Improved tissue perfusion during isolated regional perfusion
Fontijne, Willem Peter Johan
SUMMARY

This thesis describes a research project which is focused on the improvement of the isolated regional perfusion technique, in which chemotherapeutic drug(s) are used.

Chapter I is a short introduction, in which the connection between the different chapters is described. Furthermore, the use of polarographic oxygen electrodes for evaluation of microcirculation is described during normal and during extra-corporeal circulation of an extremity. Insight into microcirculatory changes during isolated regional perfusions is a prerequisite to achieve an optimal circulation.

In chapter II the effect of acute hypovolemia on the microcirculatory changes in tissue oxygen tension \( (p_O_2) \) of the skeletal muscle in the hindlimb of dogs is described. Dogs were bled until mean arterial pressures of 25 and 50 mm Hg below the initial value were reached. A multiwire polarographic \( p_O_2 \) electrode, placed on the sartorius muscle, permitted quantitative evaluation of microcirculation by means of \( p_O_2 \) histograms (104 \( p_O_2 \) values measured on the muscle surface). By means of this technique we demonstrated that the oxygen supply to the skeletal muscle was severely impaired after a relatively small drop in systemic mean arterial pressure \( ((2 \times \text{diastolic pressure} + \text{systolic pressure}) :3) \) of 25 mm Hg. The surface oxygen tension measurements and histogram constructions enabled a rapid and reliable determination of microcirculatory changes.

Chapter III describes the study in which the circulation in the hindlimb of dogs was taken over by means of an extracorporeal circuit after isolation of the hindlimb from the systemic circulation. The purpose of this study was to evaluate the effect of various perfusion pressures during isolated hindlimb perfusions in dogs on the oxygen supply to the skeletal muscle by means of the multiwire polarographic \( p_O_2 \) electrode. The conclusion of this study was that tissue perfusion was adequately maintained, when the perfusion pressure was not more than 15 mm Hg below the systemic mean arterial pressure. To maintain this perfusion pressure a perfusion flow was needed which was about 5 times higher than the control flow. It was also concluded that, when the perfusion flow was approximately equal to the control flow, the hindlimb pressure was 50 mm Hg below the systemic mean arterial pressure and that tissue perfusion was severely impaired.

Chapter IV describes the study in which an isolated hindlimb of dogs was perfused for sixty minutes, according to the standard clinical technique, in which...
hyperthermia (40-41°C) and a chemotherapeutic drug Melphalan® are used. The dogs were divided into three groups. In group I and II the perfusions were performed at a perfusion pressure of respectively 15 and 50 mm Hg below the systemic mean arterial pressure. In group III the perfusion pressure was also 15 mm Hg below the systemic mean arterial pressure, but in this group the chemotherapeutic drug Melphalan® was added, to determine whether this toxic drug would affect tissue perfusion. Besides measurement of tissue oxygenation by means of polarographic pO₂ electrodes, any leakage of blood from the hindlimb to the systemic circulation was measured by means of radio-isotopes. In group I and III tissue pO₂ values were equal to control values, indicating adequate tissue perfusion. In group II however, tissue perfusion was severely impaired. In all groups the leakage of blood to the systemic circulation was less than 10%, which indicates that a high perfusion pressure in the hindlimb does not always lead to an increase in leakage to the systemic circulation.

In the study described in chapter V we evaluated the results of isolated hindlimb perfusions in dogs during clinical perfusions. Iliacal perfusions, performed on patients in the Department of Surgical Oncology of the University Hospital Groningen, were divided into three groups. In group I and II the flow of the extracorporeal circuit was thus regulated, that the mean arterial pressure in the leg was respectively 15 and 50 mm Hg below the systemic mean arterial pressure of the patient. In group III the perfusions were regulated at a fixed flow of about 300 ml/min, a technique which was commonly used during clinical perfusions. During the perfusions tissue oxygenation was determined by means of a transcutaneous pO₂ electrode, placed on the skin of the lower leg. In group I the perfusion technique resulted in an adequate tissue perfusion. In group II and III tissue perfusion was severely impaired. Despite the higher perfusion flows in group I, the leakage in this group was less than 10% and even lower than in the other two groups. These clinical results led to the conclusion that during isolated regional perfusions, regulation of the extracorporeal circuit at a mean arterial pressure in the leg of not more than 15 mm Hg below the systemic mean arterial pressure will accomplish an optimal perfusion of the skin and probably also of the tumor. By means of this perfusion technique a better distribution of the chemotherapeutic drug will be obtained and therefore it will probably be necessary to change the dose of the chemotherapeutic drug. It could also be possible that this perfusion technique obviates complications due to tissue hypoxia or anoxia during perfusion. Moreover, inadequate distribution of the chemotherapeutic drug in the perfused extremity, which may lead to severe edema and associated muscular and/or neural lesions, could be prevented. Therefore the routine fasciotomy, introduced to prevent these complications, might be redundant.

In the epilogue, chapter VI, the conclusions of chapter II, III, IV and V are summarized and some speculations for further investigations are made.