LUNG TRANSPLANTATION TODAY

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TRANSPLANTÁCIA PĽÚC V SÚČASNOSTI

Abstract

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Lung transplantation has become an accepted surgical modality, and it is indicated in patients with a long-term benign pulmonary disease in stage when all the other therapeutic possibilities failed. Nowadays it presents a real possibility to significantly improve the quality of life. Success, (mainly in the last decade), establishing international professional centers, national coordinations, shifts transplantation towards the standard treatment procedures.
The objective of the paper is to offer an overview of the international activities, trends and results in the area of lung transplantation. Authors present a review of the current situation based on their own experiences gained from the bilateral cooperation with Vienna Transplant Group. ***(Tab. 4, Fig. 4, Ref. 19.)***
***K*ey words: lung transplantation, benign pulmonary diseases.**

Abstrakt

Pereszlényi Jr. Á., Haruštiak S., Taghavi S., Birsan T., Huber E., Deviatko E., Klepetko W.:
Transplantácia pľúc v súčasnosti
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Transplantácia pľúc sa stala akceptovanou chirurgickou modalitou, indikuje sa u pacientov s dlhotrvajúcim benígnym pľúcnym ochorením, v štádiu, keď už iné terapeutické možnosti zlyhali. V súčasnosti predstavuje reálnu možnosť podstatného zlepšenia kvality života. Úspechy (najmä v poslednom desaťročí), vypracovanie medzinárodných profesionálnych centier a nadnárodných koordinácií posúvajú transplantácie k štandardným liečebným postupom.
Práca ponúka prehľad medzinárodných aktivít, trendov a výsledkov na poli pľúcnych transplantácií. Autori prezentujú prehľad súčasného stavu aj na základe vlastných skúseností z obojstrannej spolupráce s Transplantačnou klinikou vo Viedni. (Tab. 4, obr. 4, lit. 19.)
Kľúčové slová: transplantácia pľúc, benígne ochorenia pľúc.

Introduction and historical overview

Exhausting all the ineffective medical treatment modalities, nowadays Lung Transplantation (LTX) offers the patients with end-stage pulmonary diseases a real possibility to substantially improve the quality of their lives. Today, having the correct indication and the optimum procedure, modern operative technique and adequate postoperative care, this can be achieved in more than 75 % of cases.

The first human lung transplantation was performed by Dr. James Hardy at the University of Mississippi in June 1963. Although the patient survived only 18 days, however, the operation proved the technical feasibility of human LTX (Cooper et al., 1987). Between 1963 and 1974, 36 patients underwent LTX at medical centers around the world, but only two recipients lived longer than one month (Veith and Koerner, 1974). In 1981 the Stanford Group performed the first successful Heart-Lung Transplantation (HLT), after which the patient lived more than 5 years. This very first success and mainly the introduction of cyclosporine (CyA) opened a new era of solid organ transplantations. The next two successful transplantations followed: Single Lung Transplantation SLT) for pulmonary fibrosis in 1983, and Double Lung Transplantation (DLT) for obstructive lung disease in 1986 (both performed at the University of Toronto) (Cooper et al., 1987, 1989). Achieving this long-term clinical success, LTX became an accepted surgical treatment modality for patients suffering from benign end stage pulmonary diseases. In the 1990s LTX experiences its resurgence. Activities in the field of LTX are rapidly increasing and the results are improving.

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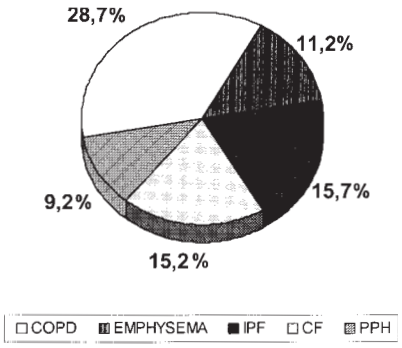

Fig. 1. The most frequent indications for lung transplantation.
Obr. 1. Najčastejšie indikácie transplantácie pľúc.

Abbreviations:
Zoznam použitých skratiek:
LTX — lung transplantation
transplantácia pľúc
SLT — single lung transplantation
jednostranná pľúcna transplantácia
HLT — heart-lung transplantation
srdcovo-pľúcna transplantácia
DLT — double lung transplantation
obojstranná (bilaterálna) pľúcna transplantácia
CyA — cyclosporine A, immunosuppressant
cyklosporín A, imunosupresívum
ISHLT — International society for heart and lung transplantation
Medzinárodná spoločnosť srdcovej a pľúcnej transplantácie
HLA — human leucocyte antigen system
hlavný humánny histokompatibliný systém
PRA — panel reactive antibodies
protilátky reagujúce s HLA-typizovaným panelom
COPD — chronic obstructive pulmonary disease
chronická obštrukčná choroba pľúc
CF — cystic fibrosis
cystická fibróza
IPF — idiopathic pulmonary fibrosis
idiopatická pľúcna fibróza
PPH — primary pulmonary hypertension
primárna pľúcna hypertenzia
TLC — total lung capacity index
index celkovej pľúcnej kapacity
ICU — intensive care unit
jednotka intenzívnej starostlivosti
MMF — mycophenolate mofetil, imunosuppressant
mykofenolát Mofetil, imunosupresívum
ATG — anti-thymocyte globulin, immunosuppressant
antitymocytárny globulín, imunosupresívum
CMV — cytomegalovirus
cytomegalovírus
BOS — bronchiolitis obliterans syndrome
bronchiolitis obliterans

Indication scale and overview of current activities

According to the official data given by Eurotransplant 6126 LTX were performed worldwide until the end of 1996 (Eurotransplant — Annual Report, 1996). According to the newest information provided by the International Society for Heart And Lung Transplantation (ISHLT) 11 608 LTX were performed until the end of 1998 (Hosenpud et al., 1999). From the total number of the official Eurotransplant statistics it is known that 3 555 (58 %) were SLT, and 2571 (42 %) were DLT (Eurotransplant — Annual Report, 1996).

The most frequent indications for LTX are the following diagnosis: chronic obstructive pulmonary disease (COPD) — 28,7 %; alfa$_1$-antitrypsin deficiency emphysema — 11,2 %; idiopathic pulmonary fibrosis (IPF) — 15,7 %; cystic fibrosis (CF) — 15,2 % and primary pulmonary hypertension (PPH) and Eisenmenger's syndrome — 9,2 % (Fig. 1) (Eurotransplant — Annual Report, 1996).

Less common indications have included bronchiectasis, sarcoidosis, lymphangioleiomyomatosis, and eosinophilic granuloma of the lung.

Recipient selection

Most lung transplant programs screen referrals and select candidates according to a predetermined protocol. Representative guidelines and contraindications are itemized in Tables 1 and 2, respectively. Other factors, such as ventilator dependence, previous cardiothoracic surgery, and preexisting medical conditions like hypertension, diabetes mellitus, and osteoporosis that must be judged individually (Trulock, 1993; Lynch and Trulock, 1996).

Typical age restriction is less than 45 to 50 yr for HLT, less than 50 to 55 yr for DLT, and less than 60 to 65 yr for SLT. There is an increasing number of pediatric transplantations and therefore the bottom age is not so strictly limited as before.

Corticosteroids or cytotoxic drugs that are needed to manage the underlying lung diseases are not an obstacle to transplantation. Perioperative corticosteroid treatment was prohibited in the first few years of LTX because of concerns about airway healing. Nowadays the pre-transplant corticosteroid therapy is not consi-

Tab. 1. Recipient selection — General guidelines.

Clinically and physiologically severe disease
Medical therapy ineffective or unavailable
Limited life expectancy, usually less than 12 to 18 months (when listed)
Ambulatory with rehabilitation potential
Acceptable nutritional status, usually 80—120 % of ideal body weight
Satisfactory psychosocial profile and support system

Tab. 1. Indikačné kritéria na recipienta — všeobecné smernice.

Klinicky a fyziologicky ťažký stupeň ochorenia
Neúčinná alebo už v danom štádiu nefektívna medikamentózna liečba
Limitovaná dĺžka života, obyčajne menej ako 12 až 18 mesiacov v čase zaradenia na čakaciu listinu
Ambulantný pacient so schopnosťou aktívne spolupracovať pri rehabilitácii
Akceptovateľný nutričný stav (80 – 120 % telesnej hmotnosti)
Uspokojivý psychosociálny profil (rodinné a sociálne zázemie pacienta)

Tab. 2. Recipient selection — contraindications.

Acutely ill or unstable clinical status
Uncontrolled or untreatable pulmonary or extrapulmonary infection
Uncured neoplasm
Significant dysfunction of other vital organs, especially liver, kidney, and central nervous system
Significant coronary disease or left ventricular dysfunction
Active cigarette smoking
Drug or alcohol addiction
Unresolvable psychosocial problems or noncompliance with medical management

Tab. 2. Kontraindikačné kritéria pre recipienta.

Akútne štádium ochorenia, alebo nestabilný klinický stav
Neliečiteľná alebo nezvládnuteľná pľúcna alebo mimopľúcna infekcia
Malignity známe z predchorobia (kožné tumory akceptovateľné)
Signifikantné dysfunkcie dôležitých orgánov (pečeň, obličky, CNS)
Signifikantné koronárne ochorenie, dysfunkcia ľavej komory
Aktívne fajčenie
Závislosť na liekoch alebo alkohole
Neriešiteľné psychosociálne problémy, neschopnosť pacienta podrobiť sa liečbe (spolupráci)

dered as a contraindication to LTX. This corticosteroid therapy has not been associated with airway complications, and a maintenance prednisone dosage of 0,2 to 0,3 mg/kg/d is acceptable before transplantation (Schaefers et al., 1992).

Chronic infection is a special issue in patients with bronchiectasis, especially CF. Infection with antibiotic-resistant Pseudomonas species is not uncommon after years of treatment, and prevalence of infection with Burkholderia cepacia is high at some CF centers. Moreover, infection with Aspergillus or non-tuberculous mycobacteria is not unusual (Miller et al., 1995). The incidence of infectious complications has been comparable in CF and non-CF recipients after transplantation (Kotloff and Zuckerman, 1996). Infection with Burkholderia cepacia or other pan-resistant Pseudomonas species has been considered a contraindication to transplantation by some centers (Yankaskas et al., 1998).

The highly allosensitized recipient presents a special problem. Antibodies to human leukocyte antigens (HLA) can be induced by blood transfusions, pregnancy, or previous transplantation. These HLA-specific alloantibodies are identified in vitro by routinely screening the potential recipient's serum against an HLA-typed lymphocyte panel (panel reactive antibodies, PRA). If antibodies are present, there is a risk of hyperacute rejection if the donor's phenotype includes the reactive HLA, and patients with a significantly positive PRA are sometimes disqualified from transplantation (Tyan et al., 1994).

Timing and choice of procedure

Transplantation is appropriate when other therapeutic options have been exhausted and when the patient's prognosis will be improved by the procedure. The main goal of transplantation is the quality of patient's life. Transplantation timing for the most frequent diseases, as: COPD, CF, IPF, PPH, has been adequately worked out. Guidelines for planning the referral are presented in Table 3 (Maurer et al., 1998; Arcasoy and Kotloff, 1999).

Tab. 3. Guidelines for Timing referral.

COPD (+alfa$_1$-antitrypsin deficiency emphysema)
FEV 1<25 % predicted
Clinically significant hypoxemia
Hypercapnia
Secondary pulmonary hypertension
Clinical course: rapid rate of decline of FEV 1 or life-threatening exacerbations
Cystic fibrosis
FEV 1 <30 % predicted
or FEV 1 >30 % with rapidly declining lung function
Hypercapnia
Clinical course: increasing frequency and severity of exacerbations, progressive weight loss
Idiopathic pulmonary fibrosis
VC, TLC <60-65 % predicted
Symptomatic disease unresponsive to medical therapy
Secondary pulmonary hypertension
Clinical, radiographic, or physiologic progression on medical therapy
Primary pulmonary hypertension
NYHA functional class III or IV
Mean right atrial pressure >10 mmHg
Mean pulmonary arterial pressure >50 mmHg
Cardiac index <2,5 L/min/m^2

Tab. 3. Všeobecné smernice na „načasovanie" (Timing) transplantácie.

CHOCHP (+alfa$_1$-antitrypsin deficient. emfyzém)
FEV 1 <25 % referenčnej hodnoty
Klinicky signifikantná hypoxémia
Hyperkapnia
Sekundárna pľúcna hypertenzia
Klinický priebeh: rapídny zostup FEV 1 alebo život ohrozujúce exacerbácie
Cystická fibróza
FEV 1 <30 % referenčnej hodnoty
alebo FEV 1 >30 % ref. hodnoty, rapídne sa zhoršujúca
Hyperkapnia
Klinický priebeh: vzostup frekvencie a stupeň exacerbácie, úbytok hmotnosti
Idiopatická pľúcna fibróza
VC, TLC <60-65 % referenčnej hodnoty
Štádium ochorenia už nereagujúce na konzervatívnu terapiu
Sekundárna pľúcna hypertenzia
Klinická a rtg verifikovaná progresia ochorenia (zintenzívnenie medikamentóznej terapie)
Primárna pľúcna hypertenzia
Funkčný stupeň III alebo IV podľa NYHA
Stredný tlak v pravej predsieni >10 mmHg
Stredný tlak v pľúcnici >50 mmHg
Kardiálny index <2,5 L/min/m^2

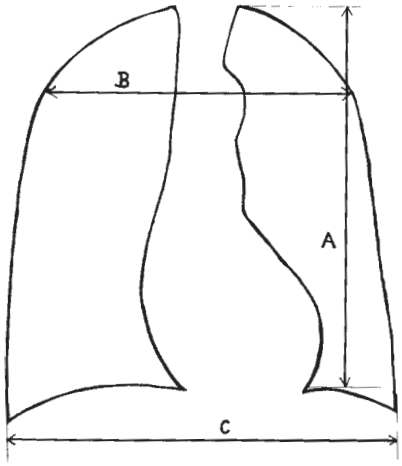

Fig. 2. Thoracic somatic dimensions. A — apex—diaphragm (right side or left side), B — transverse length of chest in the aortic arch place, C — transverse length between the two frenico-costal angles).
Obr. 2. Somatické rozmery hrudníka. A — rozmer apex—diafragma, B — priečny rozmer v mieste oblúka aorty, C — priečny rozmer medzi 2 freniko-kostálnymi uhlami.

Up to now SLT is the most frequently performed transplantation due to the relative shortage of donor organs and due to the relatively long stay on the waiting list. HLT should be reserved for the patients who cannot be treated by LTX alone; the compulsory indications are Eisenmenger's syndrome with a surgically uncorrectable anomaly or end-stage lung disease with concurrent severe cardiac diseases.

Bilateral LTX is mandatory for patients with generalized bronchiectasis or other forms of chronic pulmonary infection.

The organ donor

The shortage of donor organs has been one of the major problems to solid organ transplantation. Xenotransplantation is the most promising solution to the organ shortage, but there are still a lot of unsolved questions due to which it is still not being practiced. Most solid organs for transplantation are obtained from heart beating, brain-dead donors (Darby et al., 1989). After brain death criteria have been fulfilled and permission has been granted, organs that are suitable for transplantation can be procured from these heart-beating donors. The legislative conditions differ from country to country, e.g. in the USA organ donation is entirely voluntary and depend on the approval of the relatives.

In the Slovak Republic and Austria donation is based on the so-called presumed consent. In Slovakia the topic of transplantology is included in the Act of the National Council of the Slovak Republic No 227/1994 of the Statute Book on Health Care in Articles 45 and 52 and in expert direction for organ harvesting from corpses issued by the Ministry of Health valid from 1 December 1996 (Laca et al., 1998).

So, what are those criteria for the organ donors? Organ donor supposes to be a healthy person. General exclusionary criteria for organ donation include untreated septicemia, active tuberculosis, human immunodeficiency virus (HIV) infection, viral hepatitis, viral encephalitis, current intravenous drug abuse and malignancy (except primary brain tumor). Criteria, which an optimum organ donor supposes to meet, mainly respect the lung oxygenation ability and absence of abnormalities in bronchoscopic inspection. These criteria are summarized in Table 4 (adequate oxygenation – PaO_2 > 300 mmHg at FiO_2 = 1,0 at PEEP = 5 cm H_2O). Some of the criteria, as age and smoking are rational, however not rigid, they are needed to be judged individually.

Fiberoptic bronchoscopy and direct inspection at the operating table are the final steps in assessing the suitability of the donor lungs. Donors with endoscopic evidence of abnormalities of aspiration, mucopurulent secretion are excluded from donation.

Microorganisms from the bronchial secretion of the donor and the recipient are being examined routinely. In case of negative findings broad-spectrum antibiotics (antiviral and antimicotic regiments) are being applied. In case of positive findings the antibiotic treatment is adjusted accordingly.

Donor — recipient size matching is being realized by comparing thoracic somatic dimensions with the measures from chest radiographs. The following values are important: A — Apex-Diaphragm (right side or left side), B — Transverse Length of Chest in the Aortic Arch Place, C — Transverse Length between the two Frenico-Costal Angles). The above mentioned values see on Figure 2.

It is also important to calculate the Total lung capacity index (TLC) according to the formula 7,99 times height in meters minus 7,08 at men and 6,60 times height in meters minus 5,79 at women. The mentioned values are being recorded at candidates in to the waiting list. These are later being compared with the parameters of the potential donors — a so-called size-matching is being carried out.

Preparation of lungs:

— opening of both pleural spaces,
— separation of truncus arteriae pulmunalis from aorta.

Tab. 4. Guidelines for donor selection.

Age ≤60-65 yr
No history of significant lung disease
Limited cumulative cigarette smoking history
Clear lung field on chest radiograph
Adequate oxygenation (PaO_2>300 mmHg at FiO_2=1,0 and PEEP=5 cmH_2O)
Satisfactory gross appearance by bronchoscopic inspection

Tab. 4. Smernice na výber optimálneho darcu.

Vek ≤60-65 rokov
Negatívna anamnéza pľúcnych ochorení
Nefajčiar (údaje o fajčení v minulosti posudzovať individuálne)
Negatívna rtg snímka hrudníka
Adekvátna oxygenácia (PaO_2>300 mmHg pri FiO_2=1,0 a PEEP=5 cmH_2O)
Neprítomnosť abnormalít pri bronchoskopickej inšpekcii

— *systematic application of Heparine anticoagulant (3 mg/kg = 20 000–25 000 i.u.)!*
— checking perfusion systems, sterile solutions, ice-salines, etc.,
— inserting perfusion catheter into abdominal aorta towards arteria mesenteria inf. (to the perfusio of intraabdominal organs),
— vessel loop on vena portae behind pancreas and double vessel loop on vena mesentrica superior below pancreas,
— inserting perfusion catheter through vena mesentrica sup.up to the hepatic hilus, tourniquet constricting of vena portae; outflow of perfusion fluid from pancreas ensured by wide incision of vena mesenterica sup.,
— clamping on lienal hilus (peripheral insicion v. lienalis below the clamp, respectively),
— perfusion catheter into aorta ascendens (tightening by purse-string suture),
— perfusion catheter into truncus pulmonalis (tightening by purse-string suture).

— *systematic application of Prostaglandin (Alprostadil, or Eproprospenol, resp., PGE 1 = 1 amp FlolanR)!*
— double ligature vena cava sup. (its transection between ligatures),
— closure of vena cava inferior (intra – or extra-pericardial clamping), discision above the clamp (right atrium blood outflow),
— left atrium auricular incision (emptying of left heart during permanent atrificial respiration of the donor),
— subdiaphragmatic (clamp) closure of aorta descendens, intrapericardial closure of aorta ascendens (cross clamping of aorta peripheral from perfusion catheter), peripheral ligature of art. mesenterica superior.

— *from this moment synchronous perfusion of all systems begins!*
— cooling by ice-slush during the synchronous perfusion of organs,
— stopping artificial respiration only after lung harvesting (pulmonary insufflation prevents atelectasis development!!).

Lung harvesting:

— discission of mediastinal pleura (separation of pulmonary hilus),
— blunt trachea separation, closure and transection of trachea by a stapler (in inspirium),
— removal of both lungs and their sterile placing into the cold preservation solution (= 4 Celsius, Euro-Collins),

Lung implantation – operation technique

This chapter will briefly deal with the operation technique of lung implantation (Single – and Double – Lung Transplantation).

Immediately after receiving the information about the potential donor, the selected recipient is contacted and transported to the Transplant Centre. Anesthesiological preparing with recent laboratory examination follows, but induction of anesthesia is postponed until the donor lung has been inspected and approved by the retrieval team. The implantation team starts to operate on the recipient. The critical moment of lung explantation must be in coordination with the delivery of the organ.

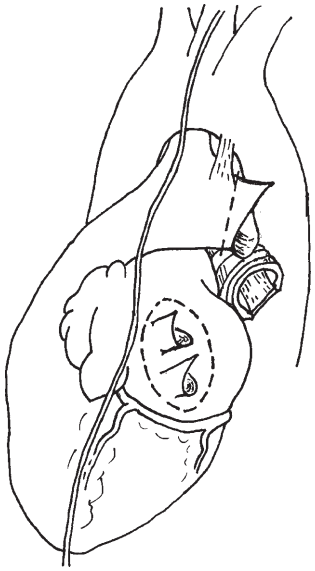

Fig. 3. Pulmonary veins with left atrium cuffs (scheme).
Obr. 3. Pulmonálne vény s „terčíkmi“ ľavej predsiene (schéma).

Single lung transplantation (SLT)

A standard posterolateral (VLTG — anterolateral) thoracotomy incision is made for SLT. With ventilation to the contralateral lung, the standard pneumonectomy is being perfomed. The difference is only in intrapericardial separation of vessel structures. If refractory hypoxemia or hemodynamic instability develops, it means an indication for cardiopulmonary bypass, which is always on standby.

During the preparation — explantation of the organ integrity of nervus phrenicus as well as of nervus vagus on the left side and of nervus laryngeus recurrens must be safeguarded. During the implantation **bronchial anastomosis** is performed as the first one. An emphasis is given to the maximum shortening of the stump of the receiver's and donor's main bronchi. Anastomosis itself is performed with absorbable, monofilament 4-0 PDS sutures. As the first pars membranacea is sutured by running sutures, then pars cartilaginacea by single sutures, which are tied out. Immediately after completing anastomosis its tightness is checked by 20—30 cmH_2O possitive airway pressure. The lung is not ventilated any more. The procedure continues with **anastomosis of pulmonary veins.** (Sufficient approach to recipient's pulmonary veins is ensured by the atrial clamp placed on the left atrium). Practically anastomosis is performed in such a way, that the pulmonary veins with the part of the atrium (the above-mentioned cuff) is being anastomosed onto the pre-prepared pulmonary veins of the recipient. These are readjusted in such a way, that from the original two trunks one is being created by discission of the link (Fig. 4). Anastomosis is being performed by the standard way — it is sutured by monofilament nonabsorbable Prolene 4-0 sutures. The running suture after completing anastomosis is not tied, its endings for the time being are left free.

Pulmonary artery anastomosis follows. It is also performed by a standard way — by monofilament nonabsorbable 5-0 Prole-

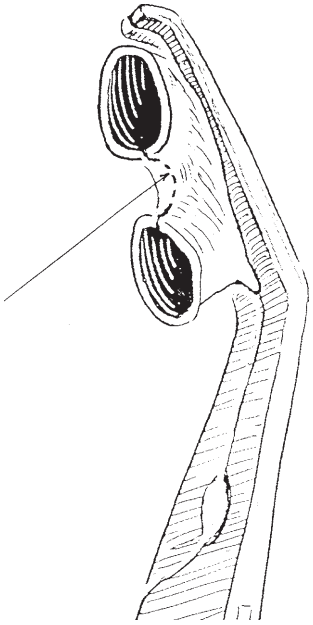

Fig. 4. Discission between pulmonary veins (scheme).
Obr. 4. Discízia medzi pľúcnymi žilami (schéma).

ne sutures. In this case as well, after completing anastomosis, the suture is not tied. **De-airing** of venous system follows. Venous system is tighten by pulling the ends of the above mentioned venous suture, which is still not tied. The left atrial (Satinsky) clamp is gradually released, while the pulmonary artery clamp is still locked. Pulmonary venous system is flushed by retrograde flow via the pulmonary veins. This will produce brisk back bleeding (with air bubles, i.e. — de-airing) from the still untied arterial anastomosis. Then the arterial anastomosis is completed (the suture is knotted). The atrial clamp will be locked again so that the pulmonary artery clamp will be opened to flush the pulmonary artery. About 400—500 ml of the recipient's blood leaves the pulmonary circulation from the still untied atrial (venous) anastomosis. This is done due to the fact that the graft blood is kalium-rich as a result of the previously applied perfusion Euro-Collins solution.

Then the atrial (venous) anastomosis is completed (the suture is knotted) and the both clamps (arterial and atrial) are completely removed. Circulation and ventilation of the implanted lungs is renewed.

Chest drainage and thoracotomy closure are done in standard ways. Immediate bronchoscopic anastomosis inspection with tracheobroncheal toilet is obligatory.

Double lung transplantation (DLT)

Nowadays sequential Double Lung Transplantation is preferable (Grimm et al., 1995). Clam-shell approach, which is transverse thoracosternotomy (the lungs are implanted separately and sequentially), is being used. In the majority of cases cardiopulmonary bypass can be avoided by supporting the recipient with the contralateral lung. Practically it can be considered that this procedure is conducted like sequential right and left Single Lung Transplantation. The process of anastomosis and the following de-airing is identical, too.

The use of cardiopulmonary bypass is indicated in that particular case, if during the procedure hemodynamic instability or malfunction of graft appears.

The necessary condition for a successful operation procedure is the return of one's own blood losses — "Cell-Saver".

Postoperative management

Early postoperative management on intensive care unit (ICU) in principal does not differ from the management of other complicated postoperative cases.

Immunosuppressive therapy is introduced immediately after transplantation. Nowadays more protocols of immunosuppressive therapy are known. The following protocol used by the Vienna Lung Transplant Group (VLTG) is listed below:

1. Cyclosporine A (CyA) is the basic element of immunosuppressive therapy. CyA is administered in dose 1 mg/kg/day by continuous intravenous infusion. Later the dose is adopted according to the CyA blood level about 300 ng/ml (1x300 mg intravenously, 3x100 mg orally, respectively).
2. Glucocorticoids are basic classical immunosuppressive and anti-inflammatory agents. They are already administered intraoperatively. Single intravenous dose of Methylprednisolone is applied (500—1000 mg/ according to the patient's weight). Further dosage is within 1 mg/kg/day postoperatively.
3. Mycophenolate mofetil (MMF) replaced Azathioprine, which was used before. (MMF is a semisynthetic derivate of mycophenolic acid antimetabolite, which suppresses T and B-cell activations). Its daily dosage is 2x1000 mg. It is produced only for oral application.
4. The forth immunosuppressivum is Anti-thymocite globulin (ATG). Its dosage is variable. It is applied as an induction therapy only during the early post-transplant period. The VLTG uses it in all indications except cystic fibrosis (CF).

For infection prophylaxis in postoperative management the following regiments are used: antibiotics, antivirotics, antimycotics, antiprotozoics. The following protocol is also the VLTG's scheme:

1. Broad-spectrum antibacterial antibiotics are routinely administered perioperatively. The regimen should include coverage for any potential pathogens that have been isolated from the donor and/or recipient. If no cultures are available, an empirical regimen is being applied. VLTG uses Tasobactame-piperacillin in dose 3x4,5 g intravenously.
2. The next from anti-infection regimens are antivirotics. Gancyclovir intravenously in dose of 10 mg/kg is applied in the first three weeks after transplantation. After this period an oral form of the same drug is introduced (3x1000 mg). Besides this CMV-Hyperimmunoglobulin in dosage of 100 mg intravenously is applied on the 1st, 7th, 14th, 21st postoperative days.
3. Amphotericin B as inhalant in dose of 3x10 mg/day is introduced in early postoperative period. The treatment is supplemented by Itroconasol for mouthwash (3x50 mg/day).
4. Finally, Thimethoprim — Sulphametoxasol in dose of 2 tablets/day as anti-protozoic prophylaxis is used.

Outcomes, survival

The actuarial survival is well-known from the registries and statistics of different Transplant Centres. The values are as follows: 1-year survival — 66—94 %, 2-year survival — 55—72 %, 3-year survival — 51—62 % (Eurotransplant — Annual Report, 1996; Klepetko and Birsan, 1997).

Infection (29 %), acute allograft rejection (20 %), early graft disfuction (13 %), heart failure (9 %) are the most frequent causes of death in the early postoperative period (3 months). In further postoperative period chronic allograft rejection (29 %), infection (24 %), neoplasms (6 %) causes death (Klepetko and Birsan, 1997).

The most frightening and most frequent cause of later mortality and morbidity is still the chronic allograft rejection. Nowadays the term of "Bronchiolotis obliterans syndrome (BOS)" is defined as chronic graft disfunction with obstructive symptomatology. Pathogenesis of this disease is still not clearly defined. Better understanding of the pathogenesis of this disease will help to define the strategy of prevention in the future more precisely, and in such a way to treat this still threatening complication more efficiently.

The questions connected with the quality of life of the patients and questions concerning re-transplantation and lobar transplantation from living related donors are still controversaly belong among the discussed ones (Klepetko and Birsan, 1997).

Conclusion

Solid organs and tissue transplantations surely belong among the greatest progresses and discoveries of mankind in the 20th century. Successful transplantation ensures an acceptable quality of life for patients with otherwise fatal end stage.

The technical success mainly in the last decade, more perfect immunosuppression, precise coordination, establishing international professional centres are those important steps, which shifts transplantation among the standard treatment procedures. In our conditions it is necessary to speed up personal training and establish technical conditions to carry out transplantation programme. All these are not possible without effective interest of governmental and non-governmental institutions.

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