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Periosteal and endosteal microcirculatory injury following excessive osteosynthesis ☆

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ABSTRACT

Introduction: We examined the endosteal and periosteal circulations in a patient with fracture non-union who had undergone excessive osteosynthesis applications (two long plates had been placed medially and laterally on the left tibia extending from the proximal 2/7 to the distal 6/7 parts of the bone, while a tibial component of a total knee prosthesis with a long stem had been inserted at the same time).

Methods: Concomitant perfusion changes were determined in the anterolateral and anteromedial periosteal sheath of the non-united bone ends and intramedullary nearest the osteosynthesis materials during their surgical removal on re-operation. The blood flow in the periosteum and endosteum was recorded by a laser-Doppler flowmetric device using a novel approach. Control measurements were made at identical points of the right tibia.

Results: Considerably lower blood flow values were measured along the tibial periosteal region of the re-operated limb than on the contralateral side (the average perfusion unit (PU) was 76 vs. 106 PU, respectively). Perfusion values were markedly lower in the endosteal region (average values of approx. 30 PU) in the control tibia and were even more diminished in the re-operated tibial endosteum (average 9 PU).

Conclusions: Our study was conducted to characterize the microcirculatory changes of a long bone in response to intramedullary implantation and to provide quantitative data on the insufficiency of local perfusion in a patient with fracture non-union. Our results highlight the association between local perfusion failure and the unfavorable outcome (i.e. fracture non-union), confirming that the vital aspects of the microcirculation should not be disregarded when aiming for mechanical stability.

Microcirculatory measurements constitute a new area of improvement in planning the adequate treatment for fracture non-unions with an unclear aetiology. Further refinement of the laser-Doppler technique could have potential benefits for bone surgery and postoperative trauma care in the future.

Introduction

Fracture healing is a complex, multifactorial process requiring the anatomical and functional integrity of the surrounding biological membranes [1]. Experimental data suggest that osteosynthesis techniques applied to the fixation of fractures (plate osteosynthesis and intramedullary nailing) can induce circulatory disturbances of the bone; for example, plate osteosynthesis (e.g. DC plates) impairs periosteal circulation, while intramedullary reaming destroys the endosteal circulation, resulting in necrosis in the inner 2/3 of the cortical bone [2–6]. Although the importance of the integrity of the microcirculation has been emphasized in numerous textbooks, no clinical evidence has been provided on the extent of microcirculatory injury in these conditions, mostly owing to methodological limitations.

Both experimental and clinical observations suggest that disruption of the continuity of the periosteum or endosteum delays

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bone healing, but impairment of only one or the other of these structures does not hinder overall fracture healing [7–11]. The anatomical connection between the two systems is not well characterized in humans, but it is extensive in young animals, where the arterial supply and venous drainage traverse both the endosteal and periosteal surfaces; therefore, either of the two systems is sufficient to provide adequate bone circulation [9,11].

The destruction of the endosteum with nailing using different materials causes distinct changes in the periosteal vascular organization [10,12]. Furthermore, the dependence of the healing capacity of the cortex on the endosteal and periosteal blood supply following osteosynthesis has been demonstrated in different species [11,13]. Perfusion changes of the periosteum have been investigated using the laser-Doppler technique in animals; however, there is limited experience with human models [12–15]. In addition, no such data are available regarding the human endosteum. Therefore, a clinical study was conducted to provide evidence of the magnitude of local blood perfusion deficit in response to intramedullary implants. The microcirculation of the tibial periosteum and endosteum was examined using a laser-Doppler flowmetric approach in a patient with non-union. Two years prior to our analysis, the patient had a tibial fracture at the level of the end point of the stem of a cemented total knee endoprosthesis. We were unable to achieve healing either with DC plate osteosynthesis or with subsequently applied angular stable plates on the medial and lateral sides of the tibia. Consequently, non-union developed. We assumed the role of microcirculatory disturbances in the development of non-union; measurements were thus performed to detect concomitant microcirculatory perfusion deficit nearest the osteosynthesis materials at the time of implant removal.

Methods

Intraoperative microcirculatory measurements were performed with the permission and signed consent of the patient. The study was approved by the Ethical Committee of the University of Szeged Clinical Center and the Regional Ethical Committee on Human Medical Research (No. 0623.2014).

The following surgical interventions were performed: Two years prior to our analysis, the patient had a tibial fracture at the level of the end point of the stem of a cemented total knee endoprosthesis. We were unable to achieve healing either with DC plate osteosynthesis or with subsequently applied angular stable plates on the medial and lateral sides of the tibia. Consequently, pseudarthrosis developed. At the time of re-operation, the patient was experiencing pain, and both plates were broken.

As the initial step of the re-operation, the two angular stable plates were removed together with their partially broken screws. Subsequently, the tibial component of the knee prosthesis was extracted. A special total knee prosthesis was designed and manufactured to manage the non-union. Its tibial component had an extended stem with distal holes that bridged the fracture. Locking screws were placed in the distal holes so that the bone ends were held closely opposed. Cement fixation was not used. The polyethylene component (15 mm in size) of the tibial tray was also replaced. The bone ends were refreshed and the fracture gap was tightly filled with autologous spongiosa from the left iliac crest to induce osteogenesis. Microcirculatory measurements were performed during the removal of the old implants.

Measurement of the tibial periosteal and endosteal microcirculatory variables with laser-Doppler flowmetry: The blood flow in the periosteum and endosteum was recorded with a laser-Doppler flowmetric device (supplied with a 780-nm laser diode; PeriFlux System 5000, Perimed, Järfälla, Sweden) with a sterilized fibre optic probe (#416, “dental probe”; fibre separation: 0.25 mm, penetration depth ~ 1 mm). The tibial periosteum was explored via a conventional anterior incision in the re-operated limb and via a small (~ 2 cm) skin incision in the contralateral limb. The flow probe was held perpendicularly to the surface of the periosteum with a plastic holder, which reduced the contact pressure on the observed area and restricted the angular movements of the probe. The endoprosthesis was then removed, and the endosteal membrane compartment was approached through the bone cavity. A small hole was drilled in the anterior cortex, providing access to the endosteum at the opposite (inner surface of the posterior) medullary wall (Fig. 1). The size of the drilled hole allowed a perfect fit for the flow probe. Since an endoprosthesis was present on the contralateral (non-operated) side, it was possible to measure the endosteal circulation distally to the stem of the endoprosthesis, somewhat below the level of the measurement on the re-operated side; the difference was ~ 1 cm. Given the examination depth of the laser-Doppler device and the thickness of the periosteal and endosteal membranes, it was mostly the periosteum and endosteum that could be examined with a portion of the underlying cortex.

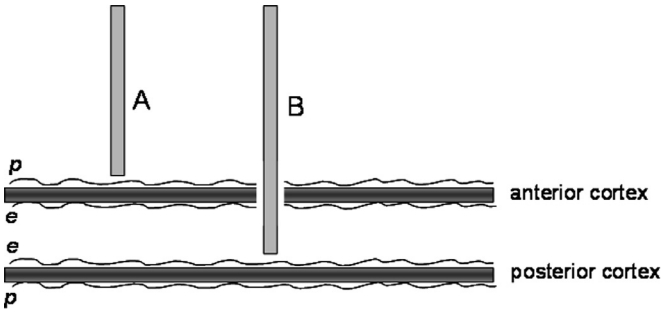

Fig. 1. Scheme of the laser-Doppler flowmetry approach to the observation of perfusion of the periosteum (A) and the endosteum (B). The periosteum (*p*) was observed through a small incision made in the skin and the underlying tissues, while the endosteal region (*e*) was reached through a small hole drilled in the anterior cortex, providing access to the endosteal region at the opposite (inner surface of the posterior) medullary wall.

Characteristic flow curves synchronized with the heart circles were reproducibly detected in the $\tau = 0.2$s mode, showing that pressure artefacts were avoided. After the required signal quality had been reached, recordings were made in 30s periods and repeated three times. Tissue perfusion was expressed arbitrarily in perfusion units (PU); before the measurements, the probe was calibrated with the special motility standard supplied by the manufacturer. Data were collected and stored on a computer and subsequently analyzed with the computer software supplied with the device. Throughout the observation period, the room temperature (20±2°C) and core temperature of the patient were maintained; the stable macrohaemodynamic parameters were recorded continuously.

Since this study relates to only one patient and the measurements were conducted repeatedly at basically the same locations, no statistical comparisons were performed. Raw data (expressed in arbitrary units) are presented in Fig. 2E to illustrate potential differences.

Results

Considerably lower periosteal blood flow values were measured in the re-operated tibial periosteum (Fig. 2B) than in the contralateral, non-operated limb (Fig. 2A) (average levels of 76 and 106 PU, respectively) (Fig. 2E). A great deal of lower perfusion was observed in the proximity of the endosteum; however, an average endosteal perfusion of 30 PU was found in the non-operated tibia (Fig. 2C). An even lower perfusion level was measured in the re-

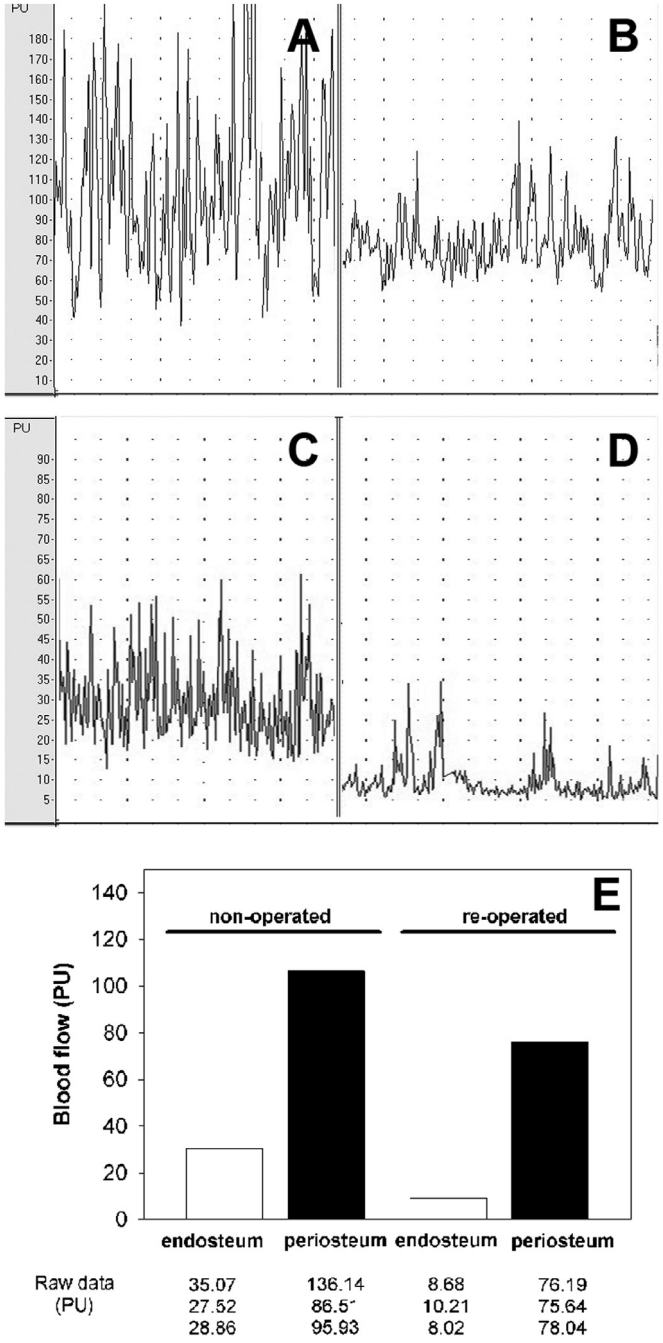

Fig. 2. Original laser-Doppler flowmetric recordings of the periosteal (A and B) and endosteal regions (C and D) in the non-operated (A and C) and operated (B and D) tibia. Data related to the perfusion of the above compartments are presented in part (E). The mean values of three measurements constitute the presented data.

operated tibial endosteal region (average 9 PU; Fig. 2D) even in the presence of characteristically good signal quality (Fig. 2E).

Radiographs taken six weeks after the operation revealed callus formation in the dorsal part of the fracture and good alignment of the fracture ends (Fig. 3). The patient now walks with the aid of a knee-ankle-toe orthosis without loading the osteosynthesis.

Discussion

Our patient underwent a series of internal fixations that provided adequate stability. The diamond model of bone fracture healing describes the interactions between the extrinsic mechanical

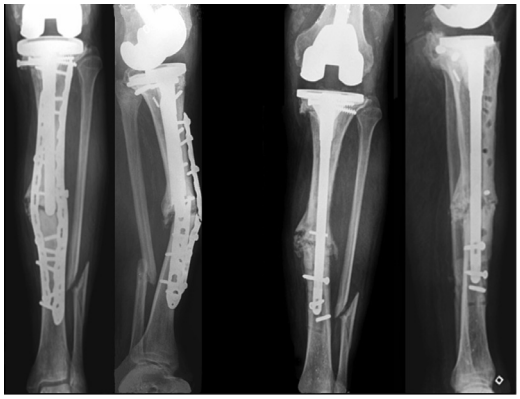

Fig. 3. Anteroposterior and lateral views of the left tibia prior to the re-operation (A) and 6 weeks after surgery (B). In addition to the proper alignment of the bone ends, callus formation was detected in the dorsal part of the fracture.

environment and endogenous factors; however, the microcirculation of the biological membranes of the bone are also essential and sometimes overlooked, as demonstrated in our study [16,17].

From a physiological/biological aspect, the endosteal and periosteal blood flow was diminished in the fractured limb (as compared to the contralateral limb), and, as a result, non-union developed. In long bones, endochondral bone repair is the primary form of bone healing when micro-motions exist between the fractured parts of bones covered with the periosteum [14,6]. This process is based on the ability of periosteum-derived cells to proliferate and to form periosteal callus in the initial phase of fracture healing [15,18]. In line with this, in an ovine “periosteal sleeve” model, the periosteum alone was shown to be capable of regenerating the long bone defect when the endosteum was completely destroyed [16,19]. Probably because of the decisive role of the periosteum, the importance of the endosteum in bone healing is generally underestimated [15,18]. Similarly to the periosteum, the endosteum covering all interior surfaces of bones (including all of the inner surfaces of the cortex and the spongiosa) also provides a rich vascular environment and harbors osteoprogenitor cells for fracture healing, but cellular mechanisms differ greatly [18,20,21]. Selective disruption of the endosteum occurs in clinical practice mostly via the reaming of the medullary cavity. As a result, avascularity and even the partial necrosis of the cortex can be detected, suggesting that a significant proportion of the cortical blood flow is provided by the intramedullary vessels.

Our patient underwent a sequence of distinct osteosynthesis techniques that provided excellent mechanical stability in the short term. However, the integrity of the periosteum and endosteum were affected simultaneously, resulting in inhibition of adequate fracture healing and formation of non-union.

Doppler flowmetry is a suitable method for the analysis of microvascular blood flow, which could be utilized in bone surgery and postoperative trauma care. However, further research is needed to refine its practicality and invasiveness.

The ethical and technical limitations of performing a high number of periosteal and endosteal circulatory measurements under clinical circumstances constitute our greatest limitation.

Therefore, further clinical studies are warranted to assess long-term circulatory derangements after osteosynthesis using noninvasive techniques. There are promising results with a combined laser-Doppler and spectrophotometry system (Oxygen-to-see) that allows microcirculatory measurements both intraoperatively and at the bedside [22]. Therefore, it could be used in a comprehensive clinical study to evaluate the microcirculatory consequences of different osteosynthesis techniques.

Conclusions

The present study provides the first evidence-based demonstration of the consequences of iatrogenic cessation of the interior and exterior blood supply of a long bone. A concurrent deterioration of both endosteal and periosteal components of the microcirculation may explain the unfavourable clinical outcome. Although there may be other reasons for the non-union of a fracture, such as mechanical or endogenous factors [23–26] – see the "diamond concept" noted above – the laser-Doppler data from the current study suggest that the cessation of the periosteal and endosteal microcirculation was the main cause of fracture non-union in this particular patient.

Appropriate preoperative planning and preservation of the local microcirculation may both contribute to the final favorable outcome after re-operation. Therefore, microcirculatory measurements constitute a new area of improvement in planning adequate treatment for fracture non-unions with an unclear aetiology. Further refinement of the laser-Doppler technique could have potential benefits for bone surgery and postoperative trauma care in the future.

Declaration of Competing Interest

None of the authors has any conflict of interests related to this manuscript.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.injury.2020.11.053.

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