the waiting list and the patient's likelihood of survival for 1 year after transplantation. The LAS can range from 0 to 100, and precedence for transplantation is ranked from highest to lowest scores. Both the lung disease and its severity affect a patient's LAS; parameters in the LAS must be updated biannually but can be submitted for recalculation whenever the patient's condition changes. The median LAS for all candidates on the waiting list is usually ~35, but the LAS tends to be higher among patients with IPF and CF than among patients with COPD and IPAH.

Under this system in the United States, the median waiting time for transplantation has been ~135 days. The overall death rate on the waiting list has been ~6.5%, but death rates vary substantially with the diagnosis (e.g., COPD, ~3%; IPF, ~7%) and with the LAS (e.g., 40–49, ~7%; 50–59, ~15%; ≥60, ~25%). The indications for transplantation depend not only on the prevalence and natural history of the various lung diseases but also on the LAS typically associated with these diseases. While patients with IPF constitute ~20% of the waiting list, they make up ~34% of recipients because their allocation scores are typically higher than those of patients with other diseases.

TRANSPLANT PROCEDURE

Bilateral transplantation is mandatory for CF and other forms of bronchiectasis because the risk of spillover infection from a remaining native lung precludes single-lung transplantation. Heart-lung transplantation is obligatory for Eisenmenger syndrome with complex anomalies that cannot readily be repaired in conjunction with lung transplantation and for concomitant end-stage lung and heart disease. However, cardiac replacement is not necessary for cor pulmonale because right ventricular function will recover when pulmonary vascular afterload is normalized by lung transplantation.

Either bilateral or single-lung transplantation is an option for other diseases unless there is a special consideration, but bilateral transplantation has been utilized increasingly for most indications. Recently, ~65% of procedures in the United States have been bilateral, and ~70% of transplants for COPD, ~55% of those for IPF, and ~95% of those for IPAH in the international registry have been bilateral.

Living-donor lobar transplantation has had a limited role in adult lung transplantation but is now rarely performed. It has been used predominantly for teenagers or young adults with CF and has usually been reserved for patients who were unlikely to survive the wait for a deceased-donor organ.

POSTTRANSPLANTATION MANAGEMENT

Induction therapy with an antilymphocyte globulin or an interleukin 2 receptor antagonist is utilized by ~55% of centers, and a three-drug maintenance immunosuppressive regimen that includes a calcineurin inhibitor (cyclosporine or tacrolimus), a purine synthesis antagonist (azathioprine or a mycophenolic acid precursor), and prednisone is traditional. Subsequently, other drugs (e.g., sirolimus) may be substituted into the regimen for various reasons. Prophylaxis against *Pneumocystis jirovecii* pneumonia is standard, and prophylaxis against cytomegalovirus (CMV) infection and fungal infection is part of many protocols. The dose of cyclosporine, tacrolimus, or sirolimus is adjusted by blood-level monitoring. All of these agents are metabolized by the hepatic cytochrome P450 system, and interactions with medications that affect this pathway can significantly alter their clearance and blood level.

Routine management focuses on monitoring of the allograft, regulation of immunosuppressive therapy, and expeditious detection of problems or complications. Regular contact with a nurse coordinator, physician follow-up, chest radiography, blood tests, and spirometry are customary, and periodic surveillance bronchoscopies are employed in some programs. If recovery is uncomplicated, lung function rapidly improves and then stabilizes by 3–6 months after transplantation. Subsequently, the variation in spirometric measurements is small, and a sustained decline of ≥10–15% signals a potentially significant problem.

OUTCOMES

Survival Major registries publish survival rates (Table 320e-2) and other outcomes annually (*www.ishlt.org; www.srtr.org*). In the international registry, the survival half-life for recipients with IPF is 4.4 years; IPAH, 5 years; COPD, 5.3 years; and CF, 7.5 years. However, age and transplantation procedure have a significant impact on outcome. For recipients 18–59 years of age, the survival half-life is 5–6 years, but this figure decreases to 4.4 years among patients 60–65 years old and to 3.6 years for those >65 years old. Survival rates at >15 years have been significantly higher after bilateral transplantation than after unilateral transplantation for COPD, α_1-antitrypsin deficiency emphysema, IPF, and IPAH.

The main sources of perioperative mortality include technical complications of the operation, primary graft dysfunction, and infections. Acute rejection and CMV infection are common problems in the first year, but neither is usually fatal. Beyond the first year, chronic rejection and non-CMV infections cause the majority of deaths.

Risk factors for mortality have been analyzed in the international and U. S. registries. In these analyses, factors associated with an increased risk of death, especially in the first year after transplantation, have included the following: recipients hospitalized at the time of transplantation; recipients supported by mechanical ventilation, extracorporeal membrane oxygenation, inotropic drugs, or dialysis at the time of transplantation; and recipients undergoing retransplantation.

TABLE 320e-2 RECIPIENT SURVIVAL, BY PRETRANSPLANTATION DIAGNOSIS (1990–2010)

		Survival Rate, %					
Diagnosis, Transplant Type	*n*	3 Months	1 Year	3 Years	5 Years	10 Years	15 Years
Chronic obstructive pulmonary disease							
Bilateral	5147	92	83	68	57	34	20
Single	6797	90	81	63	49	21	7
α_1-antitrypsin deficiency emphysema							
Bilateral	1403	88	80	68	59	39	22
Single	1086	87	78	62	52	29	14
Cystic fibrosis	5608	90	82	69	59	42	32
Idiopathic pulmonary fibrosis							
Bilateral	3057	84	75	62	52	33	19
Single	4481	86	74	57	43	20	8
Idiopathic pulmonary arterial hypertension							
Bilateral	1037	78	72	61	53	38	24
Single	271	71	63	51	41	25	18
Sarcoidosis	849	84	73	58	51	30	

Source: Data from *www.ishlt.org/registries/slides.asp?slides=heartLungRegistry*.