Acta Orthop. Belg., 2005, **71**, 635-645

REVIEW ARTICLE

Tourniquet injuries : pathogenesis and modalities for attenuation

Colin G. MURPHY, Desmond C. WINTER, David J. BOUCHIER-HAYES

From the Royal College of Surgeons and Beaumont Hospital, Dublin, Ireland

Although it is widespread in orthopaedic surgery, tourniquet use is associated with appreciable morbidity and even mortality. We review the use of tourniquets, highlighting how an understanding of their design and application can reduce the complications and injuries associated with their use. We also review the attempts being made to modulate these injuries through physical and pharmacological advances, in particular looking at the phenomenon of preconditioning.

Key words : pneumatic tourniquet.

INTRODUCTION

Pneumatic tourniquets are widely used in extremity surgery to provide a bloodless field and facilitate dissection. However, it is important to appreciate their potential complications, which may be minimised by understanding the principles of tourniquet use and with careful patient evaluation. Maximising the length of safe continuous ischaemia time and minimising the potentially deleterious effects of reperfusion has focused attention on a variety of experimental methods and pharmacological agents, but none have yet been incorporated into routine clinical management. The frequently rigid approach to the use of the tourniquet has lead many surgeons to underestimate the potential complications of using this piece of equipment *(70)*. Modern pneumatic tourniquets are designed to minimise the incidence of potential complications, but their use is still associated with potentially serious morbidity *(48, 59, 61, 101, 102, 123, 139)* and even mortality *(27, 44)*. Given the extent of potential complications, and even with guidance available to improve safety *(15, 18)*, some authors are seeking to remove ritual use with a more conservative and selective approach *(62, 64)*. Advances in the understanding of cellular mechanisms and specific mediators involved in ischaemia reperfusion (IR) injury may provide potential therapeutic modalities to improve the safety and possibly the duration of surgery under tourniquet control. However, it is essential that surgeons be familiar with the potential complications of using tourniquets in extremity surgery, and be aware of the patho-physiology of tourniquet-induced IR injury.

HISTORY

The tourniquet concept dates back to antiquity when band constriction was used to control haemorrhage during amputation. The term was coined by Jean Louis Petit (derived from the French word 'tourner' meaning to turn), who described a mechanical twisting device in 1718 *(72)*. von Esmarch advanced the design in the late 19th century,

■ Colin G. Murphy, MD, Research Registrar
■ Desmond C. Winter, MD, Senior Registrar
■ David J. Bouchier-Hayes, MD, Professor of Surgery
Correspondence : Colin Murphy, 144 Rock Road, Booterstown, Co. Dublin, Ireland
E-mail : cmurphy@rcsi.ie

adding a concentric flat rubber bandage wrap, before Harvey Cushing introduced the first pneumatic tourniquet in 1904. Its use has become almost routine since, as the use of a bloodless field has become an integral part of limb surgery.

SAFETY AND REGULATION

Mechanism

Modern pneumatic tourniquets comprise microprocessor-controlled components which combine to ensure that the cuff, gas source and pressure regulator provide precise regulation and self-compensation during limb movement or air leak. Most systems prevent excessive pressures (500-600mm Hg) being applied, along with audio and visual alarms to provide warnings if cuff pressure fails or pressure exceeds the fail-safe limit *(138)*. Machines should be checked pre-operatively and at frequent intervals intra-operatively to ensure good working condition and between uses where rigorous monthly tests are recommended to ensure safe function and accurate calibration *(92)*.

Staff

Only experienced personnel, knowledgeable about the use and potential complications of pneumatic tourniquets should be involved in their application. The surgeon should be alerted to the tourniquet time at regular agreed intervals, and information regarding the specific location, duration and pressure of the cuff recorded in the notes. Relative contra-indications to tourniquet use should be identified before application. These include co-morbidities such as arteriosclerosis, prosthetic vascular grafts, significant soft tissue injury, peripheral abscesses, morbid obesity or sickle cell disease *(1, 128)*.

Application

The principles of tourniquet use were established in antiquity. The limb is generally exsanguinated either by elevation for three to five minutes, or ideally by external compression either by application of Esmarch or gauze bandage or a roll-cuff squeeze method *(11, 12)*. The tourniquet should be used with a soft padded protection between the skin and the cuff to prevent skin abrasions, blisters and breaks *(30)*. It should be applied proximally to the upper arm or thigh, to ensure there is sufficient muscle and soft tissue protection of the nerves from compression, and its position checked during surgery to prevent migration of the cuff down the limb *(93)*. Curved cuffs are ideal for obese or very muscular patients as they require lower arterial occlusion pressures than rectangular cuffs *(111)*. Wide cuffs require lower inflation pressures to ensure haemostasis than narrow cuffs *(26)*. Recently, evidence is emerging that more proximal positioning of the cuff along the forearm and above ankle level is safe and effective for hand and foot surgery respectively *(28, 35, 89)*. Reusable cuffs have the potential for contamination with blood and bacterial pathogens, and pose an infection risk if used carelessly *(46)*. In this regard, disposable tourniquets may offer a safer, if more costly, alternative.

TOURNIQUET INFLATION, DURATION AND DEFLATION

Optimal pressure

The pressure to which the cuff should be inflated is dependent on a number of variables, including the patient's age, blood pressure, and the shape and size of the extremity in question, as well as the dimensions of the cuff. Lower tourniquet pressures to achieve haemostasis may be tolerated in younger patients due to youthful vessel compliance *(82)*. There are a number of methods described to determine the optimal inflation pressure for extremity surgery. One method is to add 50-75 mm Hg and 100-150 mm Hg above the arm systolic blood pressure, for surgery on the upper limb and lower limb respectively *(25)*. Alternatives include adding 50-75 mm Hg to the pressure required to obliterate the peripheral pulse on Doppler probe *(116)*, or adding 90-100 mm Hg to the pre-operative blood pressure measured in the arm when operating on the lower limb *(34)*.

Duration

Application of the inflated tourniquet cuff causes interruption of blood supply leading to tissue hypoxia, hyperkalaemia and acidosis *(141)*. High-energy phosphate depletion results in loss of membrane potential of the ischaemic myocytes due to failure of the sodium pump with leakage of potassium into the interstitium *(19)*. If uncorrected, cellular necrosis ensues. Experimental data demonstrates that severity of tourniquet ischaemia is time-, tissue- and species-dependant, and a function of collateral circulation. For identical duration of ischaemia, rat skeletal muscle exhibits more rapid and severe metabolic deterioration than canine or human *(100,129)*. In canine skeletal muscle, widespread sublethal injury to myocytes occurred after three hours of sustained tourniquet ischaemia *(119)*. Even one hour of tourniquet application at clinically relevant pressures in the cat causes subtle changes in muscle function which can persist up to seven days *(43)*.

A time-dependent hypoxia and acidosis in venous blood taken from distal to the cuff has been demonstrated in human trials *(125, 141)*. Venous pH fell to 7.0 at two hours, and resulted in muscle fatigue, ultrastructural changes and muscle damage. Serum creatine phosphokinase (CPK) concentration is elevated locally and distally if the ischaemia time exceeds 1.5 hours *(20, 119)*. If intracellular adenosine triphosphate (ATP) is depleted after three hours of ischaemia, metabolic recovery of muscle is impaired *(100)*. One practical means of avoiding ischaemic injury to muscle cells that is commonly used is the so-called 'breathing period' whereby the tourniquet is released during surgery for a period of time, then re-applied for a second or third period of ischaemia time. Unfortunately the time limits for subsequent ischaemia are unknown *(16)*. The suggested reperfusion time between successive ischaemic periods has ranged from three minutes *(57)* to twenty minutes *(141)*, with some authors questioning the benefit of tourniquet release if surgery time does not exceed three hours *(73)*. The obvious benefit of increased operating time with a bloodless field must be weighed carefully against the potential local and systemic complications of tourniquet release.

Strategies for safely prolonging ischaemia time include alternating dual tourniquets, inflated at hourly intervals to increase continuous ischaemia time *(99)*. Potential complications include higher risk of machinery failure, and an increase in transient hypoaesthesia or paraesthesia for limbs exposed to greater than two hours ischaemia.

With respect to the safe limits for continuous duration of application of tourniquets, the literature has suggested ischaemia times ranging from one to three hours *(20, 55, 71, 73, 119)*. Despite the lack of randomised controlled trials to define the optimal time of lower limb surgery, it has been suggested that two hours is considered safe for upper limb surgery *(37)*.

Deflation

Deflation and reperfusion permits replenishment of energy supplies and elimination of toxic metabolites. However, careful monitoring of the patient is essential at this stage of surgery, as pulmonary embolisation is most likely to occur *(94, 95, 107)*. Intraoperative echocardiography has demonstrated that embolisation of echogenic material is a common event following deflation of the tourniquet, but the composition and clinical relevance of these emboli is uncertain *(107)*. Peak embolisation occurs approximately fifty seconds after tourniquet release *(58)*, but this may even be inversely proportional to the duration of tourniquet time *(94)*.

Despite the significant risk for postoperative deep venous thrombosis in orthopaedic extremity surgery, the pneumatic tourniquet does not appear to be implicated as an independent risk factor *(6, 63, 78, 121, 142)*. However, in the context of intramedullary instrumentation, cementing or insertion of a prosthesis in the lower limb, pneumatic tourniquet use adds a significant risk to the release of large venous emboli *(108)*. Given the prevalence of echogenic material propagated proximally following tourniquet release, and the numerous reports of significant embolic events secondary to tourniquet deflation *(8, 58, 94, 107)*, close attention must be paid to high risk patients. Although there is no consensus for prophylaxis, standard risk factors must be managed aggressively. Screening such patients pre-

operatively and judicious avoidance of pneumatic tourniquets in high risk cases may prevent unnecessary embolisation of material *(108)*.

Inflation of a tourniquet may cause hypercoagulability and fibrinolysis. The tourniquet itself, the pain from surgery and tissue trauma cause a release of catecholamines, which promote platelet aggregation and a hypercoagulable state *(2,75)*. Paradoxically, tourniquet deflation is associated with thrombolytic activity ; anoxia promoting activation of the antithrombin III and protein C pathways which may be implicated in post tourniquet bleeding *(74, 113)*. Tourniquet release prior to wound closure is associated with significantly greater blood loss and demands in blood transfusion, suggesting release following wound closure would offer better control *(22)*.

COMPLICATIONS

All tourniquets can cause complications ranging from minor and self limiting to severe, and even fatal. Systemic effects are usually related to inflating and deflating the tourniquet and the resultant ischaemia and reperfusion phases respectively, while local effects are due to compression ; the mechanical pressure combines an axial stretching force with a sagittal compressive force.

SYSTEMIC COMPLICATIONS

Cardiovascular

While the vast majority of patients tolerate inflation of the tourniquet around an extremity, mobilisation of blood volume at tourniquet placement and release may have detrimental effects on those with coronary or cardiac insufficiency *(33)*. Exsanguination of both lower limbs can account for a 15% increase in circulating blood volume *(14)* and cardiorespiratory decompensation and arrest have been reported *(88)*. This fluid shift accounts for the transient rise in central venous pressure and systolic blood pressure that occur in two thirds of patients having tourniquets applied under general anaesthesia, while occurring in only 2.7% of patients undergoing spinal anaesthesia *(135)*.

This syndrome of tachycardia and hypertension is often referred to as ‘tourniquet pain’, and is thought to be driven by a cutaneous neural feedback mechanism *(33)*. It is tolerated without analgesia for about 30 minutes *(51)*, but for longer periods with incremental sedation *(42)*. A rise in the pCO_2 associated with tourniquet release causes an increase of up to 50% in the flow to the middle cerebral artery, which usually lasts less than ten minutes *(41, 65, 80)*. This may be associated with secondary brain injury in patients with an increased intracranial pressure *(23, 127)*. Changes in cerebral blood flow velocity can be prevented by maintaining normocapnia after tourniquet deflation *(65)*.

Metabolic

Application and release of the extremity tourniquet causes several metabolic changes. Arterial pH, PaO2, PaCO2, lactic acid and potassium levels change significantly after release, the degree largely dictated by the duration of ischaemia time. These changes are generally well tolerated, but in elderly patients, those undergoing mechanical ventilation who are unable to compensate for the metabolic load, and in patients with poor cardiorespiratory reserve, these changes may become clinically important *(45, 110, 133)*. Leakage of potassium, the major intracellular cation, leads to hyperkalaemia in the early reperfusion period *(81)*, and has been implicated in sudden mortality *(24)*. Methods to minimise this risk include ensuring the availability of agents to reduce acidosis and hyperkalaemia respectively, and a high index of suspicion for such problems.

Temperature

Core body temperature increases during tourniquet inflation, and decreases following tourniquet release *(32)*. The increase may be attributable to a combination of reduced convection from extremity skin, and reduced heat loss from central to peripheral compartments. The particular body habitus of children (high surface area to volume ratio) causes a greater increase in core temperature, and they should not be actively warmed during surgery *(9,*

10). Redistribution of body heat and the reflow of hypothermic venous blood from limb distal to the tourniquet into systemic circulation following deflation probably accounts for the temperature drop. This may switch off the thermoregulatory vasodilatation, leading to the decreases in skin-surface temperature seen *(4)*.

Drug kinetics

Application of extremity tourniquet affects the concentration and penetration of intravenous perioperative medication. For example, timing between administration of antibiotic and inflation of the tourniquet can affect the concentration and penetration of the drug at the site of surgery. Although different antibiotics are absorbed at differing rates, a one-minute interval between administration and application of tourniquet may achieve the minimum inhibitory concentration for expected microorganisms *(40)*. In general though, at least five minutes is optimal to achieve the appropriate tissue penetration *(7, 39)*.

Reperfusion syndrome

The re-establishment of blood flow following a period of ischaemia is essential to restore energy and remove toxic metabolites, however reperfusion can induce a paradoxical extension of ischaemic damage *(54)* and it can cause a group of complications known as the 'Reperfusion Syndrome'. The process is complex, mediated in part by oxygen free radicals, and results in cells that have sustained sublethal ischaemic damage being lethally injured on reperfusion. In a feline model, three hours of ischaemia followed by one hour of reperfusion was worse than four hours of consecutive ischaemia *(106)*. Further evidence implicating the return of oxygenated blood is that hypoxic reperfusion of ischaemic tissue results in little injury *(112)*. Although first noted among patients following reperfusion of a previously ischaemic extremity, it has also been problematic across a broad range of surgical specialties. It can be seen following tourniquet use in lower limb surgery *(38)*, hand surgery *(5)* and during surgery involving organ transplantation *(76)* cardiac bypass *(104, 134)*, vascular cross clamping *(52, 60, 69, 126)*, tissue grafting *(68)* and a range of intestinal resections *(87)*.

A key component in the pathogenesis of reperfusion syndrome is the upregulation of surface adhesion molecules on the vascular endothelium *(130)* and their subsequent interaction with the activated neutrophils *(47,56,137)*. Transendothelial migration of neutrophils, with release of reactive oxygen species and cytokines, causes further damage to the injured tissue *(140)*. There are two main components to the reperfusion syndrome : the local component that causes an exacerbation of the regional ischaemic damage, and the systemic sequelae that may cause secondary organ failure remote from the site of ischaemia. Resulting pulmonary microvascular permeability can lead to ARDS, while both renal and cardiac injuries can lead to other severe and often fatal complications *(19, 36)*.

LOCAL COMPLICATIONS

Skin

Excessive tourniquet time or poorly placed tourniquets may result in cutaneous abrasions, blisters and even pressure necrosis *(21)*. Chemical burns can occur with alcohol based skin preparations *(29, 109)*, while friction burns arise if the tourniquet is unpadded, or telescopes away from its padding during surgery *(30)*.

Vascular

Direct vascular injury is an uncommon complication of tourniquet use with an incidence of 0.03% to 0.14% in knee arthroplasty *(115)*. It occurs most commonly in patients with peripheral vascular disease undergoing lower limb surgery *(50,90)* and is likely caused by atheromatous plaque fracture, or by thrombosis of severely atheromatous vessels *(118)*. A thorough preoperative assessment can identify at-risk patients with peripheral arterial disease in whom tourniquet use is a relative contraindication *(124)*. Acute arterial injury may not be identified on the day of surgery in up to 50% of patients *(17)*, highlighting the importance of

neurovascular examination at intervals following surgery. Judicious use of arteriography and aggressive revascularisation are critical to achieving limb salvage. Outcomes following correction of direct injury are excellent, but poor for thrombotic injury even if corrected early *(79)*.

Nerve

There have been several reports of nerve injuries associated with tourniquet use *(3,13,37,77,117)*. A survey of surgeons in the Australian Orthopaedic Association thirty years ago reported the incidence of nerve palsy to be 1 in 5000 and 1 in 13000, after upper limb and lower limb tourniquet use respectively *(97)*. This probably underestimates the incidence of nerve injury, as the data provided for this survey was voluntary, and electrodiagnostic testing was not routinely performed. Mechanical pressure seems more important in the injury than distal ischaemia *(85)*. Compression of the nerve causes microvascular congestion and oedema, causing inadequate tissue perfusion and axonal degeneration *(86)*. High tourniquet pressures and faulty pressure gauges are implicated in many reports, as are Esmarch bandages, which can generate pressures in excess of 1000 mmHg immediately under the tourniquet *(96)*. Excessive continuous compression times cause a higher likelihood of neuropathy and delayed recovery of function *(77)*.

The duration of tourniquet application is proportionate to quadriceps dysfunction following tourniquet-controlled knee surgery *(120)*. While some degree of pain and muscle necrosis may be involved, delayed recovery may be the result of a slowly resolving axonal compression syndrome caused by the pneumatic tourniquet. Axonal injury induces muscle weakness, loss of sensation and leads to adaptive responses and neuropathic pain, but nerve regeneration following crush injury occurs at 3-4 mm per day *(131)*.

Muscle

Application of the tourniquet causes tissue ischaemia both beneath the cuff and distal to the occluded area. This causes functional and microscopic changes proportional to the duration and pressure applied, such that reversal is significantly prolonged after three hours of ischaemia *(111, 119)*. Ischaemic necrosis may occur beneath the cuff after only two hours of tourniquet inflation at pressures of 200 mmHg to 350 mmHg, while histological changes distal to the tourniquet only become apparent after four hours *(100)*. The combined effects of muscle ischaemia, oedema and microvascular congestion, leads to the 'post-tourniquet syndrome', the most common and least appreciated morbidity associated with tourniquet use. This syndrome is characterised by stiffness, pallor, paresis and paraesthesia *(66, 83)*. Rhabdomyolysis due to tourniquet use has been reported due to long tourniquet times and unusually high pressures *(105, 114, 123, 136)*. Compartment syndrome is uncommon, and is thought to result from the combination of anoxic oedema, reperfusion hyperaemia and haematoma formation *(48, 59, 84, 103, 122)*.

PHYSICAL AND PHARMACOLOGICAL ATTENUATION

The search continues for a method of safely increasing the maximum duration of continuous ischaemia time, while decreasing the effects of ischaemia and reperfusion syndrome. There has been considerable interest in attempting to complement the endogenous and induced exogenous mechanisms of modulating the local and systemic consequences of reperfusion injury with physiological, pharmacological and physical methods. Preconditioning, the phenomenon whereby cells and tissues exposed to a sublethal stress are protected from a subsequently lethal assault, has huge potential as a therapeutic agent in attenuating planned injuries. Physical preconditioning strategies such as hypothermia *(31, 67, 132)*, ischaemia *(49, 98)*, hyperthermia *(53, 91)* have demonstrated reasonable success. The legion of pharmacologic agents investigated have yet to yield a clear winner that achieves the ultimate goal of preconditioning research - the discovery of the form of treatment which exerts effective protective qualities, yet is side-effect free, noninjurious, inexpensive and clinically applicable. Its potential use in tourniquet

surgery would be significant, offering a means of increasing the maximum safe length of continuous tourniquet use, while minimising the local trauma and reducing the local and systemic effects of reperfusion injury.

SUMMARY

Tourniquet use, although widespread in many fields of surgery, is not without complications. Surgeons must be aware of the potential complications associated with their use, and understand the mechanisms by which these occur. Careful patient assessment, knowledge of the principles of tourniquet use and an understanding of the pathophysiological changes that occur are essential in minimising the morbidity of this often ritually used piece of equipment.

REFERENCES

1. **Adu-Gyamfi Y, Sankarankutty M, Marwa S.** Use of a tourniquet in patients with sickle-cell disease. *Can J Anaesth* 1993 ; 40 : 24-27.
2. **Aglietti P, Baldini A, Vena LM *et al.*** Effect of tourniquet use on activation of coagulation in total knee replacement. *Clin Orthop* 2000 ; 371 : 169-177.
3. **Aho K, Sainio K, Kianta M *et al.*** Pneumatic tourniquet paralysis. Case report. *J Bone Joint Surg* 1983 ; 65-B : 441-443.
4. **Akata T, Kanna T, Izumi K *et al.*** Changes in body temperature following deflation of limb pneumatic tourniquet. *J Clin Anesth* 1998 ; 10 : 17-22.
5. **al-Qattan MM.** Ischaemia-reperfusion injury. Implications for the hand surgeon. *J Hand Surg* 1998 ; 23-B : 570-573.
6. **Angus PD, Nakielny R, Goodrum DT.** The pneumatic tourniquet and deep venous thrombosis. *J Bone Joint Surg* 1983 ; 65-B : 336-339.
7. **Bannister GC, Auchincloss JM, Johnson DP *et al.*** The timing of tourniquet application in relation to prophylactic antibiotic administration. *J Bone Joint Surg* 1988 ; 70-B : 322-324.
8. **Berman AT, Parmet JL, Harding SP *et al.*** Emboli observed with use of transesophageal echocardiography immediately after tourniquet release during total knee arthroplasty with cement. *J Bone Joint Surg* 1998 ; 80-A : 389-396.
9. **Bloch EC.** Hyperthermia resulting from tourniquet application in children. *Ann R Coll Surg Engl* 1986 ; 68 : 193-194.
10. **Bloch EC, Ginsberg B, Binner RA Jr *et al.*** Limb tourniquets and central temperature in anesthetized children. *Anesth Analg* 1992 ; 74 : 486-489.
11. **Blond L, Kirketerp-Moller K, Sonne-Holm S *et al.*** Exsanguination of lower limbs in healthy male subjects. *Acta Orthop Scand* 2002 ; 73 : 89-92.
12. **Blond L, Madsen JL.** Exsanguination of the upper limb in healthy young volunteers. *J Bone Joint Surg* 2002 ; 84-B : 489-491.
13. **Bolton CF, McFarlane RM.** Human pneumatic tourniquet paralysis. *Neurology* 1978 ; 28 : 787-793.
14. **Bradford EM.** Haemodynamic changes associated with the application of lower limb tourniquets. *Anaesthesia* 1969 ; 24 : 190-197.
15. **Braithwaite I, Klenerman L.** Burns under the tourniquet - Bruner's ten rules revisited. *J Med Dent Defence Union* 1996 ; 12 : 14-15.
16. **Bruner JM.** Time, pressure, and temperature factors in the safe use of the tourniquet. *Hand* 1970 ; 2 : 39-42.
17. **Calligaro KD, Dougherty MJ, Ryan S *et al.*** Acute arterial complications associated with total hip and knee arthroplasty. *J Vasc Surg* 2003 ; 38 : 1170-1177.
18. **Carter KB, Shaw A, Telfer AB.** Tourniquets for surgery : Safety aspects. *J Med Eng Technol* 1983 ; 7 : 136-139.
19. **Chaudry IH, Clemens MG, Baue AE.** Alterations in cell function with ischaemia and shock and their correction. *Arch Surg* 1981 ; 116 : 1309-1317.
20. **Chiu D, Wang HH, Blumenthal MR.** Creatine phosphokinase release as a measure of tourniquet effect on skeletal muscle. *Arch Surg* 1976 ; 111 : 71-74.
21. **Choudhary S, Koshy C, Ahmed J *et al.*** Friction burns to thigh caused by tourniquet. *Br J Plast Surg* 1998 ; 51 : 142-143.
22. **Christodoulou AG, Ploumis AL, Terzidis IP *et al.*** The role of timing of tourniquet release and cementing on perioperative blood loss in total knee replacement. *Knee* 2004 ; 11 : 313-317.
23. **Conaty KR, Klemm MS.** Severe increase of intracranial pressure after deflation of a pneumatic tourniquet. *Anesthesiology* 1989 ; 71 : 294-295.
24. **Cormier JM, Legrain M.** Hyperkalemia, very severe complication of acute ischaemia syndromes of the limbs. *J Chronic Dis* 1962 ; 83 : 473-483.
25. **Crenshaw A.** *Surgical Techniques and Approaches.* 9th ed. DK Canale S, Jones L, editor. St Louis : Mosby ; 1998, pp. 29-142.
26. **Crenshaw AG, Hargens AR, Gershuni DH *et al.*** Wide tourniquet cuffs more effective at lower inflation pressures. *Acta Orthop Scand* 1988 ; 59 : 447-451.
27. **Darmanis S, Papanikolaou A, Pavlakis D.** Fatal intraoperative pulmonary embolism following application of an Esmarch bandage. *Injury* 2002 ; 33 : 761-764.
28. **Delgado-Martinez AD, Marchal JM, Blanco F *et al.*** Distal forearm tourniquet for hand surgery. *Int Orthop* 2004 ; 28 : 267-269.

29. **Dickinson JC, Bailey BN.** Chemical burns beneath tourniquets. *BMJ* 1988 ; 297 : 1513.
30. **Din R, Geddes T.** Skin protection beneath the tourniquet : A prospective randomized trial. *ANZ J Surg* 2004 ; 74 : 721-722.
31. **Erdogan D, Omeroglu S, Sarban S *et al.*** Prevention of oxidative stress due to tourniquet application. Analysis of the effects of local hypothermia and systemic allopurinol administration. *Acta Orthop Belg* 1999 ; 65 : 164-169.
32. **Estebe JP, Le Naoures A, Malledant Y *et al.*** Use of a pneumatic tourniquet induces changes in central temperature. *Br J Anaesth* 1996 ; 77 : 786-788.
33. **Estebe JP, Malledant Y.** Pneumatic tourniquets in orthopedics. *Ann Fr Anesth Reanim* 1996 ; 15 : 162-178.
34. **Estersohn HS, Sourifman HA.** The minimum effective midthigh tourniquet pressure. *J Foot Surg* 1982 ; 21 : 281-284.
35. **Finsen V, Kasseth AM.** Tourniquets in forefoot surgery : less pain when placed at the ankle. *J Bone Joint Surg* 1997 ; 79-B : 99-101.
36. **Fitzpatrick DB, Karmazyn M.** Comparative effects of calcium channel blocking agents and varying extracellular calcium concentration on hypoxia/reoxygenation and ischaemia/reperfusion-induced cardiac injury. *J Pharmacol Exp Ther* 1984 ; 228 : 761-768.
37. **Flatt AE.** Tourniquet time in hand surgery. *Arch Surg* 1972 ; 104 : 190-192.
38. **Friedl HP, Till GO, Trentz O *et al.*** Role of oxygen radicals in tourniquet-related ischaemia-reperfusion injury of human patients. *Klin Wochenschr* 1991 ; 69 : 1109-1112.
39. **Friedman RJ, Friedrich LV, White RL *et al.*** Antibiotic prophylaxis and tourniquet inflation in total knee arthroplasty. *Clin Orthop* 1990 ; 260 : 17-23.
40. **Friedrich LV, White RL, Brundage DM *et al.*** The effect of tourniquet inflation on cefazolin tissue penetration during total knee arthroplasty. *Pharmacotherapy* 1990 ; 10 : 373-377.
41. **Fujii Y, Toyooka H, Ishikawa E *et al.*** Blood flow velocity in the middle cerebral artery response to tourniquet release. *Anaesth Intensive Care* 1999 ; 27 : 253-256.
42. **Fuselier CO, Binning T, Dobbs BM *et al.*** A study of the use of a double tourniquet technique to obtain hemostasis in combination with local standby sedation during podiatric surgery. *J Foot Surg* 1988 ; 27 : 515-527.
43. **Gersoff WK, Ruwe P, Jokl P *et al.*** The effect of tourniquet pressure on muscle function. *Am J Sports Med* 1989 ; 17 : 123-127.
44. **Gielen M.** Cardiac arrest after tourniquet release. *Can J Anaesth* 1991 ; 38 : 541.
45. **Girardis M, Milesi S, Donato S *et al.*** The hemodynamic and metabolic effects of tourniquet application during knee surgery. *Anesth Analg* 2000 ; 91 : 727-731.
46. **Golder M, Chan CL, O'Shea S *et al.*** Potential risk of cross-infection during peripheral-venous access by contamination of tourniquets. *Lancet* 2000 ; 355 : 44.
47. **Granger DN, Benoit JN, Suzuki M *et al.*** Leukocyte adherence to venular endothelium during ischaemia-reperfusion. *Am J Physiol* 1989 ; 257 : G683-G688.
48. **Greene TL, Louis DS.** Compartment syndrome of the arm-a complication of the pneumatic tourniquet ; A case report. *J Bone Joint Surg* 1983 ; 65-A : 270-273.
49. **Gurke L, Marx A, Sutter PM *et al.*** Ischaemic preconditioning improves post-ischaemic skeletal muscle function. *Am Surg* 1996 ; 62 : 391-394.
50. **Hagan PF, Kaufman EE.** Vascular complication of knee arthroplasty under tourniquet. A case report. *Clin Orthop* 1990 ; 257 : 159-161.
51. **Hagenouw RR, Bridenbaugh PO, van Egmond J *et al.*** Tourniquet pain : a volunteer study. *Anesth Analg* 1986 ; 65 : 1175-1180.
52. **Haimovici H.** Arterial embolism with acute massive ischaemic myopathy and myoglobinuria : evaluation of a hitherto unreported syndrome with report of two cases. *Surgery* 1960 ; 47 : 739-747.
53. **Healy C, Mulhall KJ, Nelligan M *et al.*** Postoperative stiffness and adhesion formation around repaired and immobilized Achilles tenotomies are prevented using a model of heat shock protein induction. *J Surg Res* 2004 ; 120 : 225-229.
54. **Hearse DJ.** Reperfusion of the ischaemic myocardium. *J Mol Cell Cardiol* 1977 ; 9 : 605-616.
55. **Heppenstall RB, Balderston R, Goodwin C.** Pathophysiologic effects distal to a tourniquet in the dog. *J Trauma* 1979 ; 19 : 234-238.
56. **Hernandez LA, Grisham MB, Twohig B *et al.*** Role of neutrophils in ischaemia-reperfusion-induced microvascular injury. *Am J Physiol* 1987 ; 253 : H699-H703.
57. **Hinman F.** The rational use of tourniquets. *Internat Abst Surg* 1945 ; 81 : 357-365.
58. **Hirota K, Hashimoto H, Kabara S *et al.*** The relationship between pneumatic tourniquet time and the amount of pulmonary emboli in patients undergoing knee arthroscopic surgeries. *Anesth Analg* 2001 ; 93 : 776-780.
59. **Hirvensalo E, Tuominen H, Lapinsuo M *et al.*** Compartment syndrome of the lower limb caused by a tourniquet : a report of two cases. *J Orthop Trauma* 1992 ; 6 : 469-472.
60. **Holoman M, Zahorec R, Kusy J *et al.*** Biochemical monitoring in patients during revascularization surgery. *Vasa* 1995 ; 24 : 23-28.
61. **Irvine GB, Chan RN.** Arterial calcification and tourniquets. *Lancet* 1986 ; 2 : 1217.
62. **Jahss M.** *Disorders of the Foot and Ankle. Medical and Surgical Management.* 2nd Ed ed. Philadelphia : WB Saunders ; 1991, pp. 55-56.
63. **Jarrett PM, Ritchie IK, Albadran L *et al.*** Do thigh tourniquets contribute to the formation of intra-operative venous emboli? *Acta Orthop Belg* 2004 ; 70 : 253-259.
64. **Johnson DS, Stewart H, Hirst P *et al.*** Is tourniquet use necessary for knee arthroscopy ? *Arthroscopy* 2000 ; 16 : 648-651.

65. Kadoi Y, Ide M, Saito S *et al.* Hyperventilation after tourniquet deflation prevents an increase in cerebral blood flow velocity. *Can J Anaesth* 1999 ; 46 : 259-264.

66. Kam PC, Kavanagh R, Yoong FF *et al.* The arterial tourniquet : pathophysiological consequences and anaesthetic implications. *Anaesthesia* 2001 ; 56 : 534-545.

67. Kelly C, Creagh T, Grace PA *et al.* Regional hypothermia protects against tourniquet neuropathy. *Eur J Vasc Surg* 1992 ; 6 : 288-292.

68. Kerrigan CL, Stotland MA. Ischaemia reperfusion injury : a review. *Microsurgery* 1993 ; 14 : 165-175.

69. Khaira HS, Maxwell SR, Thomason H *et al.* Antioxidant depletion during aortic aneurysm repair. *Br J Surg* 1996 ; 83 : 401-403.

70. Klenerman L. Is a tourniquet really necessary for knee replacement ? *J Bone Joint Surg* 1995 ; 77-B : 174-175.

71. Klenerman L. The tourniquet in operations on the knee : a review. *J R Soc Med* 1982 ; 75 : 31-32.

72. Klenerman L. The tourniquet in surgery. *J Bone Joint Surg* 1962 ; 44-B : 937-943.

73. Klenerman L. Tourniquet time : how long ? *Hand* 1980 ; 12 : 231-234.

74. Klenerman L, Chakrabarti R, Mackie I *et al.* Changes in haemostatic system after application of a tourniquet. *Lancet* 1977 ; 1 : 970-972.

75. Kohro S, Yamakage M, Arakawa J *et al.* Surgical/tourniquet pain accelerates blood coagulability but not fibrinolysis. *Br J Anaesth* 1998 ; 80 : 460-463.

76. Koo DD, Welsh KI, Roake JA *et al.* Ischaemia/reperfusion injury in human kidney transplantation : an immunohistochemical analysis of changes after reperfusion. *Am J Pathol* 1998 ; 153 : 557-566.

77. Kornbluth ID, Freedman MK, Sher L *et al.* Femoral, saphenous nerve palsy after tourniquet use : a case report. *Arch Phys Med Rehabil* 2003 ; 84 : 909-911.

78. Kroese AJ, Stiris G. The risk of deep-vein thrombosis after operations on a bloodless lower limb. A venographic study. *Injury* 1976 ; 7 : 271-273.

79. Kumar SN, Chapman JA, Rawlins I. Vascular injuries in total knee arthroplasty. A review of the problem with special reference to the possible effects of the tourniquet. *J Arthroplasty* 1998 ; 13 : 211-216.

80. Lam AM, Slee T, Hirst R *et al.* Cerebral blood flow velocity following tourniquet release in humans. *Can J Anaesth* 1990 ; 37 : S29.

81. Larcan A, Mathieu P, Helmer J *et al.* Proceedings : Severe metabolic changes following delayed revascularization : Legrain-Cormier syndrome. *J Cardiovasc Surg* 1973 ; 14 : 609-614.

82. Lieberman JR, Staheli LT, Dales MC. Tourniquet pressures on pediatric patients : a clinical study. *Orthopedics* 1997 ; 20 : 1143-1147.

83. Love BR. The tourniquet. *Aust N Z J Surg* 1978 ; 48 : 66-70.

84. Luk KD, Pun WK. Unrecognised compartment syndrome in a patient with tourniquet palsy. *J Bone Joint Surg* 1987 ; 69-B : 97-99.

85. Lundborg G. Structure and function of the intraneural microvessels as related to trauma, edema formation, and nerve function. *J Bone Joint Surg* 1975 ; 57-A : 938-948.

86. Lundborg G, Dahlin LB. The pathophysiology of nerve compression. *Hand Clin* 1992 ; 8 : 215-227.

87. Mallick IH, Yang W, Winslet MC *et al.* Ischaemia-reperfusion injury of the intestine and protective strategies against injury. *Dig Dis Sci* 2004 ; 49 : 1359-1377.

88. Maurer NH, Voegeli PT Jr, Sorkin BS. Non-cardiac circulatory overload secondary to pneumatic thigh tourniquets. *J Am Podiatry Assoc* 1983 ; 73 : 589-592.

89. Maury AC, Roy WS. A prospective, randomized, controlled trial of forearm versus upper arm tourniquet tolerance. *J Hand Surg* 2002 ; 27-B : 359-360.

90. McAuley CE, Steed DL, Webster MW. Arterial complications of total knee replacement. *Arch Surg* 1984 ; 119 : 960-962.

91. McCormick PH, Chen G, Tierney S *et al.* Clinically relevant thermal preconditioning attenuates ischaemia-reperfusion injury. *J Surg Res* 2003 ; 109 : 24-30.

92. McEwen J. Complications of and improvements in pneumatic tourniquets used in surgery. *Med Instrum* 1981 ; 15 : 253-257.

93. McEwen JA, Auchinleck GF. Advances in surgical tourniquets. *AORN J* 1982 ; 36 : 889-896.

94. McGrath BJ, Hsia J, Boyd A *et al.* Venous embolization after deflation of lower extremity tourniquets. *Anesth Analg* 1994 ; 78 : 349-353.

95. McGrath BJ, Hsia J, Epstein B. Massive pulmonary embolism following tourniquet deflation. *Anesthesiology* 1991 ; 74 : 618-620.

96. McLaren AC, Rorabeck CH. The pressure distribution under tourniquets. *J Bone Joint Surg* 1985 ; 67-A : 433-438.

97. Middleton RW, Varian JP. Tourniquet paralysis. *Aust N Z J Surg* 1974 ; 44 : 124-128.

98. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischaemia : a delay of lethal cell injury in ischaemic myocardium. *Circulation* 1986 ; 74 : 1124-1136.

99. Neimkin RJ, Smith RJ. Double tourniquet with linked mercury manometers for hand surgery. *J Hand Surg* 1983 ; 8-A : 938-941.

100. Newman RJ. Metabolic effects of tourniquet ischaemia studied by nuclear magnetic resonance spectroscopy. *J Bone Joint Surg* 1984 ; 66-B : 434-440.

101. Ogino Y, Tatsuoka Y, Matsuoka R *et al.* Cerebral infarction after deflation of a pneumatic tourniquet during total knee replacement. *Anesthesiology* 1999 ; 90 : 297-298.

102. O'Leary AM, Veall G, Butler P *et al.* Acute pulmonary oedema after tourniquet release. *Can J Anaesth* 1990 ; 37 : 826-827.

103. O'Neil D, Sheppard JE. Transient compartment syndrome of the forearm resulting from venous congestion from a tourniquet. *J Hand Surg* 1989 ; 14-A : 894-896.

104. Ortolano GA, Aldea GS, Lilly K *et al.* A review of leukofiltration in cardiac surgery : the time course of

reperfusion injury may facilitate study design of anti-inflammatory effects. *Perfusion* 2002 ; 17 : 53-62.

105. Palmer SH, Graham G. Tourniquet-induced rhabdomyolysis after total knee replacement. *Ann R Coll Surg Engl* 1994 ; 76 : 416-417.

106. Parks DA, Granger DN. Contributions of ischaemia and reperfusion to mucosal lesion formation. *Am J Physiol* 1986 ; 250 : G749-G753.

107. Parmet JL, Berman AT, Horrow JC *et al.* Thromboembolism coincident with tourniquet deflation during total knee arthroplasty. *Lancet* 1993 ; 341 : 1057-1058.

108. Parmet JL, Horrow JC, Berman AT *et al.* The incidence of large venous emboli during total knee arthroplasty without pneumatic tourniquet use. *Anesth Analg* 1998 ; 87 : 439-444.

109. Parslew R, Braithwaite I, Klenerman L *et al.* An investigation into the effect of ischaemia and pressure on irritant inflammation. *Br J Dermatol* 1997 ; 136 : 734-736.

110. Patel AJ, Choi CS, Giuffrida JG. Changes in end tidal CO2 and arterial blood gas levels after release of tourniquet. *South Med J* 1987 ; 80 : 213-216.

111. 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* 1993 ; 287 : 237-244.

112. Perry MA, Wadhwa SS. Gradual reintroduction of oxygen reduces reperfusion injury in cat stomach. *Am J Physiol* 1988 ; 254 : G366-G372.

113. Petaja J, Myllynen P, Myllyla G *et al.* Fibrinolysis after application of a pneumatic tourniquet. *Acta Chir Scand* 1987 ; 153 : 647-651.

114. Pfeifer PM. Acute rhabdomyolysis following surgery for burns. Possible role of tourniquet ischaemia. *Anaesthesia* 1986 ; 41 : 614-619.

115. Rand JA. Vascular complications of total knee arthroplasty. Report of three cases. *J Arthroplasty* 1987 ; 2 : 89-93.

116. Reid HS, Camp RA, Jacob WH. Tourniquet hemostasis. A clinical study. *Clin Orthop* 1983 ; 177 : 230-234.

117. Rorabeck CH, Kennedy JC. Tourniquet-induced nerve ischaemia complicating knee ligament surgery. *Am J Sports Med* 1980 ; 8 : 98-102.

118. Rush JH, Vidovich JD, Johnson MA. Arterial complications of total knee replacement. The Australian experience. *J Bone Joint Surg* 1987 ; 69-B : 400-402.

119. Sapega AA, Heppenstall RB, Chance B *et al.* Optimizing tourniquet application and release times in extremity surgery. A biochemical and ultrastructural study. *J Bone Joint Surg* 1985 ; 67-A : 303-314.

120. Saunders KC, Louis DL, Weingarden SI *et al.* Effect of tourniquet time on postoperative quadriceps function. *Clin Orthop* 1979 ; 143 : 194-199.

121. Schippinger G, Wirnsberger GH, Obernosterer A *et al.* Thromboembolic complications after arthroscopic knee surgery. Incidence and risk factors in 101 patients. *Acta Orthop Scand* 1998 ; 69 : 144-146.

122. Seybold EA, Busconi BD. Anterior thigh compartment syndrome following prolonged tourniquet application and lateral positioning. *Am J Orthop* 1996 ; 25 : 493-496.

123. Shenton DW, Spitzer SA, Mulrennan BM. Tourniquet-induced rhabdomyolysis. A case report. *J Bone Joint Surg* 1990 ; 72-A : 1405-1406.

124. Smith DE, McGraw RW, Taylor DC *et al.* Arterial complications and total knee arthroplasty. *J Am Acad Orthop Surg* 2001 ; 9 : 253-257.

125. Solonen KA, Tarkkanen L, Narvanen S *et al.* Metabolic changes in the upper limb during tourniquet ischaemia. A clinical study. *Acta Orthop Scand* 1968 ; 39 : 20-32.

126. Soong CV, Young IS, Hood JM *et al.* The generation of byproducts of lipid peroxidation following carotid endarterectomy. *Eur J Vasc Endovasc Surg* 1996 ; 12 : 455-458.

127. Sparling RJ, Murray AW, Choksey M. Raised intracranial pressure associated with hypercarbia after tourniquet release. *Br J Neurosurg* 1993 ; 7 : 75-77.

128. Stein RE, Urbaniak J. Use of the tourniquet during surgery in patients with sickle cell hemoglobinopathies. *Clin Orthop 1*980 ; 151 : 231-233.

129. Stock W, Bohn HJ, Isselhard W. Metabolic changes in rat skeletal muscle after acute arterial occlusion. *Vasc Surg* 1971 ; 5 : 249-255.

130. Stokes KY, Abdih HK, Kelly CJ *et al.* Thermotolerance attenuates ischaemia-reperfusion induced renal injury and increased expression of ICAM-1. *Transplantation* 1996 ; 62 : 1143-1149.

131. Stoll G, Muller HW. Nerve injury, axonal degeneration and neural regeneration : basic insights. *Brain Pathol* 1999 ; 9 : 313-325.

132. Swanson AB, Livengood LC, Sattel AB. Local hypothermia to prolong safe tourniquet time. *Clin Orthop* 1991 ; 264 : 200-208.

133. Townsend HS, Goodman SB, Schurman DJ *et al.* Tourniquet release : systemic and metabolic effects. *Acta Anaesthesiol Scand* 1996 ; 40 : 1234-1237.

134. Valer G, Khoschsorur GA, Almdahl SM *et al.* Lipid peroxidation in open-heart surgery. *Perfusion* 1994 ; 9 : 277-283.

135. Valli H, Rosenberg PH, Kytta J *et al.* Arterial hypertension associated with the use of a tourniquet with either general or regional anaesthesia. *Acta Anaesthesiol Scand* 1987 ; 31 : 279-283.

136. Vold PL, Weiss PJ. Rhabdomyolysis from tourniquet trauma in a patient with hypothyroidism. *West J Med* 1995 ; 162 : 270-271.

137. Wakai A, Wang JH, Winter DC *et al.* Tourniquet-induced systemic inflammatory response in extremity surgery. *J Trauma* 2001 ; 51 : 922-926.

138. Wakai A, Winter DC, Street JT *et al.* Pneumatic tourniquets in extremity surgery. *J Am Acad Orthop Surg* 2001 ; 9 : 345-351.

139. Ward CM. Oedema of the hand after fasciectomy with or without tourniquet. *Hand* 1976 ; 8 : 179-185.

140. Welbourn CR, Goldman G, Paterson IS *et al.* Pathophysiology of ischaemia reperfusion injury : central role of the neutrophil. *Br J Surg* 1991 ; 78 : 651-655.

141. Wilgis EF. Observations on the effects of tourniquet ischaemia. *J Bone Joint Surg* 1971 ; 53-A : 1343-1346.

142. Williams JS, Jr., Hulstyn MJ, Fadale PD *et al.* Incidence of deep vein thrombosis after arthroscopic knee surgery : a prospective study. *Arthroscopy* 1995 ; 11 : 701-705.