pain or slight pain at break and no or slight limitation of joint movement; Level II, moderate injury – partial fracture of muscle, obvious pain at break and aggravated by active contraction or passive pull of muscles, and significant limitation of joint mobility; Level III, severe injury – complete fracture of muscle, visible partial muscle bulge during contraction and inability to move the joints. Sometimes the symptoms and signs of level I muscle strain are not obvious, and it is clinically feasible to assist the diagnosis together with ultrasound, CT, MRI and other auxiliary examinations; Level III is easy to diagnose when muscle issue is completely broken, local muscle displacement is visible, and there is bulge when contraction occurs.

Main causes: (1) Inadequate warming-ups, non-standard and uncoordinated training movement and weak muscle strength; (2) Muscle fatigue, long-term muscle load or short-term continuous high-intensity training without adequate break; (3) The older the age, the less elasticity of muscle fiber, and the higher the risk of muscle strain.

Prevention measures:^{27–29} (1) Trainees should have adequate warming-ups before training and have a break at training interval to prevent muscle fatigue and effectively reduce muscle injury; (2) Stretching exercise can change elasticity of muscle to avoid muscle strain; (3) The training intensity should be gradual and individualized, and some non-standard movements should be avoided; (4) Avoid trauma.

Treatment measures:^{26–28} Many treatment approaches are available for muscle injuries, but the best management is still debated in literature. An evidence-based summary of treatment protocols is provided as follows: (1) Early “PRICE” principle (within 3 days after trauma): Protection (P), abdominal band, elastic bandage or lumbar and abdominal support can be used for local immobilization to promote muscle recovery and prevent re-injury; Rest (R) and Ice (I), which can reduce the bleeding in the part of muscle fibre fracture, mitigate hematoma or edema and relieve inflammation; Compression (C) of injured muscle has significant effect to relieve hematoma and promote muscle recovery; Elevation (E) of injured part can reduce interstitial fluid pressure and alleviate tissue edema. Bleakley et al.³⁰ promoted a “POLICE” (Protection Optimal Load Ice Compression Elevation) protocol, with a major innovation of optimal load. In this way, the injured muscle will rest, but a balanced progressive rehabilitation program should be gradually introduced to control mechanical stresses; (2) Physiotherapy, hyperbaric oxygen treatment and drug therapy: hot compress, infrared ray and ultrasonic therapy can improve micro-circulation and enhance muscle recovery. Hyperbaric oxygen is able to elevate oxygen saturation and facilitate muscle fibre regeneration. Non-steroidal anti-inflammatory drugs can mitigate pain, and decrease inflammation and the secondary damage caused by local inflammation. Traditional Chinese medicine for activating blood

circulation and removing clots is also widely used in clinical practice, and it can promote microcirculation, mitigate edema and potentiate muscle regeneration; (3) Surgical treatment: severe ruptures of muscle and tendon need to be evaluated by surgical consultation. If necessary, surgical operation for repair will be performed; (4) Rehabilitation training²⁷: in the acute phase of muscle strain, or that is to say, rehabilitation training should be started as soon as possible in the pain-free range within 3 days after injury, after the implement of immobilization, detumescence and pain killing. In the intermediate period, that is, in 3–10 days after the injury, muscle stretching exercises, hydrotherapy, etc., should be started to promote muscle recovery. The functional recovery period is 10 days after muscle strain, which is designed to recover the normal movement function. Specific activities include muscle flexion and extension training, endurance training, resistance training, etc.^{31,32} The norm of muscle strain recovery is as follows: the flexibility of both limbs is equal; there is no apparent abnormality in muscle contraction; muscle strength returns to 85%–90% of normal level.^{28,29}

Volvulus

Volvulus refers to closed-loop intestinal obstruction resulted by the rotation of a segment of intestinal loop along the long axis of its mesentery. Since mesenteric vessels are compressed, strangulating intestinal obstruction is caused at the same time.³³ It is often seen in strenuous exercise after a large meal, particularly training subjects of sudden transformations in body position, such as the Navy's swimming training, the air force's roller and ladder training. The cause is that the content of intestinal cavity after a large meal is more, and when the body position is changed suddenly, the intestinal tract cannot rotate synchronously with the abdominal cavity because of the weight drooping.

The occurrence of volvulus is related to intestinal activity. The small intestine with high flexibility, is the most common part of volvulus accounting for more than 70% of all of volvulus,³⁴ followed by volvulus of sigmoid colon and volvulus of cecum. However, it was reported that volvulus of cecum is commonly seen in long-distance runners, such as infantry who do a lot of running.^{35,36} The cause may be due to the repeated upper and lower mechanical stress on the abdominal organs during long-distance running, which pulls and weakens the fixation of the mesocolon, coupled with the hypertrophy of the psoas major muscle in long-distance runners, called "cecal slapping syndrome" (the frequent and repeated slapping of the posterior wall of the cecum against the abdominal muscle tissue during long-distance running), which leads to increased friction between the cecum and the abdominal wall.^{37–39} These factors will all raise the cecal flexibility during long-distance running training, and then increase the risk of volvulus.

Symptoms of different parts of volvulus have different characteristics. The volvulus of small intestine is more presented as sudden periumbilical colic, which can extend to the back of the waist together with vomiting; volvulus of sigmoid colon is manifested as persistent abdominal distending pain and left abdominal distension; volvulus of cecum may present as abdominal pain, vomiting, and mass in the right lower abdomen. When volvulus incurs strangulating intestinal obstruction, the patient will have the symptoms of poisoning and shock, with dehydration and electrolyte disturbance.

When volvulus is highly suspected in accordance with the trainee's medical history and clinical manifestation, the patient should be urgently sent to the clinic. Meanwhile, X-ray, barium meal examination and CT examination can be feasibly used to assist the diagnosis. Abdominal CT, possessing high sensitivity and

specificity to the diagnosis of volvulus, can be taken as the preferred choice of imaging examination. In addition to the manifestations of intestinal obstruction, the CT characteristics of volvulus of small intestine also include the "whirl sign", that is, the torsional intestine, the mesentery and the mesenteric vessels are arranged in a spiral shape around a center, forming the whirl sign of the intestine and the vessels. In the case of volvulus, attention should also be paid to differentiating it from other acute abdominal symptoms such as acute perforation of gastroduodenal ulcer, acute cholecystitis, and paralytic ileus.

Prevention measures: (1) Avoid training immediately after meals, and high-intensity training should be started 2–3 h after meals; (2) Do not overeat before training; (3) Trainees with the medical history of intestinal ascariis, habitual constipation, intestinal diverticulum, and abdominal surgery should attach importance to the occurrence of volvulus.

Treatment measures:^{33,40} (1) Surgery is the preferred treatment for volvulus and timely surgical treatment should be performed on the basis of early diagnosis, which plays a pivotal role in the prognosis of patients. The purpose of the surgery is to reduce the twisted loop of the intestine, resolve the obstruction, and restore intestinal patency. For patients who have the strangulation of intestinal obstruction for a longer time to appear intestine necrosis or perforation, intestinal resection is required; (2) Fiber colonoscopy for treatment or adjuvant therapy of volvulus can be options^{41,42}; (3) General treatment measures, including fasting and water deprivation, decompression of gastrointestinal tract, anti-infection, regulating water, electrolyte disturbance and acid-base imbalance.

Peptic ulcer (PU)

PU means that mucous membrane, under the action of various pathogenic factors, develops inflammatory response to present necrosis and exfoliation, and then forms ulcer.⁴³ The relationships between exercise or physical training have received little attention. Two studies showed that mild to moderate physical activity reduced peptic ulceration.^{44,45} However, prolonged endurance and high-intensity training seems likely to have a negative effect, resulting in gastrointestinal blood supply shortage and weakened immune function.⁴⁶ The stress induced by strenuous training will also make the sympathetic nerve excited, gastrointestinal mucosal blood vessel contracted, and the gastrointestinal secretion and motor function enhanced, causing stress ulcer and the subsequent bleeding or perforation.⁴⁷ There has been few studies focusing on high-intensity activity or military training and PU, calling for more attention and exploration. Animal studies reported very high prevalence of PU in racehorses and racing sled dogs, suggesting negative effects at high intensities and competitiveness of exercise.^{48,49} It could be believed that the high intensity and competitiveness, and the harsh territory of military training are risk factors for PU. Studies reported that the gastroscopic positive rates for PU in military officers and soldiers were higher (13.2%–46.74%) than general population (6.8%–18.37%).^{50–52} But it remains difficult to separate effects of environment, diet and psychological factors in these studies.

PU is typically presented as abdominal pain at the top middle and sour regurgitation, which are rhythmical and periodical, with nausea, anorexia and abdominal distension. Gastroscopy is an effective way to diagnose PU. PU complicated with gastrointestinal bleeding is manifested as hematemesis or melena, and some patients may be asymptomatic, with fecal occult blood test being positive. Gastrointestinal perforation, with rapid onset and serious condition, is the severest complication of PU. Patients with gastrointestinal perforation generally have aggravated ulcer symptoms or excessive fatigue, manifested as sudden severe pain in

the upper abdomen, like “a knife cut”. Besides, the abdominal pain quickly spreads to the whole abdomen. Peritonitis and shock could be present, and the typical sub-septum crescent-shaped free gas shadow could be seen on the orthostatic X-ray.³³

Prevention measures:^{51,53} (1) Arrange training and rest properly to avoid stress; (2) The training and living environment of the trainees should be improved. Timely psychological counseling and intervention are needed if necessary; (3) Regular diet and the attention to food hygiene are necessary; do not eat too much spicy raw or cold food; (4) Patients with helicobacter pylori infection should undergo formal helicobacter pylori eradication therapy.

Treatment measures:^{47,54} (1) Proton pump inhibitor is the preferred drug for the treatment of PU, which can effectively inhibit gastric acid secretion, significantly improve the gastrointestinal symptoms of patients, prevent gastrointestinal bleeding, and promote ulcer healing; (2) The application of gastric mucosal protectant can effectively prevent and treat gastric mucosal injury and promote tissue repair and healing; (3) Patients with ulcer complicated with gastrointestinal bleeding should take emergency gastroscopy as soon as possible (within 12 h). If active bleeding is found, the bleeding can be stopped directly under the gastroscope. At the same time, intravenous high-dose proton pump inhibitor is used for 72 h and fluid resuscitation. (4) Ulcer complicated with gastrointestinal perforation should be treated with emergency surgery and perforation suture, or complete subtotal gastrectomy, together with fluid resuscitation, prevention and treatment of shock and infection. Regular anti-ulcer drug therapy is still needed after surgery.

Abdominal trauma

Due to the high intensity, difficulty of military training and the heavy training equipment and lethal weapons, all kinds of injuries frequently occur, among which abdominal injuries account for 6%–14.9% of all of them,⁵⁵ and are often accompanied with limb, craniocerebral or thoracic injuries. In severe cases, multiple organ dysfunction syndrome may occur and even endanger life, with the overall mortality rate up to 8%–25%.⁵⁶

The diagnosis of abdominal trauma needs to be rapid and accurate, which is very important to the prognosis of patients and even to save lives. In our experience, open abdominal trauma often has exposure of abdominal viscera (intestine, omentums, etc.), and it is not difficult to diagnose according to the wound effusion. However, the symptoms and signs of closed abdominal trauma are often hidden, and the severity may be greater than that of open abdominal trauma. Nevertheless, regardless of open or closed abdominal trauma, it is crucial to identify the injured organs, injury degree and associated injuries such as injuries of blood vessels, ureters and nerves.

Based on the classic ultrasound and CT, it is reported that dual-phase CT has a much better accuracy of the diagnosis for the visceral blood vessel injury.⁵⁷ Compared with CT, focused assessment with sonography for trauma is considered to have the same accuracy but more timesaving for closed trauma, being already applied in military training and battlefield.⁵⁸

The best treatment is to prevent the occurrence of any kind of trauma. Prevention measures: (1) Improving the training security system, strictly implementing safety measures, enhancing the safety awareness of trainers and trainees, and keeping alert; (2) Necessary protective measures should be taken for high-risk training projects, such as the use of protective gear; (3) Sufficient simulation training or rehearsal before training with live ammunition, to ensure that the participant's actions are standardized and to avoid accidents caused by improper operation; (4) Checking training equipment and weapons before training to ensure the

safety; (5) Improving medical security: medical personnel should educate participants before training, and go to the training site to provide medical security and find problems and correct them in time.

Abdominal trauma is usually combined with multi-system and multi-organ injuries. The patient's condition is critical, complex and changeable. The main treatment measures^{59–66} are: (1) General treatment: vital signs monitoring, fluid resuscitation, regulating water and electrolyte disturbance, and other symptomatic supportive treatments; (2) Infection prevention: serious infection is the crucial factor of death after abdominal trauma, sometimes accompanied with wound infection, peritonitis, abscess, sepsis and other symptoms. The primary precautions involve thorough debridement, control of infection sources, correction of physiological disorders, rational use of antibiotics and prevention of secondary infections; (3) Operative treatment: laparotomy after abdominal trauma is sometimes the key measure to save lives. The 3 main purposes of exploratory laparotomy are (1) to control bleeding and gain effective time for resuscitation; (2) to identify the injured part, remove and control abdominal contamination; (3) to repair or reconstruct the injured part. In order to save life, there is no absolute contraindication for laparotomy, and the main surgical indications are⁵⁹: (1) Abdominal penetrating firearm injury; (2) Shock and unstable hemodynamic indicators after active treatment; (3) Signs of peritonitis; (4) Presence of free gas in the abdominal cavity; (5) Gastrointestinal bleeding or severe hematuria; (6) Non-coagulant blood or gastric contents acquired by abdominocentesis; (7) Large amount of blood loss, or outflow of gastrointestinal contents, bile and urine; (8) Prolapse of the great omentum and intestinal canal through the abdominal wall wound, or the wound in connection with the abdominal cavity during debridement.

With the revolution of technology and concept, damage control surgery for major abdominal trauma received increasing attention and acceptance.⁶⁷ It involves 3 steps: surgical control of lesions (hemostasis, sealing of intestinal spillage), physiological restoration and surgery for definitive repair. Based mainly on specific hemodynamic resuscitation targets associated with early and aggressive hemostasis, damage control surgery aimed at prevention or correction of the lethal triad of hypothermia, acidosis and coagulation disorders. This greatly improves the survival rate of the wounded from military training and even war.⁶⁸

Conclusion and prospect

In summary, common types of abdominal injuries and diseases during military training include functional gastrointestinal disorders, abdominal muscle spasm and strain, volvulus, peptic ulcer and abdominal trauma (Table 1). For any of them, prevention should come first. We should improve safety awareness, strictly implement safety regulations, prepare for safety protection, pay attention to reasonable and regular diet, and warm up and relax before training, so as to reduce unnecessary non-combat attrition. When abdominal military training-related injuries happen, quick evaluation and initial treatment should be provided by healthcare personnel.

Some abdominal injuries can be very serious and life-threatening, such as abdominal organ injury. The injured often need an urgent diagnosis and should be transported to a hospital as soon as possible. Nowadays, the diagnosis and treatment capacity for serious abdominal injuries have been remarkably improved. The artificial intelligence and robot diagnosis system that has emerged in recent years are expected to enable first-responders to make accurate diagnosis and assessment of injuries on scene, and to take reasonable treatment measures earlier.^{69,70} It is expected to

Table 1
Summary of all common types of military training-related abdominal injuries and diseases.

Types	Causes	Prevention	Treatment
Training-related functional gastrointestinal disorders	<ul style="list-style-type: none"> ● Improper diet ● Insufficient warming-up ● Strong air input 	<ul style="list-style-type: none"> ● Avoid meals around training ● Proper food and water intake ● Adjust breathing to slow down the inhaled airflow 	<ul style="list-style-type: none"> ● Stop training ● Anti-spasmodic drugs along with acid suppression drugs ● Pain killer when necessary
Abdominal muscle spasm	<ul style="list-style-type: none"> ● Inadequate warming-up ● Overexercise and muscle fatigue ● Non-standard training movement ● Excessive temperature difference 	<ul style="list-style-type: none"> ● Adequate warm-ups ● Reasonable training intensity ● Standard training movement ● Muscle relaxation after training 	<ul style="list-style-type: none"> ● Relaxation ● Stretching ● Physiotherapy
Abdominal muscle strain	<ul style="list-style-type: none"> ● Inadequate warming-up ● Muscle fatigue ● Muscle elasticity reduction ● Trauma 	<ul style="list-style-type: none"> ● Adequate warm-ups ● Avoid muscle fatigue ● Stretching exercise ● Gradually increase training intensity 	<ul style="list-style-type: none"> ● PRICE principle: protection, rest, ice, compression and elevation ● Physiotherapy, hyperbaric oxygen and NSAIDs ● Surgery
Volvulus	<ul style="list-style-type: none"> ● Strenuous exercise after a large meal ● Sudden body position transformation ● Long-distance running ● Abdominal disease or surgery history 	<ul style="list-style-type: none"> ● Avoid training after meals ● Avoid overeating ● Trainees with abdominal disease or surgery history should keep alert 	<ul style="list-style-type: none"> ● Rehabilitation training ● Surgery ● Fiber colonoscopy ● General support measures
Peptic ulcer	<ul style="list-style-type: none"> ● Training-induced stress ● Blood supply shortage during exercise 	<ul style="list-style-type: none"> ● Avoid stress ● Psychological counseling and intervention ● Proper diet ● <i>H. pylori</i> eradication 	<ul style="list-style-type: none"> ● Proton pump inhibitor ● Gastric mucosal protectant ● Bleeding control under gastroscopy and hemostatic
Abdominal trauma	<ul style="list-style-type: none"> ● Any external force during training ● High intensity and risk of military training ● Weapon injuries <p>NSAIDs: nonsteroidal anti-inflammatory drugs.</p>	<ul style="list-style-type: none"> ● Improve training security measures ● Protective gear ● Sufficient simulation training ● Medical education and support 	<ul style="list-style-type: none"> ● Surgery for perforation ● General management ● Infection prevention ● Operative treatment ● Damage control surgery

perform surgical intervention for the injured in the first time with the same effect as in hospital. It is believed that in the near future, the research and development of technical equipment will greatly help improve the prevention and treatment capacity for military training-related abdominal injuries and diseases.

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Ethical statement

Not applicable.

Declaration of competing interest

The authors declare that they have no competing interests.

Author contributions

Chuan Pang and Zhi-Da Chen wrote the paper and Hong-Qing Xi outlined this manuscript. Hong-Qing Xi, Bo Wei and Wen-Tong Xu provided detailed guidance on this article and proofread the manuscript. All authors read and approved the final manuscript.

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