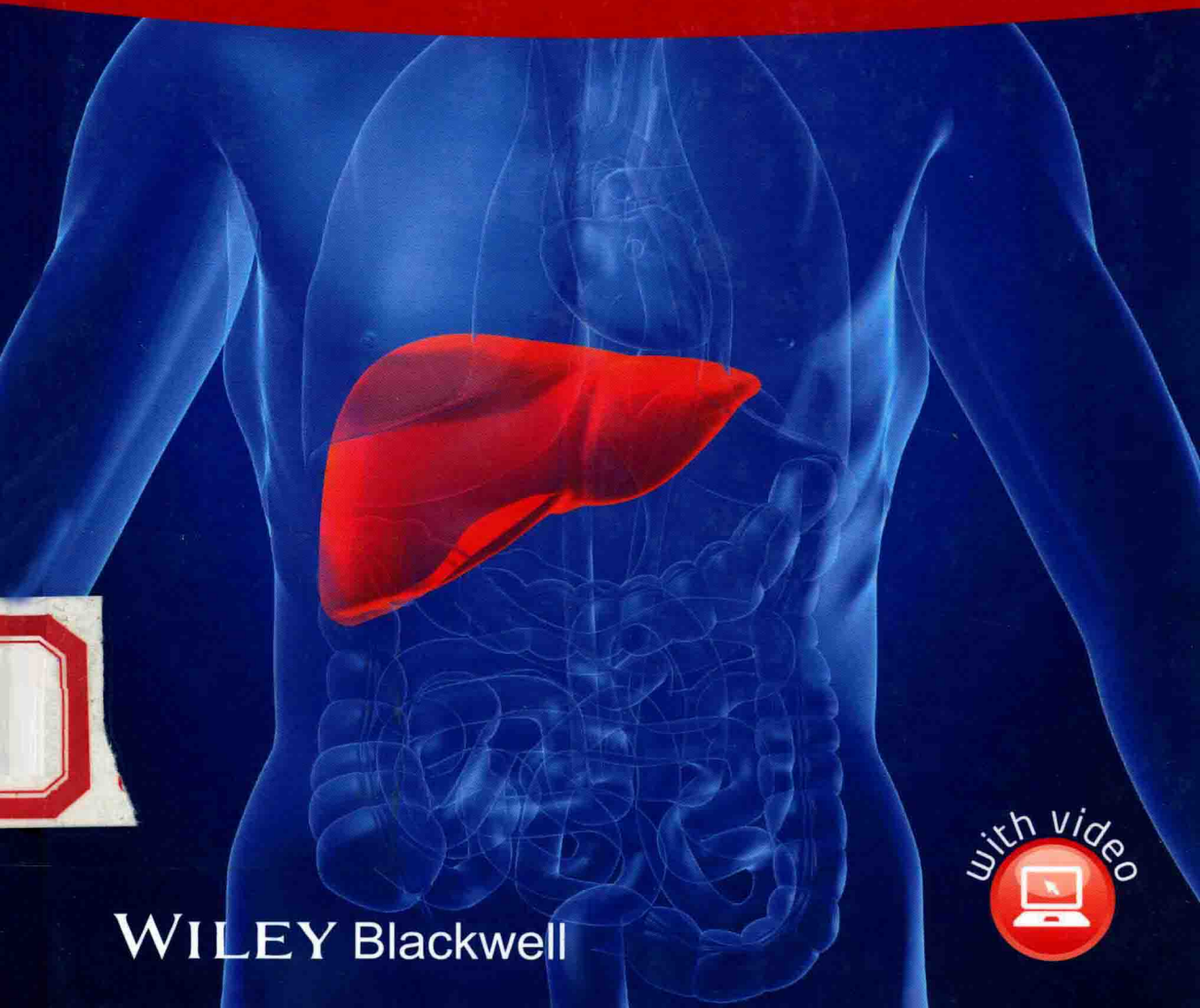
LIVER TRANSPLANTATION

CLINICAL ASSESSMENT AND MANAGEMENT

Edited by
James Neuberger | James Ferguson | Philip N. Newsome



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This edition first published 2014 © 2014 by John Wiley & Sons, Ltd.

Registered office: John Wiley & Sons, Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial offices: 9600 Garsington Road, Oxford, OX4 2DQ, UK
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
111 River Street, Hoboken, NJ 07030-5774, USA

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Library of Congress Cataloging-in-Publication Data

Liver transplantation (2014)
Liver transplantation : clinical assessment and management / edited by James Neuberger, James Ferguson, Philip N. Newsome.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-118-27738-6 (hardback : alk. paper) – ISBN 978-1-118-67591-5 – ISBN 978-1-118-67592-2 (mobi) – ISBN 978-1-118-67601-1 (pub) – ISBN 978-1-118-67605-9 (pdf)
I. Neuberger, James, editor of compilation. II. Ferguson, James, 1975– editor of compilation. III. Newsome, Philip N., editor of compilation IV. Title.
[DNLM: 1. Liver Transplantation. 2. Liver–surgery. 3. Liver Diseases–surgery. WI 770]
RD546
617.5'562–dc23

2013007102

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Cover image: © Sebastian Kaulitzki iStockphoto.com #4303856
Cover design by Meaden Creative

Set in 9.5 on 13 pt Meridien by Toppan Best-set Premedia Limited
Printed and bound in Singapore by Markono Print Media Pte Ltd

1 2014

Liver Transplantation

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Foreword

Liver transplantation in humans has come a very long way in a short period of time. My first studies of liver transplantation in animals began in 1958 when I showed that such a procedure was technically possible. I identified three key challenges: the need to preserve the liver between retrieval and implantation, the need to preserve the recipient in haemodynamic stability and the need to prevent rejection.

The first human liver transplant was performed in 1963 and identified a number of issues that needed resolution, so the programme was put on hold but restarted with the first successful transplant in 1967. The programme, initially in Denver and subsequently in Pittsburgh, grew rapidly and was followed by the successful programme in Cambridge, UK, in 1968, led by Sir Roy Calne and Roger Williams. Those early pioneering days were exciting but stressful, physically and emotionally. Outcomes improved slowly but surely. In 1983, the procedure came of age when liver transplantation was recognised by the NIH as an effective treatment. Other programmes developed around the world and liver transplantation is now routine, with many recipients surviving 20 and more years with an excellent quality of life.

The progression from a high-risk and resource-intensive procedure, where blood use of less than 100 units was considered a success and outcomes were measured in 1-year survival, to a low-risk, routine and usually blood-free procedure has been achieved as a result of the dedication, hard work, enthusiasm, imagination and sheer persistence of a large number of people: surgeons, physicians, scientists, intensivists, microbiologists and many others have all made huge contributions to the success of the procedure. The contribution of both donors and recipients must also be acknowledged for, without their support, these advances could never have occurred.

Yet many challenges remain. Despite advances in medical care, the need for liver transplantation is increasing and the availability of donor livers inadequate. Liver preservation is still a concern: new perfusion fluids and machine perfusion may mitigate some of the problems. While immunosuppression has improved enormously, with the introduction initially of ciclosporin and tacrolimus and, more recently, mycophenolate, sirolimus

and biological agents, most recipients require long-term treatment, with its associated side effects; tolerance remains an elusive goal. Selection and allocation policies are attracting, quite appropriately, public scrutiny. Regulation is increasing: indeed, it is doubtful whether liver transplantation could have developed as quickly as it did under the current risk-averse climate.

Liver transplantation is expanding and outcomes are better than ever, so more clinicians will be touched by the procedure, whether for referral or for follow-up. It is hoped that this volume will provide a useful and practical guide to the successful management of these patients.

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Preface

The field of liver transplantation continues to evolve and is a highly effective therapy for many patients with acute and chronic liver disease. The numbers undergoing transplantation are increasing, the indications have widened and the list of contraindications has become shorter. Successful management of patients and the appropriate use of scarce organs require close and effective collaboration between the multi-professional teams looking after patients.

This book is intended to be a practical guide for those involved in the care of adult patients who are either potential transplant candidates or who have undergone transplantation. We are grateful to those authors who have contributed, all of whom have considerable practical experience in the management of patients before and after transplantation. We have asked authors to be didactic and clear both in outlining the issues and recommending management. We intended this volume to complement the larger, comprehensive textbooks and the in-depth reviews published in journals.

We hope you find this volume useful and practical.

James Neuberger
James Ferguson
Philip N. Newsome

Acknowledgements

We have enjoyed editing this book and would like to thank all the contributors for their input. This volume would not have happened without the close support and advice from Oliver Walter and Jennifer Seward at Wiley Blackwell.

About the Companion Website

This book is accompanied by a companion website:

http://www.wiley.com/go/neuberger/livertransplantation

The website includes:

- 80 surgical video clips
- An extended version of Chapter 13 – Surgical Aspects of Liver Transplantation

Abbreviations

AAT	alpha-1-antitrypsin deficiency
ACE	angiotensin converting enzyme
ACEi	ACE inhibitors
ACR	acute cellular rejection; albumin:creatinine ratio
AFP	alpha-fetoprotein
AGT	alanine:glyoxylate aminotransferase
AICD	activation induced cell death
AIH	autoimmune hepatitis
AIP	acute intermittent porphyria
ALD	alcoholic liver disease
ALF	acute liver failure
ALHA	accessory left hepatic artery
ALP	alkaline phosphatase
ALT	alanine aminotransferase; auxiliary liver transplant
AMR	antibody-mediated rejection
APC	antigen presenting cell
APOLT	auxiliary partial orthotopic liver transplantation
ARHA	accessory right hepatic artery
ATG	anti-thymocyte globulin
BCC	basal cell carcinoma
BCG	Bacille Calmette-Guerin
BCLC	Barcelona Clinic Liver Cancer (staging system)
BEC	biliary epithelial cell
BMD	bone mineral density
BMI	body mass index
CCB	calcium channel blocker
CF	cystic fibrosis
CHOP	cyclophosphamide, hydroxydaunorubicin, Oncovin and prednisone
CI	confidence interval
CIA	common iliac artery
CIT	cold ischaemic time
CIV	common iliac vein

CLEVER common lymphatic endothelial and vascular endothelial receptor
CMV cytomegalovirus
CNI calcineurin inhibitor
COC combined oral contraceptives
CPP cerebral perfusion pressure
CR chronic rejection
CSF cerebrospinal fluid
CT computed tomography
CTP Child-Turcotte-Pugh
CUC chronic ulcerative colitis
CYP3A4 cytochrome P450 3A4
DAA directly acting antiviral (therapy)
DAMP danger-associated molecular patterns
DAT donor advocate team
DBD donor after brain death; deceased heart-beating donor
DC dendritic cell
DCD donor after circulatory death; donor after cardiac death
DPT diphtheria, pertussis and tetanus
DRA therapeutic paracentesis CHECK
DRI donor risk index
dWIT donor warm ischaemic time
DXA dual energy X-ray absorptiometry
EBV Epstein-Barr virus
ECMO extracorporeal membrane oxygenation
EGD esophagogastroduodenoscopy
Egr early growth response protein
EPP erythropoietic protoporphyria
ERCP endoscopic retrograde cholangiopancreatography
ESLD end-stage liver disease
EVL endoscopic variceal ligation
FAP familial amyloid polyneuropathy
FCH fibrosing cholestatic hepatitis
FHF fulminant hepatic failure
GDA gastroduodenal artery
GFR glomerular filtration rate
GGT gamma-glutaryl transferase
GLP glucagon-like peptide
GCS Glasgow Coma Score
GVHD graft versus host disease
HAART highly active antiretroviral therapy
HAT hepatic artery thrombosis
HAV hepatitis A virus

HBIG hepatitis B immunoglobulin
HBV hepatitis B virus
HCC hepatocellular carcinoma
HDL high-density lipoprotein
HE hepatic encephalopathy
HiB *Haemophilus influenzae* type B
HLA human leucocyte antigen
HMGB high mobility group box
HPS hepato-pulmonary syndrome
HPV human papillomavirus
HR hazard ratio
HRS hepatorenal syndrome
HSEC hepatic sinusoidal endothelial cells
HVPG hepatic venous pressure gradient
ICAM intercellular adhesion molecule
ICP intracranial pressure
IDO indoleamine 2,3-dioxygenase
IFG impaired fasting glucose
IGF insulin-like growth factor
IgSf immunoglobulin superfamily
IGT impaired glucose tolerance
IMV inferior mesenteric vein
INR international normalised ratio
IPTH idiopathic post-transplant hepatitis
IRI ischaemia reperfusion injury
IUD intrauterine device
IVC inferior vena cava
JVB jugular venous bulb
LDL low-density lipoprotein
LHV left hepatic vein
LLS left lateral segment
LNG levonorgestrel
LPS lipopolysaccharide
LPV left portal vein
LRV left renal vein
LT liver transplantation
LVP large-volume paracentesis
MARS molecular adsorption recirculation system
MDRD modification of diet in renal disease
MELD model for end-stage liver disease
MET metabolic equivalent
MHC major histocompatibility complex
MHE minimal hepatic encephalopathy

MHV middle hepatic vein
MMF mycophenolate mofetil
MMR measles, mumps and rubella
MOPP mechlorethamine, Oncovin, procarbazine and prednisone
MPA mycophenolic acid
mPAP mean pulmonary artery pressure
MPTP mitochondrial permeability transition pore
MRA magnetic resonance angiography
MRCP magnetic resonance cholangiopancreatography
MRI magnetic resonance imaging
MS metabolic syndrome
mTOR mammalian target of rapamycin
NAFLD non-alcoholic fatty liver disease
NASH non-alcoholic steatohepatitis
NFAT nuclear transcription factor of activated T-cells
NKT natural killer T-cells
NLR NOD-like receptor
NOD new-onset diabetes
NSAID non-steroidal anti-inflammatory drug
NSBB non-selective beta-blocker
OGGT oral glucose tolerance test
OLT orthotopic liver transplantation
OTC over-the-counter
PASP pulmonary arterial systolic pressure
PBC primary biliary cirrhosis
PBG porphobilinogen
PCR polymerase chain reaction
PD programmed cell death protein
PEL primary effusion lymphoma
PELD paediatric model for end-stage liver disease
PERV porcine endogenous retrovirus
PNF primary non function
PoPH porto-pulmonary hypertension
PPI proton pump inhibitors
PSA prostate-specific antigen
PSC primary sclerosing cholangitis
PT prothrombin time
PTC percutaneous transhepatic cholangiography
PTH parathyroid hormone
PTLD post-transplant lymphoproliferative disease
RA refractory ascites
RAGE receptor for advanced glycation end products
RANKL receptor activator of nuclear factor-κB ligand

RANTES regulated on activation, normal T-cells expressed and secreted
RFA radiofrequency ablation
RHA right hepatic artery
RHV right hepatic vein
RLR RIG-I-like receptor
ROS reactive oxygen species
RR relative risk
RRHA replaced right hepatic artery
SAAG serum ascites albumin gradient
SAAH severe acute alcoholic hepatitis
SBP spontaneous bacterial peritonitis
SCC squamous cell carcinoma
SGA subjective global assessment
SIR standardised incidence ratio
SLK simultaneous liver and kidney (transplantation)
SLV standard liver volume
SMA superior mesenteric artery
SMV superior mesenteric vein
SOT spontaneous operational tolerance
SRR steroid-resistant rejection
SSI surgical site infection
STAT signal transducer and activators of transcription
SVR sustained virological response
TACE transarterial chemoembolisation
TCI transplant to conception interval
TCR T-cell receptor
TIPS transjugular intrahepatic portosystemic shunt
TIPSS transjugular intrahepatic portosystemic stent shunt
TLR Toll-like receptors
TPN total parenteral nutrition
UDCA ursodeoxycholic acid
UKELD United Kingdom end-stage liver disease model
ULN upper limit of normal
USS ultrasound scan
VAP vascular adhesion protein
VCAM vascular cell adhesion molecule
VEC vascular endothelial cell
VEGF vascular endothelial growth factor
VLDL very-low-density lipoprotein
VZV varicella-zoster virus
WIT warm ischaemic time