HISTORY OF MEDICINE EDITORIAL

The race between vascular repairs and weapon injuries in war

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Abstract Taking a cue from the first war experience in Ukraine conflict with HAV (Human Acellular Vessel) technology for vascular repair, a historical review of modern war vascular lesions repair is accomplished; it reports a progressive improvement on (lower) limbs salvation from vascular injuries amputation that was 50 % in World War II reduced to 13% in Korea and Vietnam wars. The tragedy of wars worsens, if possible, at every new step; if a contradictory positive point exists, it may be found in military medicine improvements; in this case, vascular surgery experiences enhance civil surgery by suggesting new solutions. The availability of a novel biologic conduit for bypass and repair like the HAV, if confirmed by further studies, could entry in the list of limb salvage tool in extreme conditions.

Keywords Arterial injuries, war vascular casualties, amputation, limb salvation, acellular vessel production.

He who wishes to be a surgeon must first go to war

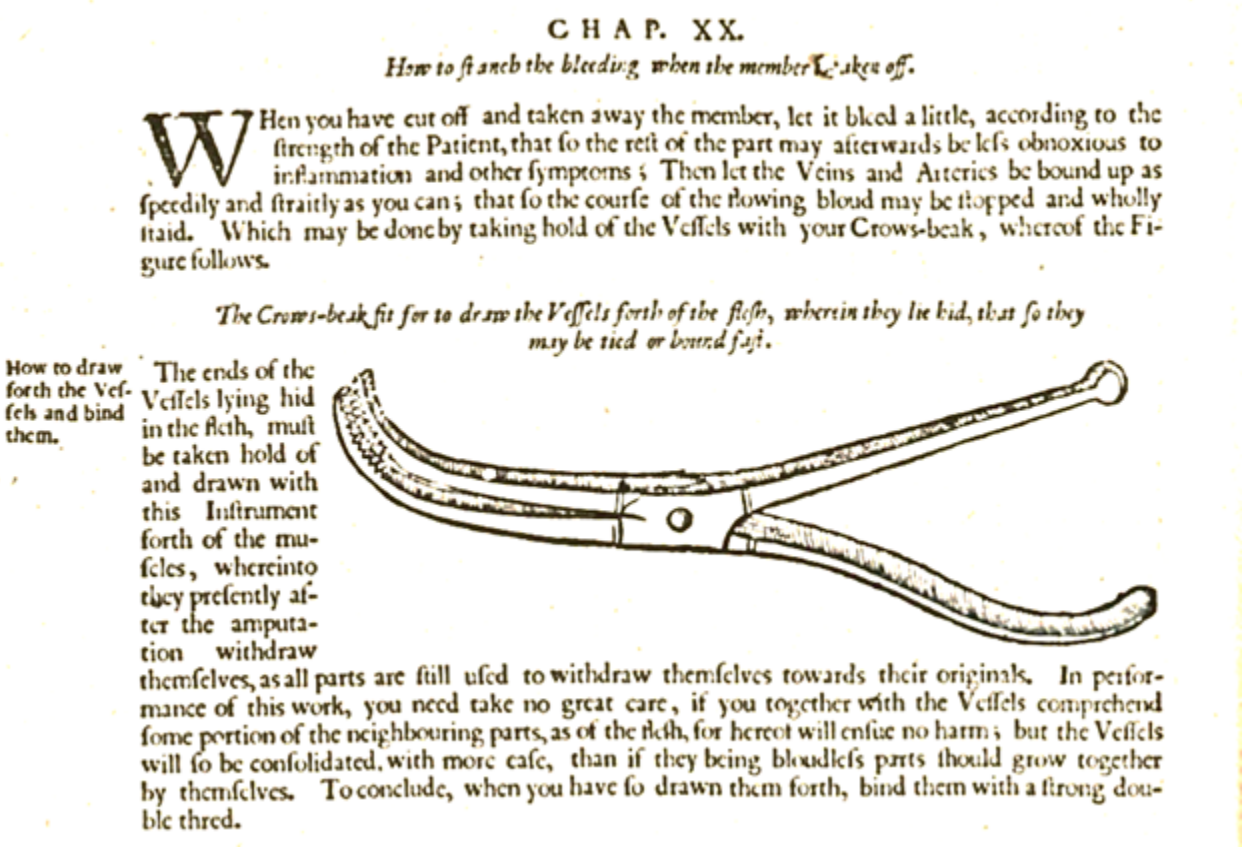
Hippokrates of Kos[1]

Wars are a constant event in human history; they give rise to horrific tragedies that seem to be quickly forgotten by later generations. Paradoxically, the collection of casualties in conflicts periods catalyse medical progress, particularly in acute trauma lesions. The battlefield provides a robust laboratory for the advancement of medicine; to quote Dr. Mayo: "Medicine is the only victor in war"[2]. Techniques, materials and equipment's proven to be safe and effective in wartime have made valuable contributions to medicine in peacetime[3].

Limb vascular injuries and consequent limb salvation challenges during modern conflicts are the typical example of this evolutions. We should also recall that treatment progress is accompanied by parallel war lesions "efficacy" enhancement creating a tragic endless challenge.

In a correspondence titled: **Use of bioengineered human acellular vessels to treat traumatic injuries in the Ukraine–Russia conflict**, published online on www.thelancet.com, dating 6 May 2023 [4], 13 patients are reported having been submitted to arterial bypass using an **acellular bioengineered vascular conduit**. This graft tool is a Human Acellular Vessel (HAV) cultured from human donors' smooth muscle cells seeded onto a biodegradable scaffold; the extracellular matrix produced is then decellularized to remove the immunogenic elements; the final structure will constitute the conduit. This is currently manufactured and delivered as a 6-mm 40-cm long conduit; it can be implanted without any preparation with current techniques. In 11 cases limb vascular injuries in the ongoing conflict, mostly comprising blast and shrapnel wounds were involved. Treated cases involved femoral, popliteal, and brachial arteries. After a follow-up times ranging from 1 to 7 months, there have been no reports of HAV conduit infection or mechanical failure. HAV development is still in a pre-clinical I/ II phase but was assigned by the manufacture (Humacyte Global Inc.) to 5 Ukraine hospitals for humanitarian reasons.

HAV for the management of wartime vascular injury seems the ideal solution due to resistance to infection, easy availability, immediate application, repeatable, not limited in length, employing current techniques confirming how battlefield provides a robust laboratory for the advancement of medicine.



CHAP. XX.

How to ſtanch the bleeding when the member is taken off.

WHen you have cut off and taken away the member, let it bleed a little, according to the ſtrength of the Patient, that ſo the reſt of the part may afterwards be leſs obnoxious to inflammation and other ſymptoms; Then let the Veins and Arteries be bound up as ſpeedily and ſtraitly as you can; that ſo the courſe of the flowing bloud may be ſtopped and wholly ſtaid. Which may be done by taking hold of the Veſſels with your Crows-beak, whereof the Figure follows.

The Crows-beak fit for to draw the Veſſels forth of the fleſh, wherein they lie hid, that ſo they may be tied or bound faſt.

How to draw forth the Veſſels and bind them.

The ends of the Veſſels lying hid in the fleſh, muſt be taken hold of and drawn with this Inſtrument forth of the muſcles, whereinto they preſently after the amputation withdraw themſelves, as all parts are ſtill uſed to withdraw themſelves towards their originals. In performance of this work, you need take no great care, if you together with the Veſſels comprehend ſome portion of the neighbouring parts, as of the fleſh, for hereof will enſue no harm; but the Veſſels will ſo be conſolidated, with more eaſe, than if they being bloudleſs parts ſhould grow together by themſelves. To conclude, when you have ſo drawn them forth, bind them with a ſtrong double thred.

Figure 1 - Paré's forceps to hold the vessel to be ligated; we can read: "To conclude, when you have so drawn them forth, bind them with a strong double thred"

Analysis of this correspondence inspired the following review on surgical evolution of vascular injuries during conflicts with the passage from amputation to possible limb salvation.

Firearms appearance

The introduction of firearms during the 13th century induced the research in treatment of consequent gunshot wounds lesions. Ambroise Paré, battlefield learned, is accredited to the most influencing diffusion of ligature of vessel lesions (1552) for achieving haemostasis after amputation in substitution to cauterization, following the previous suggestions of Hieronymus Brunschwig (1497). Parè invented also a "crow beak" forceps for vessel withdrawal to facilitate ligation[5]. (Fig 1)

The introduction of tourniquet (1674) by military surgeon Morel[6] has been the further advance in the field. Initially made by a stick into a bandage twisted till haemorrhage cessation, it was rapidly perfected by a screw system till the introduction by van Eschmark (1873) of an elastic tourniquet bandage that permitted surgeons to operate on a bloodless field. Tourniquet principles continued to be a valid tool in the following experiences till present days.

Arterial repair attempts

Starting from the last part of the 19th century, progressively arterial repair surgery took (slowly) place initially involving prevalently aneurismal corrections: The first successful end-to-end arterial anastomosis in man was described by Murphy in 1896 [7]. The next successful repair of an arterial defect came 10 years later when in 1906, Goyanes used a vein graft to bridge an arterial defect using the suture technique developed by Carrel and Guthrie in 1912: triangulation of the arterial orifice with three sutures, followed by continuous suture of cut ends between each of the three sutures. Carrel and Guthrie were performing at that time classic experimental studies on direct suture repair of arteries, vein transplantation, and transplantation of blood vessels, organs, and limbs. (Carrel wan the 1912 Nobel Prize for these studies). By 1910 more than 100 cases of arterial reconstruction by lateral suture, 46 repairs by end-to-end anastomosis or by insertion of a vein graft were reported. A high failure rate, usually by thrombosis, attended early attempts at repair, and few surgeons were convinced that repair of an artery was

worthwhile[8]. Curiously, although this promising start, more than 30 years elapsed before vascular surgery was widely employed.

World War I experience

During the first 9 months of World War I, low velocity missiles caused arterial trauma of a limited extent. In 1915, however, the widespread use of high explosives (the high explosive artillery shells replaced the Shrapnel shell in use since 1904) and high-velocity bullets, combined with wound contamination (trench warfare) and slow evacuation of the wounded, made arterial repair impractical[9].

In World War I, 4404 US soldiers lost one or more extremity. Of these, only 13% lost their limbs on the battlefield. The remaining 3713 amputations occurred in the operating room due to infection or serious damage to blood supply[9].

"The great frequency of infection with secondary haemorrhage virtually precluded arterial repair. In addition, there were inadequate statistics about the frequency of gangrene following ligation, and initial reports subsequently proved to be unduly optimistic." [9]

Contemporary accompanying veins ligation was an astonishing indication, performed even when main veins were non directly involved.

A complete picture of the WWI vascular lesions may be found in Makins book[9] of 1919.

Between the two wars heparin action as anti-thrombotic agent was confirmed, arteriography demonstrated an efficient diagnostic tool, penicillin became available since 1944, whole blood transfusion and storage proved important in vascular surgery.

World War II

Vascular lesions analysis in the classic review of DeBakey and Simeone[10] (1946) based on 2471 arterial injuries gives a very exhaustive picture of the conditions what the wounded and their treating military surgeons experienced. "It is clear that no procedure other than ligation is applicable to the majority of vascular injuries which come under the military surgeons' observation. It is not a procedure of choice. It is a procedure of stern necessity, for the basic purpose of controlling haemorrhage, as well as because of the location, type, size and character of most battle injuries of the arteries.", they concluded.

In facts, initially instructions on optimal wound management by Military Surgical Manuals keeping with doctrine established in the First World War, considered the risk of limb loss after ligation sufficiently low and the probability of devastating complications from repair so high that Carrel-style procedures were discouraged in favour of arterial ligation not ignoring the possibility of amputation after tying off arteries (50%). In particular, war wound devastating nature destroyed collateral vessels and the acute nature of the injuries precluded the development of new collateral branches[11].

Also ligating the concomitant vein suggested in previous war by Makins[9] in the hypothesis of *The elimination, in fact, of the capacious main vein is a real advantage, since this for the time affords a too ready channel of exit for the diminished arterial supply, as well as an undesirable reservoir for stagnation*, was still in use, only progressively abandoned. Chemical and surgical sympathectomies to increase collateral flow were diffusely used without any possible scientific prove of efficacy.

In 1943, Arthur Blakemore described a new sutureless technique for achieving vascular repair that would eventually be implemented in the Second World War on a small scale. He lined a Vitallium (65% cobalt, 30% chromium, 5% molybdenum) tube with a vein graft and used the tube to connect the two cut ends of the damaged vessel. At the time, vein grafts were the only practical method of anastomosing arteries, and poor outcomes after attempts at sutured anastomosis in the previous world war indicated a need for a method that avoided sutures in the combat theatre[12].

Through December 1944, in the 2471 vascular wounds DeBakey and Simeone catalogued, 40%(995 arms and legs) required amputation (primary amputations excluded). They noted 1639 ligations in 1774 vascular injuries (92%); 81 instances of repair in 2471 cases, (3.3% repair rate) with 3 were end-to-end anastomosis and no venous autografts[10].

From 1945 on the war evolute with victory perspective; front lines became stable, supplies well organised, field hospitals better diffused, confidence and hopes grown together with experience[11]. Among American military surgeons in the last 6 months of the war in the European Theatre of Operations "both combatant units and stateside surgeons began repairing an ever-increasing percentage of injured arteries in 1945. Although such operations never predominated, surgeons nevertheless demonstrated that these procedures were not only possible but also, in the hands of trained and experienced surgeons, had far superior outcomes than simple ligation." [11]

Between the end of World War II (1945) and the beginning of the Korean Conflict (1950), advances in suture, no crushing clamps, and arteriography were emerging. New technology in polymerized material (plastic) added a new opportunity for arterial repair.

Korea conflict (1950-1953)

In the initial phases of war, the Military medical care was unprepared due to the substitution of the old experienced surgical community with new generation of non-specialized personnel in combat medicine or military culture[13].

The army manual for surgical procedures was essentially a copy of the one used in the World War II. It did not include arterial repair because military surgeons were told not to attempt it, largely based on the DeBakey and Simeone report from 1946. However, the state of wounded mobility and care offer was much improved after previous war also due to the creation of MASHs (Mobile Army Surgical Hospitals) close to battlefields, with rapid jeep and helicopter wounded evacuation, resuscitation, reducing the time of intervention. Despite the prescription, some surgeons (the first was first performed in MASH 8055during the summer of 1951 by Otto Apel) [14] begun silently to experiment arterial reconstruction including reverse Saphenous bypass, initially on prisoners (fearing judicial reprisal for violating military policy) with early good results on 40 cases. By the end of 1951, more than 100 had been performed by Apel and Colemann inducing (1952) medical authorities to review the old policy.

In 1955, Spencer and Grewe reported the results of treatment of 97 major arterial injuries in which 89 repairs were attempted. Nearly half of the repairs were performed with arterial homograft, and the limb salvage rate was 78% [15]

In 1958, Hughes[16] in a review of the Korean experience, found that the overall amputation rate was lowered to about 13%, compared to the approximately 49% amputation rate that followed ligation in World War II. 304 major vessel injuries were actually treated; 269 were repaired and 35 were ligated.

Hughes[17] compiled a registry of the vascular injuries occurred during the Korean Conflict. For the first time a registry work had been used to provide comprehensive feedback to military doctrine for increasing efficacy of problems solution, using real-time data to provide physicians with best practice guidelines based on objective data.

Vietnam War 1954/1964-1975

During the Vietnam War previous experience induced to display surgeons more experienced with vascular surgery techniques (end-to-end anastomosis, vein grafts, lateral sutures, and thrombectomy).

An important advance was the use of frozen blood products. Fresh blood can only be used for 21-30 days before deteriorating. while frozen blood can be used for up to a year: in war extreme injuries, it is not uncommon to transfuse 5,10, or even more Liters of blood and have the patient survive[18]

The most valuable product of the Vietnam War was the establishment of the VVR (Vascular Vietnam Registry) [19], Instituted by Dr Norman Rich out of Walter Reed General Hospital, containing information of >7500 patients from surgeons at military hospitals in Vietnam.

To provide statistics and comments on the status of vascular repairs, 1000 cases of major acute arterial - Vietnam military and civilian excluded- were analysed, occurred in 4 years (1065-1968), documenting the long term follow up: lower extremity wounds were 56.8%; autogenous venous grafts were the most frequently used (49,5%), (initial) end-to-end anastomosis in 37,3 %, ligation in 1,5%. Amputation rate was 13,5% prevalently for popliteal artery lesions. Post operative complications occurred in 30,1% of cases with thrombosis prevalence. 92 vein graft were performed in a second attempt of restoring vascularization. There were 37,7 venous injuries and 42,4 % of nerve lesions[20].

With standard use of helicopters for evacuation, soldiers were being seen #2.5 hours of injury. Overall limb salvage rates were as high as 87%. The VVR encouraged the management of venous injuries too, previously feared for thrombotic risk, with repair, when possible, even with concomitant arterial injury. Particularly, the registry allowed long-term follow-up of these soldiers, providing invaluable insight into the long-term results of these operations in this selected population[19].

Iraq campain 2003-2011 - Afghanistan 2001-2021

Data from the Joint Theatre Trauma Registry (2002-2009) to identify vascular injuries in US troops could be analysed: the vascular injury rate of 12% was significantly higher than the 1–3% reported in WWII, Korea, and Vietnam. The widespread training and use of tourniquets in the modern battle field are likely the major reasons for the increase in vascular injuries seen. Casualties that would have died in the field in prior conflicts were now reaching medical care[21].

Explosive mechanisms accounted for 73% of vascular injuries, followed by gunshot wounds (27%). 1570 troops injured in Iraq (n = 1390) and Afghanistan (n = 180). Approximately 60% sustained injury to major or proximal vessels, operative management including 54% ligation and 46% repair. Early results of in-theatre repair are comparable with contemporary civilian reports and are improved from the Vietnam era. Rapid evacuation and damage control manoeuvres, such as temporary shunting and

early fasciotomy appear effective also assisting definitive repair. Self-applied tourniquets were in use in military training and proven as lifesaving as new haemostatic dressings deployed by the U.S. military into the battlefield: zeolite and chitosan. Studies on the battlefield directed to stopping bleeding, allowing lower blood pressure in certain patients—permissive hypotension— helped to decrease the bleeding from uncontrolled bleeding points[22].

Conclusion

"Every war has advanced medical knowledge and patient care and this conflict is notable for improvements that have been adopted into civilian practice and helped save many lives." [2]

Military vascular surgery enhances civil surgery by suggesting new solutions. This is evident for acute lesions (crash, gunshot, car accident), but has a great validity also for the successive corrections of trauma consequences, frequently characterized by haemorrhage, arteriovenous fistulas, pseudo aneurisms, occlusion, treated out of battlefield environment. Sadly, military surgeons' researches concentrate on battlefield giving less interest to the consequences of conflict on the surrounding world made of civil subjects that in modern wars are more and more involved, and due to the high number of victims, easily under concerned.

The already cited HAV technology[4, 23], inspiring this review, far from the final solution to vascular injuries during conflicts, could become, if confirmed by running research, one of the cited war's evolutions rapidly applied to civilian exigence's not only due to firearms. The availability of a novel biologic conduit for bypass and repair like the HAV, seemingly resistant to infection, easily available, immediately applicable, repeatable, not limited in length, and employing current techniques, if confirmed by further studies, could entry in the list of limb salvage tool in extreme conditions.

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