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Risk factors and outcome in clinical pancreas transplantation

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Summary of chapters

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SUMMARY OF CHAPTERS

The aim of this thesis was to evaluate and investigate factors that are associated with the outcome following clinical pancreas transplantation. Although still considered an experimental procedure by some, over the past 50 years pancreas transplantation has proven to be a lifesaving treatment for patients with diabetes mellitus and in fact the only curative option. The procedure itself comes at certain risks, which as this thesis argues, may lead to loss of a valuable graft and, even more dramatically, loss of life. Therefore donor, recipient and treatment selections are to be optimized. This thesis answers questions and addresses problems and challenges associated with pancreas transplantation. It is a product of the close collaboration of the transplantation division of the Leiden University Medical Center and the Eurotransplant International Foundation.

Chapter 2 provides an overview of the first 30 years of pancreas transplantation at Leiden University Medical Center. In those 30 years and through the effort of dedicated professionals, LUMC has become one of the largest pancreas transplant centers in Europe. The chapter describes a single-center study and is one of the few studies to evaluate long-term outcome following pancreas transplantation in the era of modern induction therapies.

Comparing the results from chapter 2 to results published in literature, it became clear that outcome, amongst other factors, largely depends on donor related risk factors and that adequate prediction models would be needed to compare outcome data. Those prediction models are frequently used in organ transplantation.¹⁻⁷ In pancreas transplantation specifically, two prediction models exist: Preprocurement Pancreas Allocation Suitability Score (P-PASS)⁵ and Pancreas Donor Risk Index (PDRI).⁴ In chapter 3, outcome data from LUMC were analyzed to validate both models in a single center. It showed that P-PASS was inferior to PDRI and the recommendation was that P-PASS should not be used in clinical decision making.

Chapter 4 evaluates the predictive capacity of both models in the Eurotransplant database. Similar to the original P-PASS article, allocation outcome was used as primary endpoint instead of transplantation outcome as used in the original PDRI article. Interestingly, even in this study, PDRI outperformed P-PASS. Another interesting finding was that large differences in donor quality and donor acceptance policies exist, even within the Eurotransplant region.

Chapter 5 describes outcome data of almost 1300 pancreas transplantations within the Eurotransplant region. This study was the first to show that pancreas transplantation outcome is associated with center volume. Even though the higher volume centers accepted higher risk donor graft, outcome in terms of graft and patient survival were superior compared to low volume centers. This study advocates centralization of this highly complex procedure.

In chapter 6, pancreas graft thrombosis was studied. This feared complication and leading cause of graft failure is still a very challenging problem. Many strategies have been under-

taken to detect and prevent thrombosis.⁸⁻¹⁴ In this chapter, in particular, detection using CT imaging and treatment of (usually subclinical) partial graft thrombosis was analyzed. Using the current protocol, with heparin and vitamin K antagonists, partial graft thrombosis rarely progressed to full, occlusive thrombosis and graft function was preserved. However, it remains unclear whether such anticoagulation therapy is warranted for all kinds of partial thrombosis.

Chapter 7, describes another risk factor related to the pancreas donor. Donation after determination of circulatory death (DCD) remains a controversial topic in pancreas transplantation. This study showed that, with strict donor selection, excellent results can be achieved with DCD pancreas donors and that these results are similar to those of donation after determination of brain death (DBD) pancreas donors.

