

Infectious Complications and Malignancies Arising After Liver Transplantation

Dame W. Idossa, MD^a, Douglas Alano Simonetto, MD^{b,*}

KEYWORDS

• Liver transplantation • Immunosuppression • Infection • Malignancy • Mortality

KEY POINTS

- Infection is the most frequent cause of death immediately after liver transplantation.
- Bacterial pathogens are the leading cause of infection after liver transplantation, most often occurring within the first month after surgery.
- Viral infections cause the majority of febrile episodes between 1 and 6 months after liver transplant.
- Invasive fungal infections are common in posttransplant patients.
- The risk of malignancy is 2 to 4 times higher in transplant recipients compared with their nontransplanted counterparts.

INTRODUCTION

Since the first liver transplant was performed in 1963, great advancements have been made in the field of hepatic transplantation. Surgical techniques have been revised and improved; diagnostic methods for identifying and preventing infections have been developed, and more conservative use of immunosuppressive agents have resulted in better long-term posttransplant outcomes. Despite the myriad advancements made since the initial liver transplants of the 1960s, technical surgical complications, infections, rejections, and chronic medical conditions such as renal failure, diabetes, dyslipidemia, osteopenia, coronary artery disease, and malignancy persist.¹ In this review, we discuss the infectious complications and malignancies that may arise after liver transplantation as a result of the procedure itself, and from posttransplant immunosuppression.

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^a Internal Medicine, Mayo Clinic, 200 First Street Southwest, Rochester, MN 55905, USA;

^b Department of Gastroenterology and Hepatology, Mayo Clinic, 200 First Street Southwest, Rochester, MN 55905, USA

* Corresponding author.

E-mail address: Simonetto.douglas@mayo.edu

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INFECTIOUS COMPLICATIONS

In many centers, infection is the most frequent cause of death immediately after liver transplantation. Unfortunately, the diagnosis is often delayed owing to the effects of immunosuppressive agents, inhibiting the usual inflammatory responses and clinical signs of an infectious state.² Such a delay in diagnosis leads to increased morbidity and mortality in these posttransplant patients. Infectious complications can be categorized into those occurring within the first month (early), between 1 to 6 months (intermediate), and after 6 months (late) after transplantation. Understanding these complications may help to optimize management strategies, support patient quality of life, and improve long-term outcomes after liver transplantation.³

EARLY BACTERIAL INFECTIONS

Bacterial pathogens are the leading cause of infection after liver transplantation, most often occurring within the first month after transplant. These infections usually involve the surgical site, peritoneal space, bloodstream, and respiratory tract.⁴⁻⁷ The most common bacterial pathogens include *Enterococcus* species, *Streptococcus viridans*, *Staphylococcus aureus*, and members of the *Enterobacteriaceae* family.³ The rate of infection with multidrug-resistant organisms is steadily increasing in patients with previous antibiotic exposure, recurrent hospitalizations, and invasive interventions such as mechanical ventilation and indwelling devices. In some centers, the prevalence rate of methicillin-resistant *S aureus* colonization may exceed 80%,^{8,9} whereas vancomycin-resistant enterococcus colonization may reach up to 55%.¹⁰

Surgical wound infections are commonly seen within the first month of transplantation.¹¹ These infections are commonly caused by gram-positive cocci such as *S aureus* and *Enterococcus*, and less commonly by gram-negative organisms such as *Escherichia coli*, *Acinetobacter*, and *Pseudomonas*.¹² Intraabdominal infections including cholangitis, peritonitis, bile leak, and intraabdominal abscesses are also common early in the postoperative period.¹³ **Tables 1** and **2** present the most common causative pathogens and the risk factors associated with these infections.

Bloodstream infections are also a serious and common occurrence postoperatively, with associated mortality rates of 24% to 36% in liver transplant recipients.^{14,15} Specific organisms responsible for bacteremia vary between transplant centers. Gram-positive cocci were considered to be the most common causative agents of early

Table 1
Common pathogens early in the postoperative phase

Surgical Wound	Intraabdominal	Bloodstream	Respiratory Tract
<i>Staphylococcus aureus</i>	<i>Staphylococcus aureus</i>	Specific organisms vary between transplant centers	<i>Staphylococcus aureus</i>
<i>Enterococci</i> spp	<i>Enterococci</i> spp		<i>Pseudomonas aeruginosa</i>
<i>Escherichia coli</i> ^a	<i>Acinetobacter</i>		<i>Klebsiella</i>
<i>Acinetobacter</i> spp ^a	<i>Pseudomonas aeruginosa</i>		<i>Enterobacter</i>
<i>Pseudomonas aeruginosa</i> ^a	<i>Klebsiella</i>		<i>Haemophilus influenza</i>
	<i>Clostridium difficile</i>		<i>Stenotrophomonas maltophilia</i>
			<i>Serratia marcescens</i>

^a Less commonly associated.

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