

The use of tourniquet in limb surgery

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**UNIVERSITY OF ZAGREB
SCHOOL OF MEDICINE**

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The use of tourniquet in limb surgery

GRADUATE THESIS



Zagreb, 2016

This graduation paper was made at Department of Orthopedic Surgery, University Hospital Zagreb, Šalata 7, Zagreb, was mentored by dr. sc. Goran Bićanić, dr. med. and was submitted for evaluation in the academic year 2015/2016.

Abbreviations:

- AC: after Christ
- AOP: arterial occlusion pressure
- ARDS: acute respiratory distress syndrome
- ATP: adenosine triphosphate
- BC: before Christ
- ETCO₂: end tidal carbon dioxide
- IVRA: intravenous regional anesthesia
- mL: milliliter
- mmHg: millimeter of mercury
- PaCO₂: arterial carbon dioxide partial pressure
- pH: hydrogen potential
- RIPC: remote ischemic preconditioning
- ROS: reactive oxygen species

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Summary :

The tourniquet is routinely used in daily practice for upper and lower limb orthopedic surgery, in order to obtain a bloodless surgical field and thus, to allow a better visualization for the surgeon. Tourniquet use is associated to several local and systemic complications which can be disabling or even lethal, including pulmonary embolism, reperfusion injury, and permanent neurological damage. Several conditions can be considered as contraindications for the use of tourniquet, even though their classification either in relative or absolute contraindication group remains controversial. Those relative or absolute contraindications include deep vein thrombosis, atherosclerosis, vascular fragility (diabetes mellitus, arteriopathies, vasculitis, calcified vessels, arteriovenous fistula, collagen vascular diseases, vascular prosthesis), cutaneous fragility, bone malunion, cerebral hypertension and cerebral trauma, sickle cell disease, rheumatoid arthritis, the presence of a local tumour or abscess, and cardiac or respiratory deficiency. The limb exsanguination should be performed by a simple elevation of the operated limb for 5 minutes. The tourniquet should be placed as distal as possible, and inflated to a pressure 50 to 75 mmHg higher than the arterial occluding pressure, which should be calculated according to the Graham's formula. Reperfusion periods of 10 minutes after every hour of ischemia are beneficial and thus can be implemented, but such reperfusion periods should be avoided if the ischemia lasted longer than 2 hours because they can become a factor aggravating the complications. Early after deflation, in the post-surgery minutes and hours, the neurological and vascular status of the operated limb should be carefully monitored in order to detect any potential complication as early as possible. The use of tourniquet is not harmless to the patient and thus should be objectively justified by the needs of the patient and only aimed at his own benefit.

Key-words: Tourniquet; Orthopedic surgery; Limb surgery; Tourniquet complications

I/ Introduction

The word « tourniquet » is a French word derived from the French verb « tourner », which means « to turn ». By itself, the word « tourniquet » is used in French to name several objects sharing the common particularity of being useful when turning, going from the turning games for kids in kinder gardens, to the security turning doors at the entrance of football stadiums. Because of the structure of the first orthopedic tourniquets (a rope attached to a wooden stick, allowing a very strong narrowing of the rope around the limb by twisting the wooden stick), this word was also formerly used in French to describe the devices used by doctors and surgeons to interrupt the blood flow in a limb, either in the case of hemorrhages in order to decrease blood loss, or to perform exsanguination during surgical procedures. While such devices are now called « garrot » in French, the word « tourniquet » is still used nowadays in English to name the different tools that are used to decrease blood loss during severe hemorrhages (e.g special forces soldiers), or aimed at achieving limb exsanguination during surgical procedures (e.g pneumatic tourniquet). Such tools are routinely used in operating rooms, particularly in orthopedic and traumatology surgeries. The use of orthopedic tourniquets is not yet precisely guided by public health institutions (national and international ones) or medical societies guidelines, leaving the surgeon quite alone facing an important investigation field full of controversies and questions, going from precise technical details regarding the best use of this tool (e.g shape, inflation pressure, duration, releasing time) to the most basic and important one : « should I even use an orthopedic tourniquet ? ». The goal of this Graduation Paper is to give an overview of the advantages and disadvantages of tourniquet use in limb surgery, and to discuss it.

II/ History of tourniquet development

1) During antiquity

The oldest written trace of an effort to prevent arterial bleeding is attributed to Sushruta. It is thought that he lived in India in the sixth century BC, and is sometimes referred as « the father of plastic surgery ». He is thought to have written the Sushruta Samhita, a surgery treatise written in Sanskrit mentioning 300 surgical procedures and 120 surgical tools and devices. Among those surgical procedures and tools is the description of pressed arteries

with pieces of leather in order to prevent from extensive bleeding. Some doubts remain regarding the existence of Sushruta, and the Sushruta Samhita may have been a collective production. But whoever were the authors of this surgery treatise, it remains the oldest written trace of an arterial compression used to control bleeding.

In the ancient Greece, some documents attributed to the medical school that was founded by Hippocrates in Cos during the fifth century BC, describe compression dressings that were used to control bleeding.

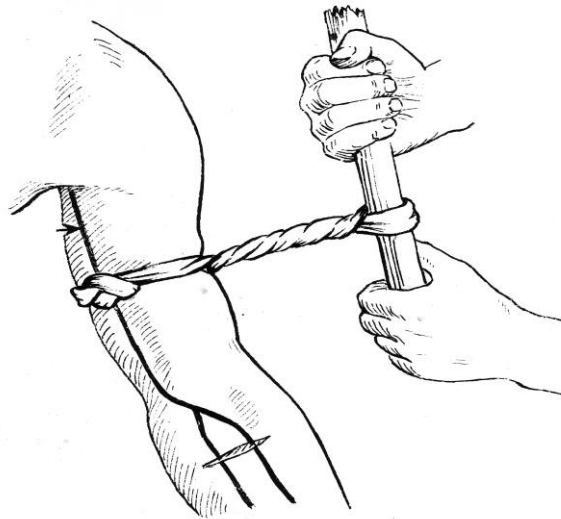
During Alexander the Great's military campaigns in the fourth century BC, some devices were used by doctors and surgeons to interrupt or decrease the bleeding of wounded soldiers.

In the Roman Republic and Empire, from the fifth century BC to the fifth century AC, probably as a consequence of military campaigns and gladiator's fights, amputation techniques using some devices in order to decrease blood loss during the procedure were invented by doctors and surgeons. At these times, narrow straps made of bronze were used to compress limbs, using leather only for patient comfort. This is an important step in the tourniquet history, since it looks like it was the first time in the known human History that such a technique was not only used in emergencies and immediate life threatening situations, but was also used as a part of scheduled surgical procedures. (1)

2) From middle age to our days

A thousand years later, during the 16th century, Ambroise Paré, a french battlefield surgeon who became the personal surgeon of the french kings Charles IX and Henri III and who is sometimes called « the father of modern surgery », described the use of a knotted long string proximally to an amputated limb during the amputation procedure. (2) (3).

During the same period, Wilhelm Fabry (1560-1624), a german surgeon ; Morel, a french surgeon(1674) (1) (4) ; and James Yonge(1679), an english naval surgeon also sometimes known as James Young ; attached for the first time the constrictive bandage to a stick, giving the possibility to twist it and thus, to control the strenght of limb compression.



TOURNIQUET

**Simple wooden-stick tourniquet, also known as Morel tourniquet, allowing a very strong compression.
(Source : Wikipedia)**

In 1718, the french surgeon Jean-Louis Petit invented a new device aimed at interrupting blood loss and displayed it at the Académie Royale des Sciences (royal academy of sciences). It was made of two metallic structures intended for limb compression, and linked to each other by two cloth bands. A screw on the top allowed a better control and an increased strenght of compression. Petit named it « tourniquet à vis » which means « screw tourniquet ». A clear advantage of the screw tourniquet was the opened possibility for the surgeon to operate alone, without the need of an assistant to hold the tourniquet to maintain the compression. (1)



Jean-Louis Petit type screw-tourniquet, allowing to maintain a constant compression force without the help of an assistant to hold the tourniquet.

In 1864, the british surgeon Joseph Lister is thought to be the first one performing limb exsanguination by elevation for three to four minutes prior to tourniquet application, thus creating a bloodless operating field. Moreover, he is also the first one who used tourniquet for surgery procedures other than amputations. The first one has been the excision of a tuberculosis infected wrist joint, with the hope of preventing the patient from arm amputation by doing so. (1)

In 1873, the german surgeon Friedrich von Esmarch, Professor of Surgery at the Kiel University, developed the use of flat rubber bandage to compress limb during surgical procedures, and gave his name to this technique. This approach has the advantage of associating exsanguination and prolonged compression in a single technique, and using only one tool. Esmarch bands are nowadays routinely used in daily practice in the operating room to perform exsanguination.



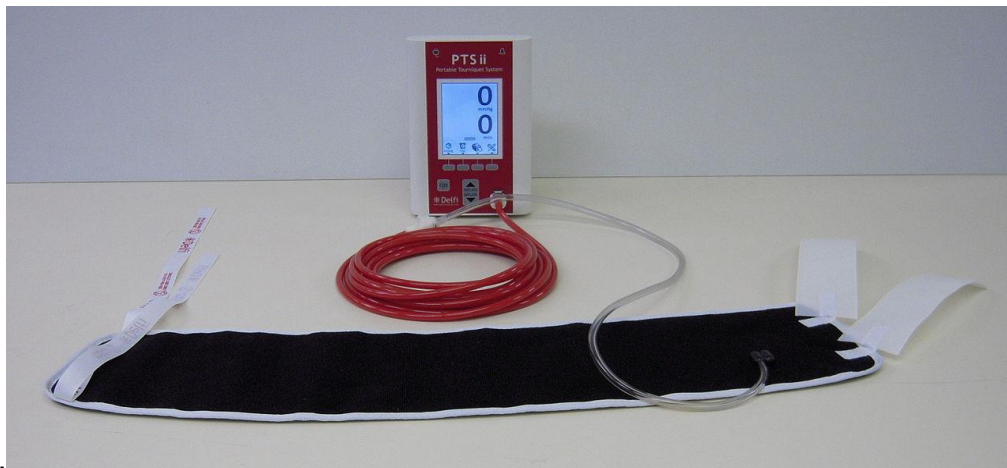
Esmarch bandage used prior to pneumatic tourniquet inflation in order to perform limb exsanguination.
 (Source : The Japanese Society for Cardiovascular Surgery website)

In 1881, the german surgeon Richard von Volkmann demonstrated that despite its benefits, the use of Esmarch bandages can lead to limb paralysis in some cases.

In 1904, the american neurosurgeon Harvey Cushing, sometimes called « the father of modern neurosurgery », invented the first pneumatic tourniquet in order to avoid the potential neurologic complications of Esmarch bandage use. This pneumatic tourniquet had the advantages of being applied and removed quite quickly, and to decrease the incidence of post-surgery nerve paralysis.

In 1908, the german surgeon August Bier had the idea of using two tourniquets to isolate the blood circulation of a specific segment of a limb from the general circulation, before to infuse intravenous anesthetics. This principle of using two tourniquets to limit the spreading of anesthetics drugs in order to induce segmental anesthesia is still commonly used nowadays and is called « IntraVeinous Regional Anesthesia » (IVRA), also known as « Bier's block » or « Bier's method ».

In the early 1980s, the canadian biomedical engineer James MacEwen invented the first microprocessor-controlled automatic tourniquet system and has been awarded for this contribution to limb surgery. This device allows to precisely control the applied pressure and can also measure the mean occlusion pressure for every patient, thus giving a strong surgical practice advantage, but also opening the research field to important issues such as investigations regarding ideal inflation pressure or ideal inflation duration



Modern pneumatic tourniquet allowing a precise control of inflation pressure.
(Source : Wikipedia)

In the 2000s, the Israeli Doctor Noam Gavrieli invented the silicone ring tourniquet. It is made of an elastic silicone ring. It is put on the extremity of the operated limb and rolled on proximally, thus exsanguinating the limb. Once the level of the intended occlusion reached, the silicone ring is kept in place. Just like the Esmarch bandage, this device has the advantage of being able to exsanguinate and maintain compression both together, but with a reduced risk of post-surgery nerve paralysis. Moreover, the device is sterile, allowing the avoidance of asepsia and antiseptia issues regarding operating room tools.

III/ Basic pathophysiology of tourniquet use

The use of tourniquet is a traumatic method, causing the onset of several local and systemic pathophysiological mechanisms in the patient's body. These mechanisms can be chronologically classified depending on their moment of arising : during exsanguination maneuvers, during tourniquet inflation, or during tourniquet deflation. These pathophysiological mechanisms and the potential subsequent complications will be extensively described below, in the following sections.

1) Limb exsanguination

The operated limb exsanguination may be performed by a simple and passive limb elevation, but is generally done by the use of an active device such as Esmarch bandage or Rhys-Davies exsanguinator. Such quite aggressive techniques have the advantage of being slightly more effective, but increase the risk of disseminating tumour cells or infection, and

of deep vein thrombosis dislodgement, potentially leading to fatal pulmonary embolism. (5)

Moreover, it is interesting to remember that obtaining a total bloodless surgical field is possible only if the operated segment is separated from the tourniquet by a joint. Otherwise, even with a proper occlusion of extraosseous circulation, some intraosseous blood supply remains. (6)

2) Tourniquet inflation

a) Hemodynamic consequences

At the moment of tourniquet inflation, a systemic hypervolemia occurs due to prior exsanguination. This added blood volume is negligible in the case of a superior limb surgery (approximately 50 mL) but can be significant in the case of an inferior limb surgery (from 500 to 800 mL). In any case, the subsequent increase of arterial blood pressure is never significant and does not persist. (7)

However, the occurrence of a delayed increased blood pressure happens secondarily to the tourniquet triggered pain. This modification is measurable 30 to 45 minutes after tourniquet inflation. (8) The measurement of cortisol and noradrenaline blood levels show some significant increased values of these two stress related hormones 60 minutes after tourniquet inflation, giving a clue of the existing link between the appearance of pain and the blood pressure increase. (8)

b) Pain

The pain is triggered by several factors not yet perfectly understood, but is caused by the activation of C fibers. Tissues compression, ischemia, and cutaneous trauma play a dominant role in tourniquet pain mechanisms. (7) Local anesthesia is more efficient than general anesthesia in this aspect, and can help to delay the onset of the pain and to decrease its intensity, thus preventing the pain triggered blood pressure increase. (9) (10)

c) Thrombo-embolic processes

The blood stasis caused by blood vessels occlusion leads to the accumulation of micro-embolic particules in the operated limb, which are released in the systemic circulation at the tourniquet deflation. Moreover, the tourniquet inflation on a preexisting deep vein thrombosis can cause an immediate fatal pulmonary embolism.

d)Muscle lesions

The tourniquet induced ischemia leads to the formation of necrotic areas in muscle tissue. Some small necrotic areas can be detected after 3 hours of tourniquet use, and extensive ones are detected 5 hours after tourniquet inflation. (11) The destruction of muscle tissue is objectively proven by an early increase of myoglobinemia and kalemia. A clinical picture of rhabdomyolysis and acute renal insufficiency has been described in few cases but remains an exception. (12) (13)

e)Metabolic and pharmacokinetic consequences

Hyperthermia develops in the whole body due to a decreased surface for thermic exchanges. (14) Inversely, the metabolic modifications and the absence of blood flow leads to hypothermia in the operated limb with tourniquet.

Moreover, the hemodynamic separation from the rest of the body and the hypothermia of the operated limb prevents the induction anesthetic molecules to be washed out and metabolized. Those molecules are locally accumulated and stored, mostly in the muscle and adipose tissue of the operated limb.

f)Cutaneous effect

Cutaneous lesions are the consequences of direct contact of skin with tourniquet cuff, and are caused by the friction and abrasion forces which are applied directly to the skin.

3) Tourniquet deflation

The tourniquet deflation leads to the restoration of continuity between the operated limb and the rest of the body. This restoration has several local and systemic consequences.

a)Hemodynamic consequences

The revascularization of a previously exsanguinated limb and its vasodilation cause a decrease of the mean arterial pressure, which can drop to values inferior to 70% of the blood pressure at the time of deflation. However, this drop of blood pressure seems to be quite unpredictable nowadays in view of our current knowledge regarding this topic. (15) This significant decrease in blood pressure causes an increase of the heart rate. In the worst case scenario, a dramatic drop of the mean arterial pressure can lead to a distributive shock.

b) Systemic dissemination (thrombo-embolisms, tumour cells, septic particles)

At the deflation of tourniquet, the accumulated micro-embolic particules are released in the systemic circulation and can be detected in 100% of cases. Trans-esophageal ultrasound and Doppler investigation detect an increase of right cardiac cavities blood pressure and of pulmonary vascular resistances few minutes after tourniquet deflation. (15) (16) As a consequence, the hemoglobin oxygen saturation percentage of the patient decreases as well in the moments following the deflation. (17)

Subclinical cerebral embolisms are detected in 60% of cases after tourniquet deflation, and subclinical pulmonary embolisms in 100% of cases. A few severe or even fatal pulmonary embolisms have been described. (5) (18) (19)

Not only thrombo-embolic particles, but also tumour cells and septic particles (coming from the disruption of an abscess due to the strong compression) can be released in the systemic circulation during deflation, potentially causing the metastatic spread of a cancer, distant infections, sepsis, or septic shock.

c) Reperfusion injury

The reperfusion injury (extensively described below) is characterized by the swelling of cells and an increase of capillary permeability, causing a leakage of liquid from the vascular compartment to the interstitial tissue. (20) Polynuclear leucocytes are recruited and their adhesion in the capillary lumen increase the arteriovenous shunt and thus, increase the tissue edema. (21) This post-ischemia edema is associated to the post-traumatic edema (caused by the surgical aggression) and to postoperative hemorrhages. Those three mechanisms together lead to an extensive global increase of limb volume. The circumference of the operated limb can reach up to 150% of its initial length 24 hours after the procedure. (18) (19) If this multi-factorial edema is too large, it can lead to a no-reflow phenomenon or to a compartment syndrome.

d) Metabolic changes

At the tourniquet deflation, the products of anaerobic metabolism are released in the systemic circulation. It causes a slight acidosis, with pH values usually not inferior to 7,30, and increased PaCO₂ and ET-CO₂. (22) In a patient operated with a local anesthesia, this acidosis is rapidly compensated by hyperventilation. This compensatory process needs a

longer time (4 to 5 minutes) to be effective in patients operated with a general anesthesia but is still efficient. Complications can arise in the case of patients with intra-cranial hypertension (e.g polytrauma) or with personal history of respiratory insufficiency (described in a following section). (23)

The release in the systemic circulation of intracellular electrolytes from necrotic areas leads to an increase of potassium blood level.

The restoration of blood circulation continuity causes a short period of hypothermia due to the low temperature of the ischemic limb, cooling down the rest of the body. This slight and short lasting hypothermia does not seem to have any significant clinical consequences.

e)Local hematoma and skin lesions

The damages caused by tourniquet use on blood vessels and muscle tissue leads to peroperative and postoperative hemorrhages. The subsequent bruises and hematomas can be directly visibles on the skin, as well as the epidermal irritation and burns caused by the tourniquet cuff.

IV/ Advantages

The use of tourniquet in orthopedic limb surgery after passive or active exsanguination enables to obtain a partially exsanguinated limb and thus, a bloodless surgical field. This can be very important in the case of micro-surgical procedures to be able to visualize micro-anatomical structures. (19) (20) In other cases, when obtaining a bloodless surgical field is not absolutely necessary, the tourniquet is used for the operative comfort of the surgeon.

The tourniquet use is sometimes said to be better for the hemodynamic function of the patient. As a matter of fact, only a few studies concluded that the use of tourniquet could decrease the peroperative blood loss. Moreover, even in these rare studies, the peroperative blood loss earning seems to be counterbalanced by an increased postoperative blood loss. Indeed, hypothermia, hypoxia and acidosis caused by the tourniquet induced ischemia lead to fibrinolysis, which increase the postoperative bleeding. (24) This is why the risk of post-surgery hemarthrosis is higher with tourniquet use. (25) Several studies have shown that the total blood loss in the case of tourniquet use is either globally similar or increased compared to surgeries without tourniquet.(26)(27)(28)(29)(30)

At last, it is also important to note that even if few studies have proved that tourniquet use decreases the duration of the surgical phase of the procedure (from incision to closure), this time earning is counterbalanced by an increased duration of other phases, such as the tourniquet preparation and installation. Thus, the duration of the whole procedure is not significantly decreased and does not save time for the surgeon, the hospital and the health care system. (31)

Therefore, it looks like apart from some specific cases of microsurgeries, the only clear advantage of tourniquet use is the operative comfort of the surgeon during the procedure.

V/ Disadvantages

1) Systemic effects

a) Pain and cardiovascular reactivity

The pain and the cardiovascular modifications occurring in the setting of tourniquet use, seem to be closely related to each other. The mechanisms behind the tourniquet triggered pain are complexes. The nociceptive C fibers are involved in the occurring pain, but further investigations have to be done regarding this complex topic. (7) Studies on volunteers showed that without anesthesia, the tourniquet triggered pain becomes intolerable after 20 to 30 minutes. (32) Under general anesthesia, an increase of cardiac rhythm and arterial pressure is observed after 20 to 30 minutes of tourniquet use. This cardiovascular reactivity increases with time, and a deeper general anesthesia does not interrupt this process. However, the local anesthesia clearly showed its efficacy in blocking this cardiovascular reactivity. (10) Nevertheless, even in the case of a proper and efficient local anesthesia, some tourniquet triggered pain and the associated cardiovascular reactivity can still arise if the tourniquet use duration lasts long enough. Indeed, the spinal plasticity causes an hyperextension phenomenon, best described as a progressive extension of cutaneous territories which are stimulated by the tourniquet. If this extension reaches tissues which are located proximally to the anesthetized tissues, pain will occur. In daily practice, even in the case of a proper and efficient general anesthesia, pain can occur after 60 to 80 minutes of tourniquet use as a consequence of hyperextension phenomenon. The appearance of this phenomenon can be delayed by the administration of opioids, (33) (34) adrenaline, (35) clonidine, (36) dextrometorphane, (37) dexmedetomidine, ketamine, (38) or by alcalinization of local anesthetic solutions when performing a nervous plexus block.

Furthermore, a short period of hypotension occurs at the moment of tourniquet deflation due to the restoration of vascularization continuity with the exsanguinated and vasodilated limb. A post-surgery hypovolemia occurs, secondary to vasodilation and to the increased vascular permeability during reperfusion. (18) (19) This hypovolemia can be worsened in the case of blood loss, either peroperative or caused by an other lesion(e.g polytrauma).

b)Thrombo-embolic events

The strong compression applied by the tourniquet on the operated limb is traumatic to all the underlying tissues, and blood vessels are not an exception. Thrombo-embolic events may happen, and can lead to a wide variety of consequences depending on their size, going from subclinical embolization only detected by Doppler investigation, to potentially dramatic respiratory and neurologic complications. In the case of a preexisting deep vein thrombosis (due to a cast or to a prolonged pre-surgery immobilization), the appearance of a massive pulmonary embolism can arise at the beginning of the procedure during the exsanguination maneuvers, particularly if Esmarch bandage is used to exsanguinate the limb. (5) But thrombo-embolic events can also happen in the absence of preexisting deep vein thrombosis. Indeed, the venous stasis caused by tourniquet use leads to an accumulation of micro-embolic particules. At the moment of tourniquet deflation, these accumulated micro-embolic particules are released in the systemic circulation and can cause pulmonary embolism. (5) (39) (40) A few massive and lethal pulmonary embolisms have been reported. (41) (42) Not only lungs but also brain can be damaged by such embolic migrations. Pulmonary embolism can cause pulmonary hypertension, thus causing an increased blood pressure in the right ventricle, leading to the opening of oval foramen and to a right-to-left shunt, potentially leading to cerebral paradoxal embolism, secondary to pulmonary hypertension. Obvious clinical strokes have been described rarely, but Doppler detected subclinical cerebral embolism have been found in up to 60% of patients after tourniquet deflation, even in the absence of an opened oval foramen. (43) However, the use of cement during orthopedic procedures probably has a role in embolic events, but this role is difficult to quantify. Moreover, some post-surgery clinical neurologic symptoms may have been caused by the neurotoxicity of cement. (44)

c)Metabolic and respiratory consequences

Apart from thrombo-embolic events, some respiratory consequences can also be caused by some metabolic reactions.

At the moment of tourniquet deflation, the products of anaerobic and hypoxic metabolism are released in the systemic circulation. The consequence of this release is an increase of PaCO₂ and ETCO₂. (22) In the case of a local anesthesia, this increase of carbonic acid level is not dangerous since a physiological adaptation occurs, causing hyperventilation, and eliminating quite fast the carbonic acid excess. In the case of a general anesthesia, this physiological adaptative hyperventilation is much slower, necessitating up to 5 minutes to come back to normal levels of carbonic acid. Even though this process lasts longer under general anesthesia compared to local anesthesia, it is most of the time very well tolerated by patients as long as they are otherwise healthy (apart from their orthopedic condition). However, in the specific case of a polytraumatic patient being operated while suffering from intracranial hypertension caused by a cranial trauma, the tourniquet release triggered hypercapnia can lead to a potentially lethal cerebral or cerebellar herniation. (23)

Later on, the reperfusion injury phenomenon occurs. The local activation of polynuclear leucocytes and their production of Reactive Oxygen Species (ROS) can cause an Acute Respiratory Distress Syndrome (ARDS) due to pulmonary oxidative damage. The consequences of reperfusion injury can be particularly dangerous in the case of a patient with a personal history of chronic respiratory insufficiency. More details regarding the mechanisms involved in the reperfusion injury phenomenon will be explained below, in the part dealing with the local effects of tourniquet use.

d) Pharmacokinetic complications

The tourniquet use has some pharmacological consequences. Indeed, it is impossible anymore for the anesthetic drugs (curariform, opioids and antibiotic ones) to reach the operated limb from the moment of tourniquet inflation. In the opposite way, it is also impossible for the anesthetic drugs used for induction to be metabolized and cleared from the operated limb tissues. Those molecules are stored in the operated limb (mostly in muscles and adipose tissues) and remain almost not degraded due to hypoxia and hypothermia. (45) When the tourniquet is deflated, those induction molecules are released in the systemic circulation and can cause a transient deepening of anesthesia, or even a depressed respiratory function in the 20 minutes following the deflation. (45) (46)

The tourniquet use also has thermic consequences on the patient's body. The tourniquet inflation separates the operated limb blood circulation from the systemic circulation. The entire operated limb cools down as long as the tourniquet is inflated. At the moment of

tourniquet deflation, the continuity of limb and systemic circulation is restored. This restored continuity of systemic circulation with colder blood and tissues transiently decreases the central temperature of the body. This could theoretically be an issue and has to be remembered, but did not show any problematic consequences in daily practice or in studies.

2) Local effects

a)Reperfusion injury, non-reperfusion

The reperfusion injury is one of the most important local complication of tourniquet use. As explained above, at the moment of tourniquet deflation, the post-ischemia reperfusion causes recruitment and activation of polynuclear leucocytes, producing and releasing reactive oxygen species, potentially causing as a distant consequence an acute respiratory distress syndrom. Locally, the reperfusion injury leads to a reperfusion edema, which develops in two following phases. The first phase is a vasodilation immediately following the tourniquet deflation. This first phase is in general responsible from a 10% increase of limb circumference. The second edematous phase develops slower in the postoperative hours, and is caused by the activation of polynuclear leucocytes in hypoxic tissues, releasing cytotoxic agents damaging the capillary endothelium, thus increasing the capillary permeability in the post-ichemic operated limb. This second phase of reperfusion edema can be quite impressive since the limb volume increase can reach more than 150% of the initial limb volume at 24 hours after the surgery. (18) (19)

In the worst cases, a no-reflow phenomenon can even occur, threatening the viability of the operated limb, potentially aggravated either by any external compression (e.g a cast) or by an impaired post-surgery hemodynamic status. (19) (20)

b)Mechanical lesions (skin, muscles, nerves, blood vessels)

The skin is the tissue which is in direct contact with the tourniquet cuff. Therefore, the strong pressure applied on the skin frequently cause cutaneous lesions, particularly if the tourniquet cuff is not perfectly installed and if some folds remain. Those cutaneous lesions are blisters most of the time and are spontaneously quite voluminous. The extent and the severity of those cutaneous lesions depends on several local factors(such as the tourniquet cuff proper installation, the inflation pressure and the prevention from antiseptic liquids flowing in between the skin and the tourniquet cuff), as well as structural factors(like

structural skin fragility, or an extreme age of the patient). (47)

The mechanisms of muscular lesions is not perfectly understood yet, but it looks like a biological cascade is triggered by ischemia, involving ATP depletion, acidosis, electrolytes imbalance, cytokines and reactive oxygen species production, fast release of large amounts of calcium and mitochondrial dysfunctions, causing cellular apoptosis and tissue necrosis. The consequences are histologically detectable after one hour of tourniquet use. (48) After two hours, the histological investigations show the necrotic lesions in the compressed muscles. Those lesions are more severe in the case of higher inflation pressures, and can lead to clinical manifestations since postural instability and worse functional outcome have been reported. (48) (49) (50) (51) Some cases of rhabdomyolysis and acute kidney failure caused by compartment syndrom have been reported in the case of tourniquet use for more than 4 hours, but also for shorter procedures (45 to 120 minutes) (18) (19)

The compression forces are particularly important when talking about their consequences on neurologic system. The function of large diameter nervous fibers is impaired before the function of thinner ones. (52) Therefore, there is a chronological block of motor function followed by a sensitive block. (53) The mechanical deformation of thick myelinated fibers, associated with ischemia, leads to myeline sheath lesions, sometimes followed by demyelination and Wallerian degeneration. A short lasting compression (4 to 13 minutes) can be enough to impair nervous conduction. (54) Such abnormalities have been detected by electromyography during the use of tourniquet, and can persist until 6 months after the surgery. (50) Some cases of permanent lesions have even been described. (55)

The high compression pressures are well tolerated by healthy arteries. But in the case of atheromatous lesion, the artery wall is fragile and loses its elastic properties, thus increasing the minimal arterial occlusion pressure (AOP). The applied pressure in order to occlude the vessels is higher, causing damages and rupture of vascular endothelium, and splitting of atheromatous plaques. Such rare complications in healthy patients are very frequent in polyatheromatous patients (up to 25%), and are extremely severe, leading to amputation if vascular reconstruction is not possible. (56) This is the reason why the revascularization of the operated limb has to be carefully checked immediately after tourniquet deflation by palpation of distal pulses, in order to detect any reperfusion impairment as soon as possible. (18) (19)

VI/ Discussion

1) Optimal protocol in tourniquet use

a) Exsanguination technique

The two exsanguination techniques which are routinely used in limb surgery are the simple passive limb elevation, and the use of an active exsanguination device such as an Esmarch bandage.

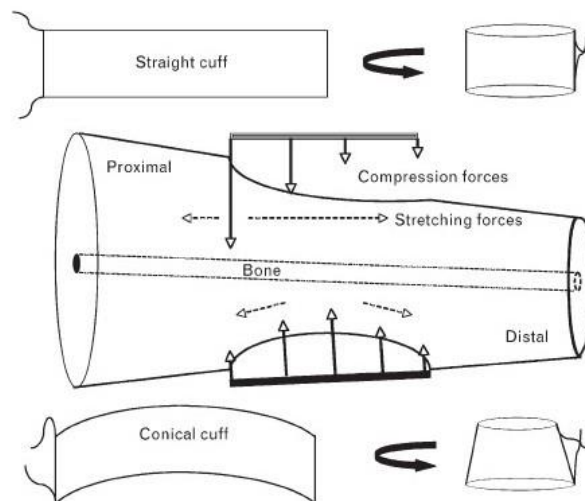
Such an aggressive technique has the advantage of being slightly more effective in exsanguinating the limb, but carries with it an increased risk of dramatic complication such as a severe to lethal pulmonary embolism, or a tumour dissemination. (57)

Conversely, the passive exsanguination by simple limb elevation is slightly less effective but has the advantage of being easy to perform and safe. This approach is nonaggressive, and thus does not carry any thrombo-embolic or tumoral distant dissemination risk. It also does not imply the use of any device, thus decreasing the risk of postoperative infectious complications. At last, it allows a better visualization of superficial vessels compared to a complete and aggressive exsanguination, leading to a better hemostasis. (58)

When performing this simple limb elevation technique, it is recommended to elevate the limb at 90 degrees for 5 minutes if it is an arm surgery, or at 45 degrees for 5 minutes if it is a leg surgery, in order to reach the maximal exsanguination. (59) (60)

b)Equipment: tourniquet shape, width, inflation pressure, regular check-up

The shape of tourniquet cuff is important. A conical shaped tourniquet leads to a better distribution of pressures than a straight tourniquet, particularly in the case of obese or very muscular patients. The better pressure distribution on the limb reduces the arterial occlusion pressure, thus decreasing the incidence of pressure-related complications.



A curved tourniquet allows a better distribution of pressure than a straight tourniquet, permitting a reduction in the arterial occlusion pressure. Sagittal forces are responsible for compression and axial forces are responsible for stretching, due to uneven pressure distribution. The intensity of stretching depends on the variation in sagittal pressure.

(source :Estebe J-P, Davies JM, Richebe P. The pneumatic tourniquet : mechanical, ischemia-reperfusion and systemic effects. Eur J Anaesthesiol 2011 ; 28 :000-000)

Following the same goal of reducing the pressure applied on the operated limb, it is also important to use a wide enough tourniquet cuff, leading to a decreased arterial occlusion pressure. It has been demonstrated that the arterial occlusion pressure decreases to values close to systolic pressure when the width of tourniquet is at least equal to 0,5 times the limb circumference. (32) (61) (62) In daily practice, if such a wide cuff is not available, the widest available cuff should be used, and its width should never be thinner than 0,3 times the limb circumference. In those conditions, it should not be necessary to use inflation pressures higher than 100 mmHg above the systolic pressure for arm surgery. (63) (64) (62) (65) (66) Different strategies are used by surgeons to decide which inflation pressure they will apply on the patient limb. Regarding the fact that all the complications are somehow related to higher pressures, the use of the lowest efficient pressure should be a goal to achieve for the surgical and anesthesiological teams. The worst is the application of an arbitrary and constant pressure for any patient. A better strategy is to

apply an arbitrary but patient-adjusted inflation pressure (usually, 50 to 75 mmHg or 100 to 150 mmHg above systolic pressure, for upper limb and lower limb respectively). (67) The optimal strategy is to determine the arterial occlusion pressure, using the Graham's formula :

$$\text{AOP} = [(\text{systolic pressure} - \text{diastolic pressure}) (\text{limb circumference}) / 3 \text{ cuff width})] + \text{diastolic pressure} \quad (61)$$

Then, the inflation pressure can be set at 50 to 75 mmHg above the calculated AOP. Using this approach, the applied pressures can be decreased by 20 to 40% in adults and by more than 50% in children, compared to the previously described arbitrary approaches. (65) (68) The blood pressure should be monitored during the procedure, and the inflation pressure should be adjusted accordingly.

Since the applied pressure is the first risk factor for neurological lesions to happen with tourniquet use, it is of primary importance to implement and schedule some periodic verifications of the devices and frequent calibration. The absence of such verifications is usually found as being the cause when neurological lesions arise despite quite short surgery duration. (69)

c) Tourniquet location and installation on the operated limb

The tourniquet is frequently placed at the most proximal location of the limb, even when the operative site is distal. This should be reconsidered since several studies have shown good results with forearm tourniquet location in hand surgery, leading to decreased inflation pressures, and delayed and decreased pain. (63) (70)

A wrinkle-free padding should be placed in between the skin and the tourniquet cuff in order to reduce skin damages due to shearing stresses. (71) A self adhesive plastic drape should be used to separate the tourniquet from the surgical field before skin preparation, in order to avoid chemical burns of the skin located beneath the tourniquet to arise. (72) (73) At last, the tourniquet cuff should not be moved once it has been inflated, thus avoiding shearing forces to damage underlying tissues.

d) Tourniquet use duration and reperfusion periods

The tourniquet use duration has to be as short as possible. However, no consensus has been established, probably in part because postoperative complications have been

reported even for tourniquet use duration much shorter than 2 hours. (69) An ideal duration would probably be shorter than 1 hour. (74) (75) (76) This technique has to be performed carefully since it seems that reperfusion after 1 hour of ischemia has a positive effect, but might be an aggravating factor after 2 hours of ischemia because after such a period, the pathophysiological processes and inflammatory cascade are greater than the biological mechanisms of protection. (77)

Most of the authors recommend to plan some reperfusion periods of at least 10 minutes for every 45 to 60 minutes of tourniquet use, in order to decrease the incidence and severity of post-tourniquet complications. It is interesting to note that few authors strongly fight this approach, mostly because even though reperfusion periods seem to have a positive effect on the functional recovery of tissues located distally to the tourniquet, it looks like they can also exacerbate the lesions of tissues located beneath the tourniquet, particularly muscles. (69) (78) (79)

e) Deflation and post-deflation monitoring

In order to keep the ischemia duration as short as possible, it is better to deflate the tourniquet before hemostasis and closure.

In the minutes and hours following deflation, it is of primary importance to regularly monitor the vascular and neurological status of the patient's limb in order to detect the potential complications as early as possible.

f) Prophylactic antibiotherapy

Prophylactic antibiotherapy is used to prevent any post-surgery infectious complication. Its efficiency is maximal if the antibiotic drugs tissular concentration is the highest at the time of tourniquet inflation. It is interesting to remember that for cephalosporins, this spike level is reached 20 minutes after intravenous injection. (80)

2) Development of new therapeutic approaches

a) Ischemic pre and post conditioning

The mechanism of ischemic preconditioning has been discovered approximately 15 years ago. It can be described as a pathophysiological adaptation of a tissue to ischemia after having been previously exposed to short periods of ischemia and reperfusion, conferring

him some ischemia resistance properties and thus decreasing the severity of lesions caused by a subsequent longer ischemia. The practical implementation of this concept can be done by imposing purposely three or four cycles of 5 minutes of ischemia (by inflating the tourniquet) followed by 5 minutes of reperfusion (by deflating the tourniquet). Those ischemia-reperfusion cycles have to be imposed to the tissue immediately before the beginning of surgical procedure. Ischemic preconditioning confers an increased ischemia resistance to local tissues located beneath and distal to the tourniquet, as well as a systemic resistance of distant organs such as lungs (also known as RIPC, Remote Ischemic PreConditioning). (81) (82) (83) (84) (85) (86)

Ischemic postconditioning, described as intermittent repetitive interruptions of reperfusion after a prolonged ischemia, has been found to cause a comparable positive ischemia neuroprotective effect on spinal cord. (87)

Ischemic pre and post conditioning are quite simple procedures with a potentially very strong positive effect regarding post-tourniquet ischemic lesions, and should probably be performed for any procedure with a tourniquet use estimated to two hours or more.

b) Antioxydants

Antioxydants have a protective effect, which is probably due to inhibition of polynuclear neutrophils recruitment, adherence and activation, and also to their reactive oxygen species scavenging properties. (88) (89)

Inhalation of nitric oxide before, during and after tourniquet use reduces inflammation in lower limb extremities. (90) (91)

Heme oxygenase catalyses the breakdown of heme to several by-products including carbon monoxide, which has similar anti-inflammatory properties than nitric oxide.

Allopurinol (an endothelial xanthine oxidase inhibitor) and vitamin E (a reactive oxygen species scavenger) can decrease oxidative stress and edema in post-ischemic skeletal muscle. (75)

Edaravone (an other reactive oxygen species scavenger), if given during early reperfusion, seems to be effective in reducing nerve injury due to oxidative stress. (92)

Buflomedil and flurbiprofen can also be used to reduce post-tourniquet microvascular

reperfusion injury in striated muscle.

c) Prevention of deep vein thrombosis

Milrinone (a phosphodiesterase-3 inhibitor) can be used as an inodilator (positive inotrope and arteriovenous dilator) to reduce deep vein thrombosis incidence. A peri-operative infusion of milrinone can decrease platelet activation without increasing the peri-operative blood loss. (93)

VII/ Conclusion

The use of tourniquet in limb surgery is associated to a lot of complications, arising at different times (exsanguination, tourniquet inflation, per-operative, tourniquet deflation, early and late postoperative), in different places (local area or distant and systemic), with a large range of severity (from subclinical ones to very severe and even lethal ones). Moreover, a lot of contraindications are mentioned by authors but without reaching a consensus regarding their classification either into absolute or relative contraindication categories. They include deep vein thrombosis, atherosclerosis, vascular fragility (diabetes mellitus, arteriopathies, vasculitis, calcified vessels, arteriovenous fistula, collagen vascular diseases, vascular prosthesis), cutaneous fragility, bone malunion, cerebral hypertension and cerebral trauma, sickle cell disease, rheumatoid arthritis, the presence of a local tumour or abscess, and even cardiac or respiratory deficiency. From the patient prospect, those contraindications and potential complications are not counterbalanced by any clinical earnings or by a better outcome.

The only clear advantage of tourniquet use is the operative comfort of the surgeon by obtaining a bloodless surgical field, but this is obviously very difficult, if not impossible, to objectively measure and quantify, not to mention the fact that this advantage is not aimed at the patient's health.

Performing hemostasis is not by itself an indication for tourniquet use since several other hemostasis technics have been proven to be much more effective. A few specific situations can be considered as proper indications for tourniquet use, such as some limb extremity microsurgery. The setting of guidelines only based on the patient's benefits would be a real improvement.

Waiting to such guidelines, both surgical and anesthetic teams working with tourniquet should be well informed regarding tourniquet use contraindications, deleterious effects and complications, should know the limits of this tool, should be well informed regarding its optimal use and should be skilled accordingly.

However, even in the optimal tourniquet use conditions, it is only possible to decrease incidence and severity of complications, which is not as good as avoiding them. The earnings being so little and exclusively aimed at the surgeon, it might be appropriate to reconsider the routine use of this technique.

Medical Doctors nowadays still declame the hippocratic oath, and Medical schools all over the world are full of Hippocrates statues and quotes. One of the most famous of those Hippocrates quotes is in latin « primum non nocere », which can be translated in english by « firstly, no harm ». This basic principle of making sure not to cause harm even before to try to help, could leads us to a tremendous decrease of tourniquet use in limb surgery, and to keep this technic for few appropriate and accurate situations, when it is needed for the patient's benefit.

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To the women who love(d) me,

To the men who guided me.

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References

- (1) Klenerman L. The tourniquet manual: principles and practice. London: Springer; 2003, 108
- (2) Paré A. Les œuvres d'Ambroise Paré. Nabu press ; 2014, 826
- (3) Mareau G. Ambroise Paré et la chirurgie moderne. Paris: Imprimerie Lachaise et Dolbeau, 1883, 24
- (4) Jamain M.A. Manuel de petite chirurgie. Paris: Librairie Germer Baillière et Cie; 1880
- (5) Bharti N, Mahajan S. Massive pulmonary embolism leading to cardiac arrest after deflation following lower limb surgery. *Anaesth Intensive Care* 2009; 37:867-8.
- (6) Blønd L, Madsen L. Bone marrow perfusion in healthy subjects assessed by scintigraphy after application of a tourniquet. *Acta Orthop Scand* 2003; 74:460–464.
- (7) Hagenouw RR, Bridenbaugh PO, Van Egmond J, Stuebing R. Tourniquet pain: a volunteer study. *Anesth Analg* 1986;65:1175-80
- (8) Crews JC, Sehlhorst CS. Response to maintenance of tourniquet inflation in a primate model. *Reg Anesth* 1991;16:195-8
- (9) Valli H, Rosenberg PH. Effects of three anaesthesia methods on haemodynamic responses connected with the use of thigh tourniquet in orthopedic patients. *Acta Anaesthesiol Scand* 1985;29:142-7
- (10) Valli H, Rosemberg PH, Nurminen M. Arterial hypertension associated with the use of tourniquet with either general or regional anaesthesia. *Acta Anaesthesiol Scand* 1987;31:279-83.
- (11) Korthals JK, Maki T, Gieron MA. Nerve and muscle vulnerability to ischemia. *J Neurol Sci* 1985;71:283-90
- (12) Sheth NP, Sennett B, Berns JS. Rhabdomyolysis and acute renal failure following arthroscopic knee surgery in a college football player taking creatine supplements. *Clin Nephrol* 2006 ;65 :134-7.
- (13) Lee YG, Park W, Kim SH, et al. A case of rhabdomyolysis with use of a pneumatic tourniquet during arthroscopic knee surgery. *Kor J Int Med* 2010 ;25 :105-9.
- (14) Estebe JP, Le Naoures A, Malledant Y, Ecoffey C. Use of a pneumatic tourniquet induces changes in central temperature. *Br J Anaesth* 1996;77:786-8.
- (15) Kahn RL, Marino V, Urquhart B, Sharrock NE. Hemodynamic changes associated with tourniquet use under epidural anesthesia for total knee arthroplasty. *Reg Anesth* 1992;17:228-32
- (16) Wauke K, Nagashima M, Kato N, Ogawa R, Yoshino S. Comparative study between thromboembolism and total knee arthroplasty with or without tourniquet in rheumatoid arthritis patients. *Arch Orthop Trauma Surg* 2002;122:442-6.
- (17) Jules-Elysee K, Blanck T, Catravas J, Chimento G, Miric A, Kahn R, Paroli L, Sculco T. Angiotensin-converting enzyme activity: a novel way of assessing pulmonary changes during total knee arthroplasty. *Anesth Analg* 2004;99:1018-22.
- (18) Estebe JP, Davies J, Richebe P. The pneumatic tourniquet : mechanical, ischaemia-reperfusion and systemic effects. *Eur J Anaesth* 2011 28 :404-11.
- (19) Estebe JP. The pneumatic tourniquet. *Surgical techniques in orthopaedics and traumatology (EFORT)*. Ed Elsevier ; 2002 [55-010-B-20].
- (20) Estebe JP. Le garrot pneumatique d'orthopédie. *Ann Fr Anesth Réanim* 1996;15:162-78.
- (21) Harris AG, Skalak TC. Effects of leukocyte activation on capillary hemodynamics in skeletal muscle. *Am J Physiol* 1993;264:909-16
- (22) Hoka S, Yoshitake J, Arakawa S, Ohta K, Yamaoka A, Goto T. VO₂ and VCO₂ following tourniquet deflation. *Anaesthesia* 1992;47:65-8. Harris AG, Skalak TC. Effects of leukocyte activation on capillary hemodynamics in skeletal muscle. *Am J Physiol* 1993;264:909-16
- (23) Hirst R, Slee T, Lam A. Changes in cerebral blood flow velocity after release of intraoperative tourniquets in humans: a transcranial Doppler study. *Anesth Analg* 1990;71:503-10. Hoka S, Yoshitake J, Arakawa S, Ohta K, Yamaoka A, Goto T. VO₂ and VCO₂ following tourniquet deflation. *Anaesthesia* 1992;47:65-8.
- (24) Kohro S, Yamakage M, Arakawa J, Kotaki M, Omote T, Namiki A. Surgical/tourniquet pain accelerates blood coagulability but not fibrinolysis. *Br J Anaesth* 1998;80:460-3.
- (25) Coupens SD, Yates CK. The effect of tourniquet use and hemovac drainage on postoperative hemarthrosis. *Arthroscopy* 1991;7:278-82.
- (26) Li B, Wen Y, Wu H, Qian Q, Lin X, Zhao H. The effect of tourniquet use on hidden blood loss in total knee arthroplasty. *Int Orthop* 2009 ;33 :1263-1268 [PMID : 18751703 DOI :10.1007/s00264-008-0647-3]
- (27) Smith TO, Hing CB. Is a tourniquet beneficial on total knee replacement surgery ? A meta-analysis and systematic review. *The Knee* 2010 ;17 : 141-147 [DOI : 10.1016/j.knee.2009.06.007]
- (28) Mittal R, Ko V, Adie S, Naylor J, Dave J, Dave C, Harris IA, Hackett D, Ngo D, Dietsch S. Tourniquet application only during cement fixation in total knee arthroplasty : a double blind, randomized controlled trial. *ANZ J Surg* 2012 ;82 :428-433 [PMID : 22571508 DOI : 10.1111/j.1445-2197.2012.06083.x]
- (29) Li X, Yin L, Chen ZY, Zhu L, Wang HL, Chen W, Yang G, Zhang YZ. The effect of tourniquet use in total knee arthroplasty : Grading the evidence through an updated meta-analysis of randomized, controlled trials. *Eur J Orthop Surg Traumatol* 2013 [DOI : 10.1007/s00590-013-1278-y]
- (30) Tarwala R, Dorr LD, Gilbert PK, Wan Z, Long WT. Tourniquet use during cementation only during total knee arthroplasty : a randomized trial. *Clin Orthop Relat Res* 2014 ; 472 :169-174[PMID : 23836239 DOI : 10.1007 /s11999-013-3124-2]
- (31) Maffulli N, Testa V, Capossa G. Use of a tourniquet in the internal fixation of fractures of the distal part of the fibula: a prospective randomized trial. *J Bone Joint Surg* 1993;75-A:700-3.

- (32) Estebe JP, Le Naoures A, Chemaly L, Ecoffey C. Tourniquet pain in a volunteer study: effects of changes in cuff width and pressure. *Anaesthesia* 2000;55:21-6.
- (33) Cherng CH, Wong CS, Chang FL, Ho ST, Lee CH. Epidural morphine delays the onset of tourniquet pain during epidural lidocaine anesthesia. *Anesth Analg* 2002;94:1614-6.
- (34) Tuominen M, Valli H, Kalso E, Rosenberg PH. Efficacy of 0.3 mg morphine intrathecally in preventing tourniquet pain during spinal anaesthesia with hyperbaric bupivacaine. *Acta Anaesthesiol Scand* 1988;32:113-6
- (35) Gielen MJM, Stienstra R. Tourniquet hypertension and its prevention: a review. *Reg Anesth* 1991;16:191-4
- (36) Bonnet F, Diallo A, Saada M, Bellon M, Guilbaud M, Boico O. Prevention of tourniquet pain by spinal isobaric bupivacaine with clonidine. *Br J Anaesth* 1989;63:93-6
- (37) Yamashita S, Yamaguchi H, Hisajima Y, Ijima K, Saito K, Chiba A, Yasunaga T. Preoperative oral dextromethorphan attenuated tourniquet-induced arterial blood pressure and heart rate increases in knee cruciate ligament reconstruction patients under general anesthesia. *Anesth Analg* 2004;98:994-8.
- (38) Satsumae T, Yamaguchi H, Sakaguchi M, Yasunaga T, Yamashita S, Yamamoto S, Kida H. Preoperative small-dose ketamine prevented tourniquet-induced arterial pressure increase in orthopedic patients under general anesthesia. *Anesth Analg* 2000;92:1286-9.
- (39) Parmet J, Horrow J, Berman A, Miller F, Collins G. The incidence of large venous emboli during total knee arthroplasty without pneumatic tourniquet use. *Anesth Analg* 1998;87:439-44.
- (40) Parmet J, Horrow J, Pharo G, Collins L, Berman A, Rosenberg H. The incidence of venous emboli during extramedullary guided total knee arthroplasty. *Anesth Analg* 1995;81:757-62.
- (41) Mc Grath BJ, Hsia J, Epstein B. Massive pulmonary embolism following tourniquet deflation. *Anesthesiology* 1991;74:618-20
- (42) Cohen JD, Keslin JS, Nili M, Yosipovitch Z, Gassner S. Massive pulmonary embolism and tourniquet deflation. *Anesth Analg* 1994;79:583-5
- (43) Sulek C, Davies L, Enneking K, Gearen P, Lobato E. Cerebral microembolism diagnosed by transcranial Doppler during total knee arthroplasty. *Anesthesiology* 1999;91:672-6.
- (44) Kinoshita H, Iranami H, Fujii K, Yamazaki A, Shimogai M, Nakahata K, Hironaka Y, Hatano Y. The use of bone cement induces an increase in serum astroglial S-100B protein in patients undergoing total knee arthroplasty. *Anesth Analg* 2003;97:1657-60.
- (45) Estebe JP, Le Corre P, Levron JC, Le Moing JP, Assoune P, Ecoffey C. Pilot study on the effect of tourniquet on sufentanil pharmacokinetics. *J Clin Anesth* 2002;14:578-83.
- (46) Shimogai M, Iranami H, Yamazaki A, et al. Transient but profound reduction of bispectral index values after tourniquet deflation : did the BIS detect an alteration of brain electrocortical activity ? *Anesth Analg* 2006 ;1613-4.
- (47) Dickinson JC, Bailey BN. Chemical burns beneath tourniquets. *Br Med J* 1988;297:1513
- (48) Bengt O, Karl M, Hans R, Lars H. Tourniquet-induced ischemia and reperfusion in human skeletal muscle. *Clin Orthop* 2004;418:260-5.
- (49) Pedowitz RA, Friden J, Thornell LF. Skeletal muscle injury induced by a pneumatic tourniquet: an enzyme and immunohistochemical study in rabbits. *J Surg Res* 1992;52:243-50
- (50) Kokki H, Vaatainen U, Miettinen H, Parviainen A, Kononen M, Partanen J. Tourniquet-induced enmg changes in arthroscopic anterior cruciate ligament reconstruction. A comparison of low and high-pressure tourniquet system. *Ann Chir Gynaecol* 2001;89:313-7.
- (51) Daniel DM, Lumkang G, Stone ML, Pedowitz R. Effects of tourniquet use in anterior cruciate ligament reconstruction. *Arthroscopy* 1995;11:307-11.
- (52) Kojo I, Pertovaara A. Effect of tourniquet induced ischemia on cutaneous thermal thresholds. *Acta Neurol Scand* 1986;74:383-6
- (53) Graham B, Breault M, Mc Ewen J, Mc Graw. Perineural pressures under the pneumatic tourniquet in the upper extremity. *J Hand Surg* 1992;17-B:262-6.
- (54) Schlee G, Milani TL, Sterzing T, et al. Short-time lower leg ischemia reduces plantar foot sensitivity. *Neurosci Lett* 2009 ; 462 :286-8.
- (55) Kornbluth I, Freedman M, Sher L, Frederick R. Femoral, saphenous nerve palsy after tourniquet use: a case report. *Arch Phys Med Rehabil* 2003;84:909-11.
- (56) Del Aurentis DA, Levitsky KA, Booth RE, Rothman RH, Calligaro KD, Raviola CA et al. Arterial and ischemic respects of total knee arthroplasty. *Am J Surg* 1992;164:237-40
- (57) Lu CW, Chen YS, Wang MJ. Massive pulmonary embolism after application of Esmarch bandage. *Anesth Analg* 2004; 98:1187–1189.
- (58) Blønd L, Jensen NV, Sørensen NH. Clinical consequence of different exsanguination methods in hand surgery: a double-blind randomized study. *J Hand Surg Eur Vol* 2008; 33:475–477.
- (59) Warren PJ, Hardiman PJ, Woolf VJ. Limb exsanguination. I the arm: effect of angle of elevation and arterial compression. *Ann R Coll Surg Engl* 1992;74:320-2
- (60) Warren PJ, Hardiman PJ, Woolf VJ. Limb exsanguination. II the leg: effect of angle of elevation. *Ann R Coll Surg Engl* 1992;74:323-5
- (61) Graham B, Breault MJ, Mc Ewen JA, Mc Graw RW. Occlusion of arterial flow in the extremities at subsystolic pressures through the use of wide tourniquet cuffs. *Clin Orthop* 1993;286:257-61
- (62) Mittal P, Shenoy S, Sandhu J. Effect of different cuff widths on the motor nerve conduction of the median nerve: an experimental study. *J Orthop Surg Res* 2008; 9:1–6.
- (63) Khuri S, Uhl RL, Martino J, Whipple R. Clinical application of the forearm tourniquet. *J Hand Surg* 1994;19:861-3

- (64) Levy O, David Y, Heim M, Eldar I, Chetrit A, Engel J. Minimal tourniquet pressure to maintain arterial closure in upper limb surgery. *J Hand Surg* 1993;18:204-6
- (65) Younger AS, McEwen JA, Inkpen K. Wide contoured thigh cuffs and automated limb occlusion measurement allow lowertourniquet pressures. *Clin Orthop Relat Res* 2004; 428:286–293.
- (66) Pedowitz RA, Gershuni DH, Botte MJ, et al. The use of lower tourniquet inflation pressures in extremity surgery facilitated by curved and wide tourniquets and an integrated cuff inflation system. *Clin Orthop Relat Res* 1993; 287:237–244.
- (67) Crenshaw A. Surgical techniques and approaches. 9th ed. In: Campbell's operative orthopaedics. Volume 1. Canale ST, Jones L, editors. St Louis: Mosby; 1998. pp. 29–142.
- (68) Reilly CW, McEwen JA, Leveille L, et al. Minimizing tourniquet pressure in paediatric anterior cruciate ligament reconstruction surgery: a blinded, prospective randomized controlled trial. *J Pediatr Orthop* 2009; 29:275–280.
- (69) Rorabeck CH, Kennedy JC. Tourniquet-induced nerve ischemia complicating knee ligament surgery. *Am J Sports Med* 1980;8:98-102
- (70) Hutchinson DT, Mc Clinton MA. Upper extremity tourniquet tolerance. *J Hand Surg* 1993;18:206-10
- (71) Okum GS, Hauser AC, Keykha MM, Horrow JC. Sufentanil plasma concentrations following lower extremity tourniquet release. *J Clin Anesth* 1996;8:210-5
- (72) Schmitt H, Batz G, Knoll R, Danner UN, Brandl M. Plasma level changes of fentanyl and midazolam after release of a prolonged thigh tourniquet. *Acta Anaesthesiol Scand* 1990;34:104-8
- (73) Shannon PF. Neuromuscular stock and tourniquets [letter]. *Br J Anaesth* 1994;73:726
- (74) Estebe JP. The pneumatic tourniquet. Surgical techniques in orthopaedics and traumatology (EFORT). In: DuParc J, editor. Elsevier; 2002.
- (75) Estebe JP, Malle d'ant Y. Pneumatic tourniquets in orthopedics. *Ann Fr Anesth Reanim* 1996; 15:162–178.
- (76) Ostman B, Michaelsson K, Rahme H, et al. Tourniquet-induced ischemia and reperfusion in human skeletal muscle. *Clin Orthop Relat Res* 2004; 418:260–265.
- (77) Pedowitz RA, Gershuni DH, Friden J, Gardin SR, Rydevik BL, Hargens. Effects of reperfusion intervals on skeletal muscle injury beneath and distal to a pneumatic tourniquet. *J Hand Surg* 1992;17:245-55
- (78) Stompro RF, Stevenson TR, Wineinger MA, Sharman RB, Carlsen RC. A reperfusion interval reduces the contractile deficit in skeletal muscle following tourniquet ischemia. *Plast Reconstr Surg* 1994;94:1003-11
- (79) Jacobson MD, Pedowitz RA, Oyama BK, Tryon B, Gershuni DH. Muscle functional deficits after tourniquet ischemia. *Am J Sports Med* 1994;22:372-7
- (80) Doumis E, Tsourvakas S, Kalivas L, Giunacellow H. Effect of time interval on tissue concentrations of cephalosporins after tourniquet inflation. Highest levels achieved by administration 20 minutes before inflation. *Acta Orthop Scand* 1995;66:158-60
- (81) Eastlack RR, Groppo ER, Hargens AR, et al. Ischemic-preconditioning does not prevent neuromuscular dysfunction after ischemia reperfusion injury. *J Orthop Res* 2004; 22:918–923.
- (82) Kharbada RK, Petres M, Walton B, et al. Ischemic preconditioning prevents endothelial injury and systemic neutrophil activation during ischemia-reperfusion in humans in vivo. *Circulation* 2001; 103:1624–1630.
- (83) Van M, Olguner C, Koca U, et al. Ischaemic preconditioning attenuates haemodynamic response and lipid peroxidation in lower-extremity surgery with unilateral pneumatic tourniquet application: a clinical pilot study. *Adv Ther* 2008; 25:355–366.
- (84) Lin LN, Wang LR, Wang WT, et al. Ischemic preconditioning attenuates pulmonary dysfunction after unilateral thigh tourniquet-induced ischemiareperfusion. *Anesth Analg* 2010; 111:539–543.
- (85) Loukogeorgakis SP, Williams R, Panagiotidou AT, et al. Transient limb ischemia induces remote preconditioning and remote postconditioning in humans by a K(ATP)-channel dependant mechanism. *Circulation* 2007; 116:1386–1395.
- (86) Kanoria S, Jalan R, Davies NA, et al. Remote ischaemic preconditioning of the hind limb reduces experimental liver warm ischaemia-reperfusion injury. *Br J Surg* 2006; 93:762–768.
- (87) Jiang X, Ai C, Shi E, et al. Neuroprotection against spinal cord ischemiareperfusion injury induced by different ischemic postconditioning methods: roles of phosphatidylinositol 3- kinase-Akt and extracellular signal-regulated kinase. *Anesthesiology* 2009; 111:1197–1205.
- (88) Arieli D, Nahmany G, Casap N, et al. The effect of nitroxide antioxidant on ischemia-reperfusion injury in the rat in vivo hind limb model. *Free Radic Res* 2008; 42:114–123.
- (89) Bolcal C, Yildirim V, Doganci S, et al. Protective effects of antioxidant medications on limb ischemia reperfusion injury. *J Surg Res* 2007; 139:274–279.
- (90) Mathru M, Huda R, Solanki DR, et al. Inhaled nitric oxide attenuates reperfusion inflammatory responses in humans. *Anesthesiology* 2007; 106:275–282.
- (91) Gabriel A, Porrino ML, Stephenson LL, et al. Effect of L-arginine on leukocyte adhesion in ischemia-reperfusion injury. *Plastic Reconstr Surg* 2004; 113:1698–1702.
- (92) Iida H, Nagasaka T, Shindo K, et al. Effect of the free radical scavenger edaravone on peripheral nerve ischemia-reperfusion injury. *Muscle Nerve* 2009; 40:582–588.
- (93) Beppu S, Nakajima Y, Shibasaki M, et al. Phosphodiesterase 3 inhibition reduces platelet activation and monocyte tissue factor expression in knee arthroplasty patients. *Anesthesiology* 2009; 111:1227–1237.

Biography

Martial Coudert was born in Ris-Orangis(Paris urban area) on the 07/07/1987, and grew up in the south suburbs of Paris, enjoying his time at playing football at a good level.

He first studied medicine in Paris and then transferred to the English program at the Medical School of Zagreb to complete his medical education.

He is now very interested in the mystery of Pyramids, admires ancient civilizations, and would like to investigate the potential contribution of ancient civilizations medicines to modern medicine. Ideally, he would like to associate the benefits of curative superspecialized modern medicine to the benefits of preventive holistic approach of the Ancients, who claimed that health is the result of a proper equilibrium of body, spirit and soul, with nature and universe.

His goals in life are to be happy and helpful!