Living Related Donor Liver Transplantation

Kazue Ozawa

Living Related Donor
Liver Transplantation

Assessment of Graft Viability
Based on the Redox Theory

109 figures, 3 color plates and 26 tables, 1994

Basel • Freiburg • Paris • London • New York •
New Delhi • Bangkok • Singapore • Tokyo • Sydney

Kazue Ozawa

MD, President of Hospital, Shiga University of Medical Science,
Seta Tsukinowa-cho, Ohtsu City, Shiga-ken 520-21, Japan

with the collaboration of the following members of Kyoto University Medical School,
Kyoto, Japan:

Yoshio Yamaoka (Department of Surgery), Kohichi Tanaka, Takashi Inamoti,
Keiichiro Mori, Yasuyuki Shimahara, Taisuke Morimoto, Kazuo Honda,
Akira Tanaka, Shinji Uemoto, Eishi Yamamoto, Kaoru Sano, Shim Fujita,
Hisashi Sawada, Huminori Katoh, Yukihiro Tokunaga, Fumio Nishizawa,
Hiroyoshi Higashiya, Dai Manaka, Yasutsugu Takada, Toshoyuki Kitai,
Atsuo Tokuka, Motoki Sugano, Masaaki Awane, Masahiro Murakawa
(Department of Anesthesiology), Fuminori Moriyasu (Department of
Internal Medicine), Hitoshi Someda, Kyo Itoh (Department of Radiology and
Nuclear Medicine), and Hirohiko Yamabe (Department of Pathology)

Library of Congress Cataloging-in-Publication Data
Ozawa, Kazue, 1929- . Living related donor liver transplantation: assessment of graft viability
based on the redox theory / Kazue Ozawa [with the collaboration of Yoshio Yamaoka ... et al.].
Includes bibliographical references and index.
1. Liver - Transplantation. 2. Living related donor transplantation. 3. Transplantation of
organs, tissues, etc. in children. 4. Mitochondrial pathology - Prevention. 5. Oxidationreduction
reaction. I. Yamaoka, Yoshio. II. Title.
WI 700 099L 1994]
Drug Dosage. The author and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

All rights reserved. No part of this publication may be translated into other languages, reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, recording, microcopying, or by any information storage and retrieval system, without permission in writing from the publisher.

© Copyright 1994 by S. Karger AG, P.O. Box, CH-4009 Basel (Switzerland)
Printed on acid-free paper.
ISBN 3-8055-5800-7

In memory of the late

Dr. Yorinori Hikasa
Professor emeritus
Kyoto University

Contents

Acknowledgments X
Preface XI

1 Historical Background 1

LRLT as a Scientific Basis for Investigating Liver Transplantation 5
The Significance of the Immunological Aspect of LRLT 6
Establishing Graft Liver Function in LRLT 7
The Prospect for the Modality 9
References 10

2 Application of the Redox Theory in Liver Transplantation 12
Evaluation of the Graft Liver by AKBR in the Peritransplant Period 17
Evaluation of Graft Liver Viability before Procurement 18
Selection of the Liver Donor by Means of AKBR 19
Evaluation of Graft Liver Viability during Preservation 21
Evaluation of Early Graft Liver Viability after Liver Transplantation 24
References 27

3 Ethical Considerations 30

The Risks and the Benefits of LRLT — A Clinical-Therapeutic Method 30
The LRLT Donor Selection Procedure 32
Indications 33
The Informed Consent Procedure 33
Documents 36

4 Preoperative Evaluation 46

Diseases Indicated for LRLT 46
Biliary Atresia 46
Budd-Chian Syndrome 48
Liver Cirrhosis 51
Intrahepatic Cholestasis 53
Fulminant Hepatitis 53
Protoporphyria 53
Tyrosinemia I 54

VII

Evaluation of Donors 54
CT Volumetry for Size Matching 54
Evaluation of Histocompatibility 61
Preoperative Evaluation of Hepatic Vascular Anatomy of Donor 65
Preoperative Care of Recipients 76
Nutritional Management 76
Preoperative Management of Infection 77
Preoperative Management of Emergency Cases 78
Preoperative Immunosuppressive Treatment for ABO-Incompatible Cases 79
References 82

5 The Operative Process 85

Anesthesia 85
I wish to acknowledge my immense debt to the many fellow scientists, colleagues and friends with whom I have had the honor of working with over
the years. When I first began this program, living related liver transplantation was a new modality, with few reported experiences. Sharing with me their scientific, medical, ethical, surgical and other fields of expertise and giving me their understanding and support, they have each in their own way contributed greatly to the evolution of the living related liver transplantation program as a whole. Among these individuals, indeed too many to mention, I wish to give special recognition to the following doctors and groups at the Faculty of Medicine, Kyoto University:


Departments of Anesthesiology, Internal Medicine, Radiology and Nuclear Medicine, Pathology, Neurosurgery, Pediatrics, Clinical Laboratory, Cardiovascular Surgery, and Divisions of Intensive Care Unit, Artificial Kidney, and Blood Service

X

Preface

Since transplantation surgeons must be thoroughly familiar with every facet of an operative technique, it is imperative that they refer back to the landmark developments made by our forbears in that sphere. On the other hand, no matter how often they perform retrospective analyses of past data, they will never succeed in developing safer and surer transplantation surgery by that means. At our institute, where we have striven constantly to introduce scientific thinking into the surgical field, I believe it is our duty as surgeons to seek to perform operations on a scientific basis so as to achieve the utmost safety, however long it may take. During the past 30 years, along with my duties as a practicing surgeon, I have been engaged in mitochondria research, in which pursuit I have been fortunate to be blessed with so many excellent coworkers.
The research we did enabled me to establish what I would call the Redox theory. Applying this theory in a program of aggressive surgery for liver cancer accompanied by cirrhosis, we were able to raise both the curability and the resectability for these cases. The introduction of liver transplantation techniques, especially for the aggressive treatment of advanced liver cancer cases, 31 of which were successful, subsequently set the stage for the liver transplantation series performed at our institute.

Also, with regard to the Redox theory, through international joint research conducted with the Hannover Medical School, the University of Pittsburgh, and the University of California at Los Angeles, it has been demonstrated that the theory has utility in evaluating the viability of the graft liver throughout the entire process of cadaveric liver transplantation. These studies suggested that if the graft viability is of a high value, there is good reason to expect a successful outcome. This was the breakthrough we needed for our liver transplantation series. In other words, I was convinced that mitochondria research was the key direction in which all related research should proceed.

In living related donor liver transplantation, first and foremost is the parents' love for the child, which is so strong that they are willing to expose themselves to the dangers of a surgical operation. Our job, then, is to verify whether they are clearly aware of the risks involved, before any operation is done. Since living related donor liver transplantation involves one of two healthy parents as the donor, no guarantees can be made as to the absolute safety of the operation, or the possibility of postoperative complications. Looking back, I remember that no matter how confident I was as to our ability to perform the donor operation, my greatest fears revolved around the vascular angiography which the donor had to undergo preoperatively to determine whether there were any abnormalities in the running direction of the arteries. What I was concerned about was that some totally unforeseen and untreatable complication would arise suddenly as a result of the angiography, which is known to have its risks. For that reason, we introduced microsurgery to perform the hepatic arterial anastomoses, which allowed us to freely anastomose whatever kind of vascular pattern we might encounter. As a result, from case 13 on, we no longer performed the vascular angiography in either the donor or the recipient. We have just completed case 53, and have not once encountered any complications in the cases up to now. As always, we continue our efforts to establish an even safer donor operation.

In other countries orthotopic liver transplantation using living donors has...
been introduced as one solution to the acute shortage of cadaveric donor livers. In performing our living related donor liver transplantation series we have instead placed emphasis on the advantage of genetic matching which would exist between parent and child.

In either case, living related donor liver transplantation has come to be established as a therapeutic modality for treating pediatric cases stricken with end-stage liver disease. When it comes to selecting between cadaveric liver transplantation or living related donor liver transplantation, that decision is, of course, one which must be left to the patients and their parents.

My hope is that the present work relating the characteristics of liver transplantation will be taken up by transplant surgeons seeking a guidebook for performing living related donor liver transplantation.

Preface XII