

Approach to the Solid Organ Transplant Patient with Suspected Fungal Infection



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KEYWORDS

- Solid organ transplant • Invasive fungal infection • Candida • Aspergillus
- Endemic fungi • Cryptococcus • Mold

KEY POINTS

- Identification of invasive fungal infections (IFIs) can be challenging, because the signs and symptoms are similar to other infections and diagnostic techniques are limited.
- *Aspergillus* and *Candida* species are the most frequent causes of IFIs in solid organ transplant (SOT) recipients.
- When an SOT recipient presents with pulmonary symptoms, chest imaging should be performed to evaluate for a fungal cause, which typically presents with nodular opacities.
- Because of immunosuppression, typical morphology of fungal skin lesions may be altered in SOT recipients, making skin biopsy an essential step for diagnosis.

INTRODUCTION

In solid organ transplant (SOT) recipients, invasive fungal infections (IFIs) are associated with significant morbidity and mortality. Detection of IFIs can be difficult because the signs and symptoms are similar to those of viral or bacterial infections or noninfectious illness, and diagnostic techniques have limited sensitivity and specificity. As a result, to aid in the diagnosis of IFI, clinicians often must rely on knowledge of the patient's risk factors for fungal infection.

In this article, an approach to diagnosis of IFIs is described on the basis of the SOT patient's clinical presentation and risk factors. Specifically, the spectrum of suspected

Disclosure Statement: Dr J.A. Anesi has nothing to disclose; Dr J.W. Baddley consults for Merck, Astellas, and Pfizer.

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Infect Dis Clin N Am 30 (2016) 277–296
<http://dx.doi.org/10.1016/j.idc.2015.10.001>

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IFIs that may be present in patients who present with clinical syndromes is outlined, including respiratory illness, neurologic illness, cutaneous manifestations, and a sepsis syndrome. Relevant fungal pathogens associated with these clinical syndromes, an initial diagnostic approach, and considerations for empiric antifungal therapy are discussed.

EPIDEMIOLOGY OF INVASIVE FUNGAL INFECTIONS AFTER SOLID ORGAN TRANSPLANTATION

The timing and incidence of IFIs vary by the organ transplanted and the use of anti-fungal prophylaxis. Candidiasis and aspergillosis have historically caused—and continue to cause—most IFIs in SOT recipients, although there are increasing reports of non-*albicans* *Candida* and non-*Aspergillus* molds complicating SOT in recent years^{1–5} (Table 1).

There have been 2 recent multicenter, observational studies describing the epidemiology of IFIs in SOT patients.^{6,7} The first, by Pappas and colleagues,⁶ analyzed data from the Transplant-Associated Infection Surveillance Network. The group described 1208 IFIs among 1063 SOT recipients (kidney, liver, pancreas, lung, heart, and small bowel) over a follow-up period of up to 5 years. The overall incidence of IFIs was 3.1%.⁶ The second study, by Neofytos and colleagues,⁷ used data collected from the Prospective Antifungal Therapy Alliance registry. In this study, 515 IFIs among 429 SOT recipients (liver, lung, kidney, heart, small bowel, islet cell, and pancreas) were described, with a follow-up time of up to 3 years. Both studies revealed similar IFI epidemiology: the most common IFIs were invasive candidiasis, invasive aspergillosis, and cryptococcosis. Invasive candidiasis was the most common IFI in all transplant types except in lung recipients, where aspergillosis was most common. Non-*Aspergillus* molds, endemic fungi, zygomycosis, and pneumocytosis were less commonly observed.^{6,7}

Timing of Invasive Fungal Infections After Solid Organ Transplant

In general, invasive candidiasis is an early complication of SOT, and other IFIs are more likely late complications, although the timing may vary based on antifungal prophylaxis and transplant type (Fig. 1).^{1,6–8} With current antifungal prophylaxis strategies, the time to onset of invasive candidiasis ranges between 3 and 6 months.^{6,7}

Table 1 Epidemiology of invasive fungal infection in solid organ transplant recipients	
Organ Transplanted	IFIs in Order of Decreasing Frequency
Kidney	<i>Candida</i> > <i>Crypto</i> > <i>Aspergillus</i> > Endemic mycoses > Molds > PJP
Liver	<i>Candida</i> > <i>Aspergillus</i> > <i>Crypto</i> > Endemic mycoses > Molds > PJP
Pancreas	<i>Candida</i> > Endemic mycoses > <i>Aspergillus</i> ≈ <i>Crypto</i> > Molds > PJP
Lung	<i>Aspergillus</i> > <i>Candida</i> > Molds > <i>Crypto</i> > PJP > Endemic mycoses
Heart	<i>Candida</i> > <i>Aspergillus</i> > Molds > <i>Crypto</i> > Endemic mycoses > PJP
Small bowel	<i>Candida</i> > <i>Crypto</i> > <i>Aspergillus</i> > Endemic mycoses > Molds > PJP

Abbreviation: *Crypto*, *Cryptococcus*.

Adapted from Pappas PG, Alexander BD, Andes DR, et al. Invasive fungal infections among organ transplant recipients: results of the Transplant-Associated Infection Surveillance Network (TRANSNET). *Clin Infect Dis* 2010;50:1101–11; and Neofytos D, Fishman JA, Horn D, et al. Epidemiology and outcome of invasive fungal infections in solid organ transplant recipients. *Transpl Infect Dis* 2010;12:220–9.

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