Acta Orthop Scand *56*, 400–403, 1985

Bone marrow circulation after osteotomy

Blood flow, pO_2, pCO_2, and pressure studied in dogs

We investigated the immediate effect of osteotomy of the femoral shaft in adult dogs on intramedullary pO_2, pCO_2, relative bone blood flow (RBF) and intraosseous pressure (IOP). Single osteotomy resulted in a pO_2 decrease from 49 mm Hg to 30 mm Hg. Double osteotomy further reduced pO_2 to 21 mm Hg. Following double osteotomy, pCO_2 increased from 42 mm Hg to 55 mm Hg. IOP was decreased by single osteotomy from 29 mm Hg to 15 mm Hg, and to 4 mm Hg by the second osteotomy. Linear regression analysis showed a negative correlation between pCO_2 and RBF. We concluded that osteotomy introduces immediate haemodynamic and metabolic changes in the bone marrow canal. A periosteal supply of the endosteal bone seems possible provided this system is intact.

Hakon Kofoed
Erik Sjøntoft
Siems Otto Siemssen
Henning Peder Olesen

The Institute of Experimental Research in Surgery, University of Copenhagen, Denmark

Correspondence: Department of Orthopaedic Surgery, Rigshospitalet, DK-2100 Copenhagen, Denmark

Revascularization and healing of tubular bone is of potential interest in fracture treatment, reconstructive surgery and intramedullary reaming. In order to judge the immediate nutritional consequences for the endosteal bone, we performed single and double osteotomies of canine femoral shafts while intramedullary pO_2, pCO_2, qualitative bone blood flow and intraosseous pressure were recorded continuously.

Material and methods

Six adult female mongrel dogs, weight 25 (20–30) kg, were used. The dogs were anaesthetized with intravenous pentobarbitone (75 mg/kg/h) and kept on a respirator (Servo 900, Siemens, FRG) using atmospheric air. The midshaft of the femur on one side was freed by blunt dissection through a lateral incision. Care was taken to avoid damage to the muscles and the periosteal envelope. A special bone cannula (outer diameter 2 mm, inner 1 mm) was screwed via a drill hole into the midshaft of the medullary canal. The cannula was used for continuous intraosseous pressure (IOP) measurements (Stratham P 23 ID transducers, UK and a Minograph 80 Elema-Siemens, S). Simultaneously the regional venous pressure (VP) in the great saphenous vein was registered by the same apparatus, in order to measure perfusion pressure, i.e. IOP-VP. The mean arterial pressure (MAP) was measured on a third channel via an open-ended catheter in the carotid artery, which was also used for extraction of arterial blood samples to be analysed in a conventional acid-base and blood gas analyzer (ABL-3, Radiometer, DK) in order to document the constancy of central arterial parameters.

A mass spectrometer (SX-200, VG-Gas Analysis Ltd., UK) was used for detection of intramedullary pO_2 and pCO_2, according to a previously described method, using the argon (pAr) for continuous *in vivo* calibration (Kofoed et al. 1983), while pAr was simultaneously used for qualitative estimation of bone blood flow (Grønlund et al. 1984). The blood gas catheter (Lundsgaard et al. 1980) connected to the mass spectrometer was inserted through the bone cannula when pressure readings were stopped (after at least 10 min of stable signals), and now pO_2, pCO_2 and rel. pAr were measured simultaneously and continuously until stable readings were obtained for a period of at least 10 min. The mass spectrometer signals were always stable after a period of 5 min from introduction of the blood gas catheter. When these measurements had been accomplished in the *in situ* situation, the femoral shaft was osteotomized with an ossilating saw distal to the entry of the main nutrient artery and proximal to the bone cannula. Figure 1 shows the experimental set-up. The measurements were continued as previously for a period of 10 min with pressure measurements and another period of at least 10 min with gas measurements to make sure that the situation had stabilized. Next the

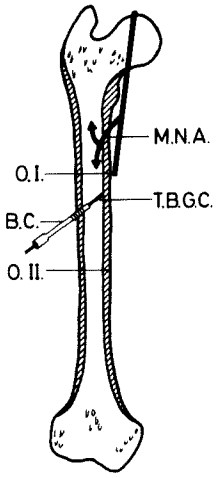

Figure 1. The experimental set-up. The blood gas catheter tip (T.B.G.C.) was always lying against the endosteal bone opposite to the lateral entrance hole of the bone cannula (BC). M.N.A. refers to the main nutrient artery. O.I. and O.II are the first and second osteotomy line respectively.

femoral shaft was osteotomized 10 cm distal to the first osteotomy (and distal to the bone cannula), and measurements were continued as previously described. Arterial blood samples were extracted and analysed immediately on completion of every measuring situation. Finally the animal was killed by an overdose of pentobarbitone. The proximal part of the femur was removed for identification of the entry of the main nutrient artery. Only animals in which the osteotomies had been performed distal to this entry were included in the study.

For statistical analysis, the paired *t*-test and linear regression analysis were used.

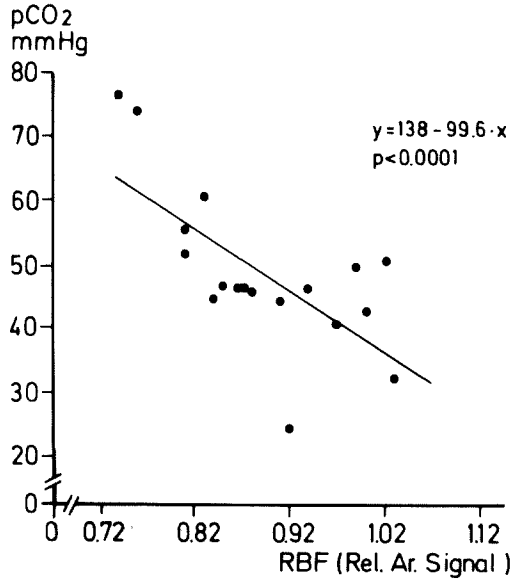

Figure 2. The regression line between qualitative bone marrow flow (rel. pAr) and bone marrow pCO_2.

Results

There was a decrease in pO_2 following single osteotomy and a further decrease following the second osteotomy. pCO_2 was not affected by the first osteotomy, but following the second osteotomy, it was increased. The decrease in the perfusion pressure following the first osteotomy did not decrease further by the second osteotomy (Table 1). The change in the relative argon signal used for detection of qualitative bone blood flow, was not consistent. MAP, paO_2, $paCO_2$ and apH stayed constant throughout the experiments.

A negative correlation was found between pCO_2 and qualitative bone blood flow (Figure 2) whereas no correlation could be established between RBF and pO_2 or IOP, respectively.

Discussion

We have demonstrated a fall in IOP followed by hypoxia and hypercapnia in the bone marrow as a result of deprival of the main nutritive supply accomplished by osteotomy. This effect of osteotomy is well documented (Arnoldi et al. 1971). However, the immediate effect on regional pO_2 and pCO_2 has not been investigated previously. Kivisaari & Niinikoski (1975) removed the intramedullary contents in rabbit

Table 1. In vivo measurements of bone marrow pO_2, pCO_2, relative bone blood flow and pressure, in situ and following single and double osteotomy of canine femoral shafts. N = 6, Mean (SEM).

		Osteotomy	
	In situ	I	II
pO_2 (mmHg)	49 (3.3)*	30 (7.0)*	21 (4.5)*
pCO_2 (mmHg)	42 (3.9)**	49 (5.7)	55 (5.0)**
RBF (rel. pAr)	0,88 (0.02)	0,92 (0.04)	0.88 (0.04)*
IOP-VP (mmHg)	29 (8.2)*	15 (5.0)*	4,2 (1.4)*
paO_2 (mmHg)	132 (12.1)	143 (13.3)	139 (12.9)*
$paCO_2$ (mmHg)	34 (1.3)	34 (0.6)	34 (0.7)*
apH	7,4 (0.01)	7,4 (0.02)	7,4 (0.02)*
MAP (mmHg)	125 (9.8)	115 (6.5)	112 (6.9)*

pO_2 pCO_2 bone marrow (mmHg),
paO_2 $paCO_2$ arterial (mmHg),
RBF relative bone blood flow,
IOP-VP intraosseous-venous pressure (mmHg),
apH arterial pH,
MAP mean arterial pressure,
* $p < 0.02$, ** $p < 0.01$.

tibiae and measured intramedullary pO_2 and pCO_2 intermittently by tonometry via an implanted Silastic tube from the first to the 52nd day. On the third day pO_2 had reached its lowest value, after which it gradually increased towards initial normal values. pCO_2 increased for the first 3 days, after which it declined, to reach normal values after 30 days. However, in their system all three nutritive sources might have been brought into action. Initially both the arteries entering the ends of the bone and the periosteal supply were at hand, and later on the main nutritive artery might have come into action. Relative hypoxia has been claimed by some authors to promote osteogenesis (Brighton & Krebs 1972, Kruse & Kelly 1974), whereas others have found the opposite (Keck & Kelly 1965, Heppenstall et al. 1976). In the clinical situation, where one is faced with treatment of tubular bone fractures, other mechanisms may threaten the bone nutrition, depending on the magnitude of the soft tissue damage, which may seriously impair the possibility of revascularization of the bone. Usually there is no disagreement with the view that in such situations hypoxia is probably to blame for the development of delayed healing. In this context, hypoxia created by destruction of the main arterial supplies should also be considered. Double osteotomy led to more serious metabolic changes than single osteotomy, and this might explain why fractures with intermediate fragments are often more difficult to heal than simple fractures. The hypercapnia found in this situation was not thought to be a result of a change to anaerobic metabolism, but merely an expression of the changed bone blood flow because a significant negative correlation was found between RBF and intraosseous pCO_2. The mechanism of nutritive supply which the endosteal bone will have to rely on after deprival of the main arterial supply is the periosteal supply. Normally a centrifugal blood supply nourishes the endosteal cortical bone (Brookes et al. 1961, Rhinelander 1968, Kelly 1968). When this possibility is abolished, a change to a centripetal bone blood flow will have to come into action. Such a mechanism seems possible and has been shown microangiographically (Brookes 1964, Danckwardt-Lilliestrom et al. 1970). Our study has demonstrated by the constancy of the oxygen partial pressure following double osteotomy that such a nutritional pathway immediately comes into action following the osteotomy as pO_2 would otherwise have declined towards zero and not stayed constant as we found. The reason why this is facilitated could be the simultaneous decrease in the intramedullary pressure, which otherwise in an intact normal bone constitutes a pressure gradient for the periosteal transcortical flow.

Provided this interpretation is correct, several factors are in favour of active revascularization:

i) hypoxia has been found to promote constant vasodilation (Guyton et al. 1964),

ii) angiogenesis is *(in vitro)* favoured by hypoxia (Knighton et al. 1983), and

iii) decreasing oxygen saturation causes an increase in blood flow (Ross et al. 1962).

However, if such mechanisms are to be able to work regionally, meticulous care should be paid to the muscular attachments to the bone and to the periosteal envelope when performing an osteotomy, as the pathways for revascularization may otherwise be jeopardized. If this is neglected, another effect of hypoxia could be favoured: production of fibroblasts at the expense of bone cells (Bassett & Hermann 1961, Vaes & Nichols 1962, Taylor et al. 1974, Balin et al. 1984), and thereby constitute the basis for fibrous pseudarthrosis or at least delayed healing.

Acknowledgements

The study was supported by the Velux Foundation.

References

Arnoldi, C. C., Lemperg, R. K. & Linderholm, H. (1971) Immediate effect of osteotomy on the intramedullary pressure of the femoral head and neck in patients with degenerative osteoarthritis. *Acta Orthop. Scand.* **42**, 357–365.

Balin, A. K., Fisher, A. J. & Carter, D. M. (1984) Oxygen modulates growth of human cells at physiologic partial pressures. *J. Exp. Med.* **160**, 152–166.

Basset, C. A. L. & Herrmann, I. (1961) Influence of oxygen centration and mechanical factors on differentiation of connective tissues *in vitro*. *Nature* **190**, 460–461.

Brighton, C. T. & Krebs, A. G. (1972) Oxygen tension of healing fractures in the rabbit. *J. Bone Joint Surg.* **54**-A, 323–332.

Brookes, M., Elkin, A. C., Harrison, R. G. & Heald, C. B. (1961) A new concept of capillary circulation in bone cortex. *Lancet* **i**, 1078–1081.

Brookes, M. (1964) The blood supply of bone. In: *Modern trends in orthopaedics*, 4th edn. *Science of fractures* (Ed. Clark, M. P.) pp. 91–125. Butterworth, London.

Danckwardt-Lilliestrom, G., Lorenzi, G. L. & Olerud, S. (1970) Intramedullary nailing after reaming. *Acta Orthop. Scand.* Suppl. 134.

Grønlund, J., Kofoed, H. & Svalastoga, E. (1984) Effect of increased knee joint pressure on oxygen tension and blood flow in subchondral bone. *Acta Physiol. Scand.* **121**, 127–131.

Guyton, A. C., Ross, J. M., Carrier, O. & Walker, W. S. (1964) Evidence for tissue oxygen demand as the major factor causing autoregulation. *Circ. Res.* Suppl. 1, **14–15**, 60–69.

Heppenstall, R. B., Goodwin, C. W. & Brighton, C. T. (1976) Fracture healing in the presence of chronic hypoxia. *J. Bone Joint Surg.* **58**-A, 1153–1156.

Keck, W. W. & Kelly, P. J. (1965) The effect of venous stasis on intraosseous pressure and longitudinal bone growth in the dog. *J. Bone Joint Surg.* **47**-A, 539–544.

Kelly, P. J. (1968) Anatomy, physiology and pathology of the blood supply of the bones. *J. Bone Joint Surg.* **50**-A, 766–783.

Kivisaari, J. & Niinikoski, J. (1975) Tissue oxygen and carbon dioxide tensions in healing rabbit tibias. *Acta Orthop. Scand.* **46**, 269–279.

Knighton, D. R., Hunt, T. K., Schuenstuhl, H., Halliday, B. J., Werb, Z. & Banda, M. J. (1983) Oxygen tension regulates the expression of angiogenesis factor by macrophages. Science **221**, 1283–1285.

Kofoed, H., Svalastoga, E., Grønlund, J., Jensen, B., Kofod, J. & Svendsen, P. (1983) Continuous measurement of subchondral pO_2 and pCO_2 by mass spectrometry. *IRCS Med. Sci.* **11**, 583–584.

Kruse, R. L. & Kelly, P. J. (1974) Acceleration of fracture healing distal to a venous tourniquet. *J. Bone Joint Surg.* **56**-A, 730–739.

Lundsgaard, J. S., Jensen, B. & Grønlund, J. (1980) Fast responding flow-independent blood gas catheters for oxygen measurement. *J. Appl. Physiol.* **48**, 376–381.

Rhinelander, F. W. (1968) The normal microcirculation of diaphyseal cortex and its response to fracture. *J. Bone Joint Surg.* **50**-A, 784–800.

Ross, J. M., Fairchild, H. M., Weldy, J. & Guyton, A. C. (1962) Autoregulation of blood flow by oxygen lack. *Am. J. Physiol.* **202**, 21–24.

Taylor, W. G., Richter, A., Evans, V. J. & Sanford, K. (1974) Influence of oxygen and pH on plating efficiency and colony development of WI-38 and vero cells. *Exp. Cell Res.* **86**, 152–156.

Vaes, G. M. & Nichols, G. (1962) Oxygen tension and the control of bone cell metabolism. *Nature* **193**, 379–380.