

Part IV. SYLLABUS FOR TRAINING IN TRANSPLANTATION MEDICINE

Common Trunk Module

Introduction and objectives

The common trunk examines the basic principles underlying solid organ transplantation and the basic knowledge every transplant physician should have. This knowledge is general and not specific for any given organ transplanted, whereas in the organ transplant module, the requirements are more focused and in depth knowledge of organ-specific aspects are examined.

Required knowledge for the exam of the Common Trunk Module:

1. Ethical and regulatory considerations

- Informed consent for organ donation
- Opt-in and opt-out rules in deceased organ donation
- Concept of brain death and cardio-circulatory death, including pathophysiological consequences
- Organ procurement esp. in DCD situation (rapid procurement vs normothermic regional perfusion (NRP))
- Living donor issues incl. organ trafficking

2. Organization of transplant medicine

The candidate should know

- his/her country organization of deceased organ allocation, the transplantation law or rules, the transplantation services (including legal aspects) and give a critical appraisal on this subject.
- the main approaches among the transplantation organisations in Europe and in other part of the world incl. in Northern America.

3. General principles of organ preservation

- Ischemia-reperfusion injury
- Basic knowledge of organ perfusion (incl. perfusion machines) and conditioning

4. Immunology

- Innate and adaptive immune response
- Relevance of ABO blood group antigens in transplantation
- Role and nomenclature of HLA
 - Concept of sensitization
 - Role of HLA antibodies
 - Concept of cross matching
- Principles of tolerance and stem cells

5. General mechanisms of rejection

- Immune response to allograft: Mechanism of recognition, activation of immune signals, effector mechanisms, memory phase
- Inflammatory response to the allograft

6. Immunosuppression

6.1 General

- Action and pharmacology of immunosuppressants
- Concept of TDM and drug interactions
- Intrinsic effects/side-effects of commonly used immunosuppressants
- Rationale for the diverse immunosuppressive combinations

6.2 Specific

Steroids

CNIs

mTOR inhibitors

Mycophenolate

Azathioprine

ATG

IL-2 receptor blockade

Alemtuzumab

Costimulatory pathway inhibitor (belatacept)

IVIg

Anti-CD20 and anti-CD38 Ab (Rituximab, Obinutuzumab, Daratumumab, Felzartamab, etc.)

Anti-IL-6/IL-6R Ab (Tocilizumab, Clazakizumab, etc)

Complement-pathway inhibitors

Proteasome Inhibitors (Bortezomib, Carfilzomib)

Imlifidase

6.3 Side effects

- Long-term side effects of immunosuppression in general
- De novo immunosuppression-related cancers including skin cancer
- Renal function
- Cardiovascular side effects
- Diabetes
- Hematology

7. Infectious diseases

- Immune response to infections in the compromised host
- Knowledge of window of the occurrence of the diverse types of infection following transplantation
- Principles of viral, bacterial, fungal and other opportunistic infections
- Specific infections:
 - Herpes viruses, CMV, EBV
 - Hepatitis viruses: A, B, C, E
 - Poliomavirus BKV and JCV
 - HIV
 - *Pneumocystis jiroveci* pneumonia
 - Tuberculosis
 - Fungal infections
- Vaccination programs before and after transplantation (European consensus)
- Occurrence and management of diseases associated with viruses (Kaposi's sarcoma, skin cancer, cervical cancer, post-transplant lymphoproliferative disorders)

Kidney Transplantation Module

Objective:

Ability to recognise, assess and prepare patients with kidney failure for renal transplantation. Ability to manage patients' care before and after the transplant, in the immediate and long-term phase.

Required knowledge for the Kidney Transplantation Module:

1. The place of kidney transplantation in the treatment of kidney failure (according to international guidelines and considering the candidate's local practice)

- Treatment options for patients with kidney failure
- Indications and major contraindications for kidney transplantation
- Type of donor and optimal recipient outcome
- Waitlist management and kidney allocation policy issues
- Renal transplantation and health economy
- Legal and ethical issues in kidney transplantation

2. Evaluation of the recipient for kidney transplantation

- General investigations, including basic serology
- Recipient diabetes and obesity
- Complex cardiovascular evaluation

- Suitability for immunosuppressive therapy (infections, malignancies, gastrointestinal diseases, etc)
- Primary renal disease and renal transplantation – special issues and contraindications
- Psychosocial issues
- Specific aspects of ethnicity among recipients
- Assessment of frailty in elderly candidates
- Overall risk assessment and strategies to improve physical condition
- Preemptive transplantation

3. Live kidney donation

- Live kidney donor evaluation process
- General contraindications for live donation
- Justification of the medically complex living kidney donor
- Evaluation of psychosocial and ethical suitability
- Alternative living donor programs (paired exchange donation, non-directed or altruistic donation)
- Surgical process of kidney donation incl. laparoscopic and robot-assisted retrieval
- Long-term follow up of live kidney donors

4. Renal transplantation specific immunology issues

- Histocompatibility of the donor and recipient, virtual and pre-transplant cross matching technologies, DSA measurement.
- HLA mismatches, virtual-PRA or CRF (UK), highly sensitized patients. Eplet matching and eplet load.
- Immune biomarker monitoring during post-transplant care
- Principles of ABO incompatible and HLA cross match positive incompatible kidney transplantation

5. Surgical procedure of kidney transplantation

- Deceased donor kidney suitability for transplantation (incl. anatomical issues, KDPI (kidney donor profile index))
- Pre-transplant procedures, indications for native nephrectomy
- Surgery of renal transplantation and postoperative surgical management
- Early and late surgical complications

6. Pre-, peri,- and early post-operative non-surgical management of the recipient

- Specific transplant related issues in fluid balance, acid-base and metabolic management

- Delayed graft function (cold and warm ischemia time, ischemia-reperfusion injury), effect of kidney preservation technologies, hypo- and normothermic machine perfusion.
- Perioperative indications of renal replacement therapy

7. Immunosuppressive therapy of kidney transplant recipient

- Indications for induction therapy, practical management of different agents: IL2-RAb, lymphocyte-depleting agents
- Initial maintenance immunosuppressive therapy, landmark studies and special indications
- Calcineurin Inhibitors: timing of initiation, dosing, choice of compound and formulation
- Mycophenolate: timing of initiation, dosing, difference between mycophenolate mofetil and sodium.
- mTORi: timing of initiation, dosing and combination with CNIs or without CNIs
- Belatacept: timing of initiation, dosing and conversion regimen from CNI
- Long-term maintenance immunosuppressive medication:
 - CNI-based protocols
 - CNI-free protocols
 - Corticosteroid avoidance or withdrawal protocols
- Therapeutic drug monitoring (TDM)
- Measuring biological efficacy of immunosuppression, biomarkers and immune monitoring
- Immunosuppressive drug interactions and role of kidney function

8. Infections and malignancies

- Kidney transplantation specific issues of infections (urinary tract infections, management of CMV, polyoma-virus, HBV, HCV, SARS-CoV and HIV)
- Renal transplantation specific issues of malignant diseases (incl. renal carcinoma)

9. Allograft dysfunction: differential diagnosis and therapy

- Differential diagnosis of early graft dysfunction
 - Clinical signs of acute rejection:
 - Risk factors for acute rejection
 - Subclinical rejection and protocol biopsies
 - Acute cellular and acute antibody-mediated rejection
- Differential diagnosis of late graft dysfunction – chronic rejection: clinical decision algorithm
- Imaging in kidney transplantation

- Performing and interpreting the result of biopsies based on Banff classification:
 - Histopathology of T-cell and antibody mediated rejection
 - Microvascular inflammation
 - Thrombotic microangiopathy
 - BK-Virus associated Nephropathy
 - Recurrent or de novo renal diseases
 - Chronic allograft damage, interstitial fibrosis and tubular atrophy
 - CNI toxicity
- “Molecular Microscope” – MMDx and other mRNA microarray diagnostics, dd-cfDNA (donor-derived cell-free DNA)
- Treatment of acute rejection forms: acute cellular rejection and antibody-mediated rejection
- Prophylaxis and management of recurrent primary renal diseases (incl. hemolytic uremic syndrome, IgAN, FSGS, C3-Glomerulonephritis)

10. CKD management in renal transplant patient

- Kidney graft function and CKD, effect on recipient and graft survival
- Cardiovascular disease: tobacco use, hypertension, role of albuminuria
- Metabolic disorders: Diabetes mellitus and NODAT, dyslipidemia management
- Nutrition aspects of the renal transplant patient
- Anemia and post-transplant erythrocytosis
- Management of the failed kidney graft

11. Other special issues

- Depression, anxiety and other psychological and psychiatric problems
- Post-transplant pregnancy
- Issues of pediatric kidney transplantation, transition from pediatric to adult care
- Diagnosis and management of non-adherence
- Management of renal transplantation in combination with other simultaneous or consecutive organ transplantations
- Systems biology in kidney transplantation, outcome prediction models

12. Evaluation of a manuscript (optional)

Liver Transplantation Module

Objective: the candidates should have special knowledge, meaningful practical experience and clinical skills to evaluate a liver transplant candidate and to manage the patient before transplantation and in the post-transplant course, on the short and long terms.

Required knowledge for the exam:

1. Indications and contraindications to liver transplantation (according to international guidelines and considering the candidate's local practice)

- Pre-transplant management of major complications of cirrhosis
- Management of acute liver failure and of acute-on-chronic liver failure.
- Indications for liver transplantation in adults and pediatrics (according to age), general principles and specificities by indications and in special situations (HIV, re-transplantation)
- Contraindications to liver transplantation: absolute and relative
- Evaluation of the liver transplant candidate: physical, social, psychological assessments, addictive behaviors
- Assessment of frailty and sarcopenia in liver transplant candidates, evaluating the issue of frailty and sarcopenia on outcome

2. Management of the waiting list

- Management of patients with HCV and HBV, alcoholic, autoimmune related and other liver diseases on the waiting list.
- Assessment and management of the liver transplant candidate with renal dysfunction: indication to combined liver-kidney versus liver transplant alone
- Prognostic scores in chronic liver disease: Child-Pugh, MELD/reMELD-Na/MELD-Na/PELD scores; disease specific scores (PBC/PSC);
- Prognostic scores in acute liver failure and acute-on-chronic liver failure
- The issue of HCC: down-staging, priority and delisting
- Standard exceptions to MELD score (incl. variability on the standard exceptions)

3. Principles of organ donation and organ allocation

- Evaluation of the deceased and living liver donors
- Extended-criteria liver donor
- Liver transplantation using donors after cardiac death
- Matching the donor to the recipient

4. The liver transplant operation

- General principles of liver transplantation surgery
 - Whole organ transplantation technique
 - Split liver transplantation
 - Living donor liver transplantation including surgical evaluation
 - Domino transplantation

- Auxiliary transplantation
- Coagulation and blood transfusion management
- Short and long term results, according to age, diagnosis, type of transplantation

5. Early post-transplant management

- Immunosuppression: initial protocols
- Acute rejection: diagnosis, histopathology and management
- Early renal dysfunction
- Respiratory, neurologic and cardiac function

6. Diagnosis and management of early complications

- Preservation and reperfusion injury including histopathology aspects
- Primary non-function and dysfunction
- Vascular complications including histopathology aspects
- Biliary complications including histopathology aspects
- Infections: diagnosis, histopathology, timing, risk factors, prevention and management

7. Long-term management

- Long-term immunosuppressive standard protocols
- Immunosuppressive strategies in special patient groups (i.e. HCV, HCC, autoimmune diseases)
- Drug interactions and toxicity
- Recurrent disease: incidence, histopathology, risk factors, prevention, treatment
- Late acute and/or chronic T-cell-mediated and antibody-mediated rejection (TCMR and AMR): diagnosis, histopathology, staging, management
- Late biliary and vascular complications
- Re-transplantation: indications and prognostic models

- Renal dysfunction: prevention and management
- Cardiovascular and metabolic complications: risk factors, prevention, treatment
- “De novo” malignancies: types, timing, prevention, treatment
- Long-term infections (CMV, EBV, etc..)

- Issue of adherence to medical regimen amongst adult and pediatric liver recipients
- Sexual function and fertility after liver transplantation
- Assessment of quality of life after liver transplantation
- Physical activity and sport

8. Evaluation of a manuscript (optional)