Fracture Healing

The Evolution of Our Understanding

Hojení zlomenin – evoluční změny v našich poznatcích

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SUMMARY

Our understanding of fracture healing has undergone an evolution over many decades with continuous improvement of fracture treatment. Solid union is a precondition of restoring the function of a fractured bone. The goal of the early treatment of the fracture was focussed upon enabling solid union in acceptable alignment of the fracture. This was achieved with reduction followed by application of external splints. The function of the articulations was often troubled by long lasting and extensive external immobilization, which required physiotherapy that lasted longer than bone union.

The surgical reduction and stabilization aimed at early recovery of movement of the articulations and maintenance of the function of the soft tissues and blood supply. The AO group initiated 1958 by Maurice E. Müller and his colleagues prioritized the recovery of limb function and propagated precise reduction and fixation using mainly compression. Absolute stability of fixation, achieved using implants, allowed to move the articulations very early without pain, while the fracture united solidly.

After such treatment the implants could not be removed before 1 1/2 to 2 years without risking increased incidence of re-fracture. This was in sharp contrast to the fact that after conservative treatment the bone was solidly united after 2 to 3 months. The analysis of this situation revealed that internal remodelling after absolutely stable fixation did not recognize the presence of the fracture. Primary healing, therefore, is not a healing in the strict sense of the word but a side effect of internal removal of necrotic bone.

To maintain early function of the limb and stimulate the healing process the so called biological internal fixation was developed. It combines minimal surgical trauma, acceptable rather than precise reduction and flexible fixation usually achieved with so called internal fixateurs. Flexibility of mind and of tools aims at safe and early healing with full recovery of function and minimal risk of biological complications.

INTRODUCTION

Our understanding of fracture, fracture treatment and healing has undergone a basic evolution in the past decade. Fracture and fracture treatment are amenable to straight forward discussion. Fracture healing, in turn, may be discussed at different layers of depth like cellular, genetic and tissue contribution. Here we will limit our self to the aspects of tissues with their immediate clinical implications (5).

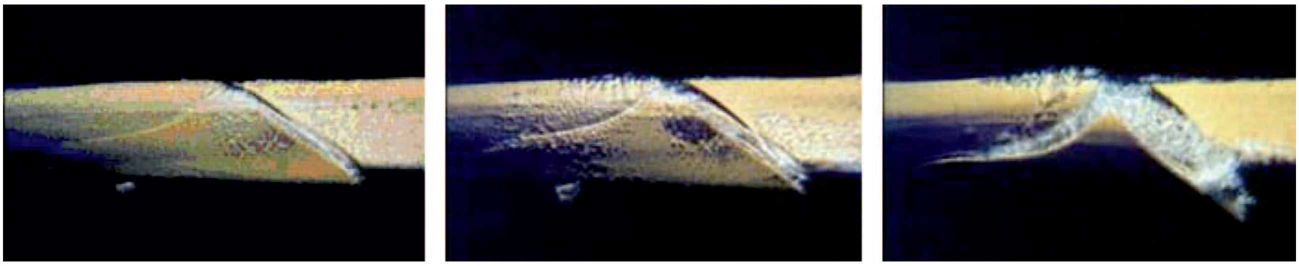
The fracture

The fracture results in a local discontinuity of structural stiffness. The main mechanical function of bone providing support and enabling locomotion is lost. This is a mechanical event with marked biological consequences. Observation of the fracture using high speed cinematography has revealed that the fracture and its abrupt opening of a fracture gap results in an important implosion (Fig. 1). With it a marked damage of the tissue results, when the surrounding tissues are forcefully aspirated into the void. The tissue trauma due to the fracture risks to be underestimated when looking at static x-ray pictures.

The biological consequences of a fracture depend on tissue disruption and with it damage to blood supply. Necrotic bone is then produced which requires biological removal. Such removal must be initiated within living bone by a signal from necrotic bone. The onset of removal of necrotic bone has attracted our attention because it explains the observation „stress protection“ (1). Today we understand so called primary bone healing also as removal of necrotic bone.

Fracture healing

is a biological event with marked mechanical consequences. The fracture which is not stabilized allows gross deformation of the tissue inside the fracture gap and of the tissue surrounding the fracture site. Healing that is restoration of original integrity of the bone. will have to bridge and thus repair the fracture to abolish discontinuity of stiffness of the bone. This discontinuity of stiffness results in an area where large displacements result in heavy deformation of the tissues. To restore the continuity of stiffness the initial repair tissues must by priority be able to survive under high deformation (technically „strain“). Such tissues are by necessity rather soft and forgiving. Later in the healing process the re-



a b c

Fig. 1. Three phases of a fracture of bone immersed in water. The fracture is produced within micro seconds. Extract from a high speed movie. The consecutive phases show that once the bone fragments separate abruptly the bubbles produced indicates a strong implosion with important tissue damage.

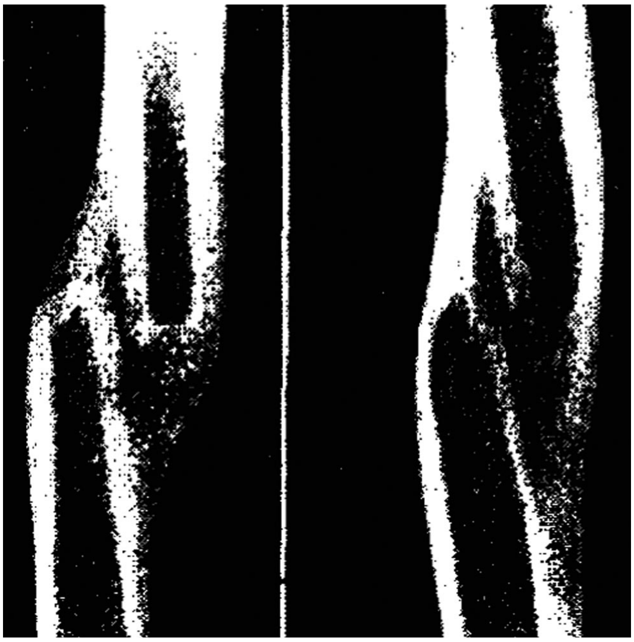


Fig. 2. Secondary healing after conservative treatment with functionally acceptable alignment. In respect to function precise alignment of diaphyseal fractures is not mandatory. For articular fractures precise reconstruction of the articulating surfaces is considered to be mandatory.

pair tissue increases its stiffness while its tolerance to deformation decreases. The concomitant increase in diameter of the callus increases the structural stiffness of the repair tissue with the fourth power of its diameter. While initial repair tissue behaves like rubber and allows without failure deformation of more than 100%, the final repair tissue the lamellar bone behaves more like glass it tolerates only about 2% deformation.

Because the main consequence of healing is restoration of the mechanical integrity of fractured bone one may expect the healing process to be mainly controlled by mechanical environment. Accordingly the biological process resulting in restoration of the structural integrity would be initiated and steered by deformation of repair tissue („strain“). Fracture healing is enabled by biological events. Is it initiated by the mechanical environment? Still, when discussing why bone behaves in a certain manner, we keep the pitfalls of such thinking in mind: We read or hear often what bone intends to do and we may, therefore, be temped to follow a teleological type of thinking and arguing. It is very difficult to assume that bone is thinking at all. The danger of teleological thinking in research consists in the easy acceptance of logical (rather pseudo-logical) argumentation which disregards the fact of the „télos“ (end, purpose) component of the word teleological. Thus, often the aim is rather the wish of the author. For what concerns our way of thinking we assume that bone simply reacts rather than acts intelligently.

Fracture treatment

The basic goal of fracture treatment formulated by Müller et al. (4) namely that the goal of the treatment is first of all to recover early the function (mobility) of the injured limb to avoid trophic disturbance (7). Still in the past decade our approach to achieving this goal has evolved (5). Absolute stability is today understood as enabling mechanical function on the price of abolishing the signal initiating biological repair (formation of callus). The obvious difference of achieving solid healing with plaster fixation within two to three months on the one hand and on the other hand requiring late (two years) removal of implants after surgical immobilization of the fracture indicates that there is room for improvement.

The fracture destroys the integrity of the bone, disables limb function and last but not least has an impact *quoad vitam*. Fifty years ago the primary goal of fracture treatment was to achieve nothing else than solid union (Fig. 2). External splinting using plaster all too often resulted in damaged joint and soft tissue function. Therefore, during the first two decades of AO technology the restoration of mechanical functions had outstanding priority. Immediate surgical stabilization could recover the function of joints and soft tissues and minimized the incidence of reflex dystrophy. If perfect reduction and excellent stabilization are the unique goals of surgical stabilization the risk of producing additional biological damage increases. Achieving function on the expense of damaged blood supply to bone and its neighboring and nourishing soft tissues cannot be the final goal. Such procedures also risk to abolish the signaling of the presence of a fracture to the repair tissues.

The decades of compression and absolute stability

In the 60s and 70s the goal of surgical stabilization mainly was to achieve absolute stability to provide the fracture with a motionless, „neutral“ environment. This was implemented using compression. Appearance of callus was assumed to indicate that this goal was not achieved. Absolute stability of fixation failed to initiate properly the healing process. The implants had to be left in place up to two years to avoid refracture of the slowly remodeling fracture site. We understand today that the stimulus for internal remodeling in primary healing is not the presence of a fracture but its concomitant tissue damage, that is necrotic bone. Observing the Haversian osteones leads to the conclusion that they may not react in relevant way to the presence of the fracture. Often the osteones crossing the fracture do not change shape nor direction and speed (Fig. 3). Beside complete removal of bone the internal remodeling is the process which allows to maintain mechanical integrity during replacement of the necrotic bone (creeping substitution by internal remodeling).

Closing and compressing the fracture gap also did not allow radiological monitoring of the repair process within the gap. Thus to prevent re-fractures of single slow healing cases, that went undetected, the implants had to be left as a rule for an extended period of time. Without direct monitoring the diagnosis of undisturbed healing had to be based on the absence of warning symptoms such as cloudy callus, widening of the fracture gap, pain and swelling. This was not a major disadvantage but it left but left room for improvement.

The review of compression technology of fracture treatment helps to elucidate the change brought about: The classical example of application of compression for stabilization is the lag screw. In the opposite cortex the thread of the screw engages solidly. In the near cortex the gliding hole or the shaft of a partially threaded screw does not engage and the fragment is held in axial position only by the purchase of the undersurface of the screw head against bone. Some aspects concerning the function of lag screws deserve mentioning:

- The compression produced by the lag screw is large (two to three kilo Newton about two to three hundred kilogram force).
- The stability produced by a interfragmentary lag screw is absolute (loading within limits of anchorage strength does not produce displacement of the fracture surfaces).
- A single lag screw does not well stabilize against torque around the long axis of the screw
- The compression is produces within the fracture plane (the plate produces eccentric compression with parasitic bending)

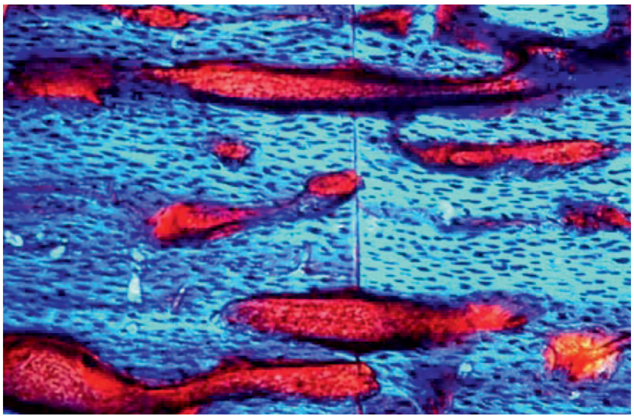


Fig. 3. Osteones crossing the osteotomy, which is adapted and compressed. The osteones do not react in a relevant manner to the presence of the fracture. The question is what induces the internal remodeling, which was understood as a process initiated by the fracture and resulting in fracture healing.

- When the axial load exceeds holding strength the compressive effect of the lag screw is irreversibly lost (the plate may give reversibly way and springs back after unloading).
- While the quality of stability of a lag screw is excellent it does not provide proper strength of fixation and can only exceptionally be used without additional protection (usually by a splinting plate).

When looking at an x-ray picture of a plate fixed with screws to a long bone one gets the impression that the forces applied along the long axis of the plate are transmitted by the plate screws from and to the bone. In conventional internal fixation the plate screw does not directly transmit forces between plate and bone The conventional plate screws does press the undersurface of the plate onto the bone surface producing friction. Each screw produces, when tightened in an average way, a force of two to three KN. This compressive force results in an amount of friction of one to $1^1/_2$ KN maintaining the contacting surfaces of plate and bone without tangential displacement. Thus, early after application the screw is not subject to relevant bending loads. When with ongoing healing the axial preload of the screw diminishes and friction can no more prevent displacement the conventional unlocked screw minimally tilts within the screw hole of the plate. Two effects then play role according to our present understanding: The interface between the screw and bone undergoes intermittent bending load and with it induces resorption with consequent loosening of the screw. Once loose the contact between screw head and plate hole is lost and no more bending is applied to the screw thread. Then bone will on grow to the now unloaded screw. At removal this on growth fakes a still functioning plate screw. A further effect of this sequence of events with displacement between screws and plate is fretting with marked increase in corrosion and/or abrasion.

The geometry of the screw to plate seating which permits inclination was chosen to allow tilting of the screw

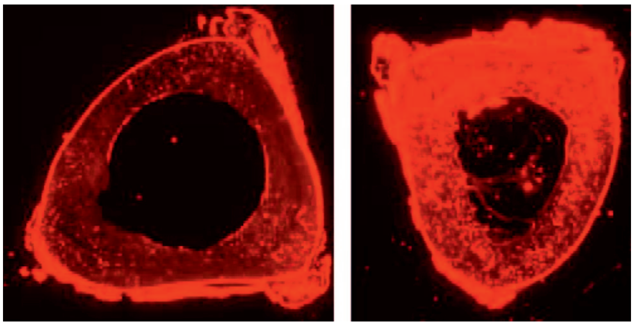


Fig. 4. Blood supply after reaming (left) and without reaming (right). Tibia of the dog after injection of procion red. There is an important deficit of blood supply after reaming.

mainly in respect to the long axis of the plate but also to a minor degree around the long axis of the plate. Such inclination allowed the plate screws simultaneously to act as fixing element for the plate and, when feasible, to produce interfragmentary compression across fracture planes with low inclination towards the long axis of the bone. Thus the screws could be oriented perpendicular to the fracture plane to produce „best“ interfragmentary compression without parasitic forces that could displace the fragments during application of interfragmentary compression. This was an obvious advantage of non locked screws during application of interfragmentary compression. A further advantage of screws which can be applied in inclined position is that they allow to avoid placing the tip or part of the thread of the screw within a fracture gap.

While a lag screw is an interesting tool, some of the above mentioned disadvantages initiated the search for more forgiving techniques. Splinting technology deserves consideration: The splint consists of a more or less rigid body fixed to the bone. In the absence of interfragmentary compression such splinting reduces but does not abolish small reversible displacements of the fracture fragments in relation to each other. The challenge was to find a new balance between stabilization that still allowed functional after treatment and enabled the repair tissue to sense the presence of the fracture.

The intramedullary nail

The intramedullary nail was since its clinical introduction by Küntscher always a pure splinting tool. A pure splint (be it plate, fixateur or i.m. nail) reduces but does not abolish (like compression does) the load dependent displacement at the fracture site. This applies to the non locked version as well as to the locked nail. A few attempts to use compression techniques with the nail were not too successful. The application of compression between the metaphyses lacked good anchorage mainly within the cancellous bone. Axial compression of long bone fractures using cortical anchorage still may help reduce initial pain during early functional after treatment. A mechanical characteristic of stabilization using locked nail is that beside the elastic deformation of the nail (2) a certain play between the locking screws and the nail allows for limited instability. New developments aim at abolishing this mechanical play.

The early i.m. nails were applied aiming at perfect geometrical fit between the rod and the cylindrically reamed marrow cavity (6). It became soon obvious that the reaming produced a major damage to the endosteal blood supply. This triggered the development of non reamed nails. It could be shown by Klein et al. (3), that non reamed procedures were biologically superior to reamed once (Fig. 4). Mechanically the non reamed i.m. nails by necessity are limited in their diameter and with it strength and stiffness.

Therefore, the clinical indication for this procedure was and still is initial temporary stabilization of multifragmented open fractures. A more extended use may require strength which these nails cannot provide.

From the external to the internal fixator

Using the external fixator the fragments of the fracture are connected to a splinting rod placed outside the body. Depending on the dimensions of the elements and their special relation (e.g. distance from bone to rod, distance between the Schanz screws) a wide variety of structural stiffness can initially be implemented and later modified according to the progress of healing. The external fixator is insofar an attractive technology as surgical trauma is minimal. The transcutaneous pins carry the risk of infection. Therefore one would try to maintain the atraumatic advantages without the transcutaneous connection by embedding the fixator completely under the skin. This is what is called today internal fixator. While splinting in compression fixation served mainly to protect stable but not strong lag screw fixation, the splinting became a self standing stabilizing tool. The internal fixator is an embedded fixator with screws replacing the pins and with a locking of screw head to plate replacing the clamps of the fixator The screws of an ;internal fixator do not compress the fracture surfaces they do as a rule not act as lag screws. Therefore, for such screws one can take advantage of locking the inclination. A improved anchorage is generally achieved using locked screws especially if they are inclined in relation to each other in longitudinally divergent or convergent position. Newer data indicates that such inclination becomes effective only over a certain limit of divergence or convergence (~ 30 °). When comparing conventional plate fixation with internal fixators the biological advantages of the latter are based on flexibility and minimal surface contact. The body of the internal fixator can be elevated from the bone surface and thus can prevent damage to the periosteal blood supply by implant surfaces contacting the bone surface.

Flexible, biological internal fixation

In contrast to compression which abolishes fracture movement, splinting elastically reduces displacement at the fracture site according to the stiffness and span width of the splint. The elastic mobility of the fracture site resulted in a better stimulation of fracture repair replacing primary or direct healing with secondary, quick and reliable healing.

The use of stabilization techniques, which are rather flexible and their application foregoing the need of precise reduction allow reducing the surgical trauma. The trauma is limited when perfect (hairline) reduction is not a goal. Furthermore, the internal fixator technique allows elevating the internal fixator avoiding extended surface contact and thus helps to maintain good blood supply. The biological advantages may be partially offset by the possible incidence of mechanically induced delayed healing or non unions.

Still the mechanical complication (due to excessive flexibility) is fairly easy to treat. The biological complication resulting from extensive surgical stripping of bone blood supply in an attempt to achieve perfect reduction and absolute stability resulting in necrotic sequestration is much more demanding to treat (Fig. 5). Multifragmented fractures are more tolerant to instability than simple short fractures (Fig. 6). The problem is that with simple and more or less transverse fracture planes establishing optimal mechano biological conditions appears to be not an easy task and requires experience. According to the strain theory for a given amount of instability the strain is the higher the smaller the gap is. The cyclic deformation inducing healing determines the lower limit of required strain while the flexibility, the loading and a narrow fracture gap increase the deformation of the repair tissues. This strain may easily exceed the upper (tolerance) limits of strain. Several preliminary reports of large series of successful flexible treatment of simple short fractures seem to indicate that flexible fixation is possible. Still one needs to know more about the optimal choice of stiffness, gap width and loading.

Flexibility of internal fixator stabilization obviously depends on the stiffness of the body of the fixator and its stiffness of coupling to the bone. With locked screws the coupling is rather tight. An additional effect needs attention: the length of span between the innermost screws determines the stiffness of the construct. With increasing length of the free span for a given displacement of the fracture the deformation of the body (plate) of the fixator is reduced.

One advocates today flexible fixation of non precisely reduced fractures generally for long bone fractures. Still articular fractures seem to require precise and stable fixation. The dream would be to avoid extensive surgery of articular comminution provided we were able to dynamically reduce the multiple fragment moving unloaded articulations: A challenging task but also a rewarding one improving biology.

Outlook

Today's main topics are to our opinion:

– A better understanding of fracture healing in respect to the balance between mechano-biological tradeoffs,
– A better understanding of the impact of molecular biology in respect to improving blood supply to enhance local defense against infection
– A better understanding where chemical induction may play a clinically relevant role in view of the excellent spontaneous onset of fracture healing and obvious

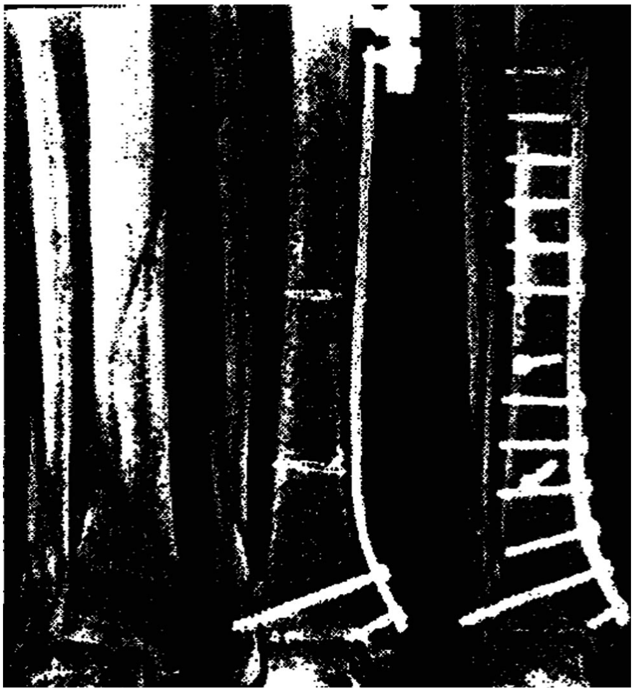


Fig. 5. Compression plating of a distal multi-fragmented Tibia fracture using plate and lag screws. Such a surgical procedure resulted as a rule in a wide stripping of the bone from its blood supply.

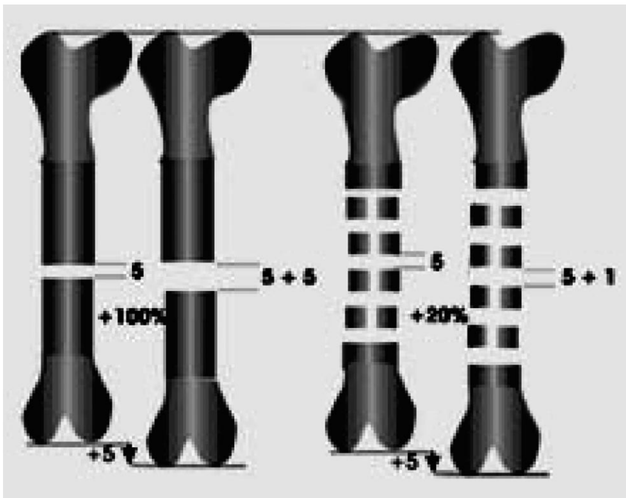


Fig. 6. Comparison of interfragmentary displacement in simple and multiple fractures. The initial gap width is 5 units, the overall displacement in both cases the same: 5 units. In the simple fracture the strain is 100%, in the multiple fracture 20%. This visualizes why multifragmental fractures are more tolerant to instability than simple ones.

absence of recognition of the presence of the fracture later on.
– Development of more tolerant, forgiving technologies of internal fixation.
– Improved fracture treatment in porotic bone.

ZÁVĚR

Naše znalosti hojení zlomenin prošly v průběhu mnoha desetiletí značným vývojem a stále se zdokonalují. Pevné zhojení je předpokladem obnovení funkce zlomené kosti. Dříve bylo cílem léčby zlomeniny zajištění jejího dokonalého zhojení v přijatelném osovém postavení. Toho bylo dosaženo pomocí repozice a následné fixace s využitím různých povrchově přikládaných dlah. Funkce kloubů však byla často narušena dlouhodobou imobilizací značné části končetiny. To vyžadovalo následnou fyzioterapii trvající často déle než vlastní zhojení zlomeniny.

Otevřená repozice a stabilizace byla zaměřena na časné obnovení funkce kloubů a zachování funkce měkkých tkání a cévního zásobení. Společnost AO založená v roce 1958 M. E. Müllerem a jeho kolegy stanovila jako prioritu obnovení funkce končetiny a propagovala přesnou repozici a fixaci zlomeniny, a to především kompresí úlomků. Implantáty dosažená absolutně stabilní fixace umožňovala velmi časný bezbolestný pohyb kloubů bez ohrožení hojení zlomeniny. Implantáty mohly být odstraněny až 1,5 až 2 roky po operaci, aby se nezvyšovalo riziko opětné zlomeniny kosti. To bylo v ostrém kontrastu s faktem, že po konzervativní léčbě se kost zcela zhojila po 2 až 3 měsících. Analýza této situace odhalila, že díky absolutně stabilní fixaci nereagují přestavbové pochody na přítomnost zlomeniny. Primární hojení proto není hojením v přesném slova smyslu, ale vedlejším jevem při vnitřní resorpci nekrotické kosti.

Pro časné obnovení funkce končetiny a stimulaci hojení byla vyvinuta tzv. biologická vnitřní fixace. Tato fixace je kombinací minimálního operačního výkonu, který je přijatelnější než přesná repozice, a flexibilní fixace, obvykle pomocí tzv. vnitřních fixatérů. Flexibilita v myšlení i používání nástrojů přispívá k časnému a bezpečnému hojení s plnou obnovou funkce a minimalizuje riziko biologických komplikací.

References

1. GAUTIER, E., PERREN, S.: Die Reaktion der Kortikalis nach Verplattung – eine Folge der Belastungsveraenderung des Knochens oder Vaskularitaetsprobleme? In: Die Plattenosteosynthese und ihre Konkurrenzverfahren, Springer Verlag 1991, 21–37.
2. KEMPF, I., GROSSE, A., LEUNG, K.: Practice of intramedullary locked nails: scientific basis and standard technique recomended by AIOD. Berlin, New York, Springer Verlag 2002.
3. KLEIN, M., RAHN, B., FRIGG, R., KESSLER, S., PERREN, S.: Reaming versus non-reaming in medullary nailing: interference with cortical circulation of the canine tibia. Arch. Orthop. Trauma Surg., 109: 314–316, 1990.
4. MUELLER, M., ALLGOEWER, M., WILLENEGGER, H.: Technik der operativen Frakturenbehandlung. Springer-Verlag 1963.
5. PERREN, S. M.: Evolution of internal fixation of long bone fractures: The scientific basis of biological internal fixation: Choosing a new balance between stability and biology. J. Bone Jt Surg., 84-B:1093–1110, 2002.
6. RAHN, B. A.: Intra vitam staining techniques. In: Handbook of biomaterials evaluation. Scientific, technical, and clinical testing of implant materials. Second edition, pp. 727-738. Ed. by AF von Recum. Philadelphia, London, Taylor & Francis 1999.
7. SCHATZKER, J., TILE, M.: The Rationale of Operative Fracture Care. Berlin, Springer Verlag 2005.

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Práce byla přijata 5. 5. 2008.