34 patients was a second operation necessary and 26 patients underwent three or more operations. Most of these operations were performed in connection with infections (44%) or bleeding (27%) in the abdomen. In addition, operations were performed because

Chapter 8

Conclusions and recommendations
34 patiënten was een tweede heroperatie noodzakelijk en 26 patiënten ondergingen drie of meer heroperaties. Meestal werden deze operaties uitgevoerd in verband met infecties (44%) of bloedingen (27%) in de buik. Darnaast werden heroperaties verricht omdat er

**Intraoperative RBC transfusion requirement during liver transplantation is the main determinant of postoperative surgical reinterventions.**

Surgical reinterventions are a reflection of post transplant morbidity. The mortality in the reintervention group was significantly higher compared to the non-reintervention group. This finding underscores the importance of reducing intraoperative blood loss. Every measure to reduce blood loss i.e. RBC transfusion requirements in liver transplantation is an important objective to improve morbidity and mortality after liver transplantation. This notion should specifically be incorporated in the training programs of anesthetists and surgeons seeking a career in this field.

**Independent predictors for RBC transfusion requirements are the Child-Pugh classification of the recipient, length of cold ischemia, plasma urea level, year of transplantation, and the use of autologous (cell saver) blood.**

The Child-Pugh classification is a measure of the severity of liver disease. Its impact on transfusion requirements can be translated directly to the timing of the transplantation. With longer waiting times the liver disease progresses, as reflected in a higher Child-Pugh score. Timely referral of patients for evaluation, placement on the waiting list and transplantation is of paramount importance. Long waiting times for transplantation are predominantly caused by a shortage of liver donors. Hence, every measure should be taken to increase the number of available grafts. Split liver procedures, living-related liver transplantation, domino liver transplantation and non-heart beating donors to shorten the waiting time should be an integrated part of the activities of each liver transplant program. The influence of the year of transplantation on peroperative transfusion requirements reflects the experience of the transplant team. This learning effect should be incorporated in training programs for new anesthetists and surgeons wanting a career in liver transplantation. The length of the cold ischemia time was directly negative related to the peroperative RBC transfusion requirements. This implicates that cold ischemia times should be kept as short as possible to reduce the intraoperative RBC transfusion requirements. Liver transplantation therefore is not an elective procedure, with consequences for hospital logistics. Autologous blood transfusion by a cell saver increases transfusion requirements. This unexpected finding emphasises a reappraisal of the cell saver in a properly designed prospective and randomized study. Until then autologous
34 patiënten was een tweede operatie noodzakelijk en 26 patiënten ondergingen drie of meer operaties. Meestal werden deze operaties uitgevoerd in verband met infecties (44%) of bloedingen (27%) in de buik. Darnaast werden operaties verricht omdat er blood by a cell saver in liver transplantation should only be used as an emergency in selected cases.

**Recombinant factor VIIa appeared to be an effective drug to reduce transfusion requirements in liver transplantation. It enhances thrombin generation in a localised and time limited manner without causing systemic coagulation.**

Our experience with rFVIIa, although limited, suggests that it can be used to minimise blood loss, despite the complexity of hemostatic abnormalities in liver transplant patients. However, the administration of rFVIIa potentially increases the risk of thrombosis. Particularly thrombosis of the liver graft vessels is unacceptable, considering its consequence as the need for retransplantation. Further studies are warranted to establish the suggested efficacy of rFVIIa, to assess the optimal dose regimen, and to define criteria for the selection of patients, in whom rFVIIa may be beneficial. Whether rFVIIa should be administered alone, together with plasma or other hemostatic drugs like aprotinin, are questions that need to be answered.

**The peroperative thromboelastography showed that recombinant factor VIIa influences not only the speed of clot formation, but also the physical properties of the clot.**

Thromboelastography appeared to provide the most direct and adequate information during the operation to assess hemostasis. It would be very helpful if a simple and rapid laboratory test becomes available to assess hemostasis and the effects of correcting measures more appropriately then the current available “classical” screening tests. Thromboelastography is a candidate technique, which provides overall information about clot formation, as well as additional information regarding the physical properties of clot formation. Although thromboelastography has potential benefits, as compared with the classical tests, its application in clinical practice needs to be validated in properly designed controlled clinical trials, including the specific setting of liver transplantation.

All together, transfusion requirements during liver transplantation have decreased considerably in our program. The proportion of primary liver transplant patients without transfusion of units RBC’s gradually increased in the past years from 4% to 30%. However, due to its still present negative influence on outcome, it merits ongoing attention of all specialists involved in this procedure.
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**Nederlandse Samenvatting**