





## Concise Communication

# Late surgical site infections among solid organ transplant recipients: an unrecognized clinical entity

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### Abstract

This study identified 26 late invasive primary surgical site infection (IP-SSI) within 4–12 months of transplantation among 2073 SOT recipients at Duke University Hospital over the period 2015–2019. Thoracic organ transplants accounted for 25 late IP-SSI. Surveillance for late IP-SSI should be maintained for at least one year following transplant.

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### 1. Introduction

Surgical site infections (SSI) are a severe complication of solid organ transplant (SOT), with rates ranging from 2% to 46%. Several factors account for the variability in SSI rates, including the surveillance period. The majority of studies limit surveillance to the first 1–3 months post-transplant surgery (Table S1), in accordance with Centers for Disease Control and Prevention (CDC) – National Healthcare Safety Network (NHSN) recommendations.<sup>1–5</sup> Notably, in 2013 CDC-NHSN modified the surveillance period from 365 to 90 days for sterile implant surgeries since the vast majority of SSI were documented within the first 90 days. In this study, we identified late SSI, occurring within 4–12 months after transplantation over a 5-year period in a major US transplant center.

### 2. Methods

#### 2.1. Study design

Observational single-center retrospective cohort study of all patients who underwent a SOT between January 1, 2015 and December 31, 2019 at Duke University Hospital (DUH). This study was approved by the DUH Institutional Review Board.<sup>6</sup>

#### 2.2. Study population

Eligible patients were 18 years or older and met the following criteria: **i**) SOT performed at DUH during the 5-year study period;

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and **ii**) 12-month post-transplant follow-up, unless death occurred before. Details on antimicrobial prophylaxis and immunosuppression protocols were previously described.<sup>6</sup>

#### 2.3. Definitions and adjudication process for surgical site infections (SSI)

SSI were defined as primary or secondary superficial incisional SSI, primary or secondary deep incisional SSI, and organ/space SSI. Deep incisional SSI and organ/space SSI were considered invasive SSI. For the primary analyses, only invasive primary SSI (IP-SSI) were considered.<sup>6</sup> SSI occurring within 3 months of transplant were defined as early SSI, while SSI occurring 4–12 months after transplant were considered late SSI. Relapse or recurrence of prior infections occurring 4–12 months after transplant were not considered late SSI. Of note, the definitions of SSI adopted in this study represent a modification of the 2021 CDC-NHSN definitions, since we extended surveillance from the recommended 90 to 365 days and we assessed the occurrence of SSI after lung and intestinal transplants, which are procedures not evaluated by CDC-NHSN.<sup>7</sup> Specifically, mediastinitis, sternal osteomyelitis, and pleural space infections occurring after lung transplant and intra-abdominal infections occurring after intestinal transplant were considered organ/space infections. Additional details on the adjudication process for SSI and additional study definitions are in our previous publication.<sup>6,8</sup>

#### 2.4. Study objectives

The primary aim of this study was to determine rate, microbiology, timing of diagnosis after transplant, and the clinical outcomes (length of transplant hospital stay, 1-year mortality, and 1-year



**Table 1.** Late surgical site infections identified among all solid organ transplant recipients at Duke University Hospital in the period Jan 1, 2015–Dec 31, 2019

Case	Year transplant	Organ transplant	Repeat transplant	Closure primary	SSI	Late SSI (days after transplant)	Area involved by late SSI	Mono-microbial SSI	Pathogen(s)	Gram negative MDR	Secondary bacteremia or fungemia	Return to the OR
1	2015	Liver	No	No	SIP	97	Primary incision	–	–	–	–	No
2	2016	Kidney	No	Yes	SIS	133	Percutaneous drain site	Yes	<i>Mycobacterium chelonae</i>	–	No	Yes
3	2017	Liver	No	Yes	SIP	106	Primary incision	–	–	–	–	Yes
4	2018	Lung	No	Yes	SIP	176	Primary incision	Yes	MRSA	–	No	Yes
5	2019	Lung	No	No	SIP	115	Primary incision	Yes	<i>Pseudomonas aeruginosa</i>	Yes	No	No
6	2019	Heart	No	Yes	SIP	359	Primary incision	Yes	MRSA	–	No	No
7	2015	Lung	No	Yes	IP-SSI	275	Left pleural cavity	Yes	<i>Staphylococcus epidermidis</i>	–	No	No
8	2015	Lung	No	Yes	IP-SSI	317	Left chest wall and sternum	Yes	<i>Candida albicans</i>	–	No	Yes
9	2015	Lung	No	Yes	IP-SSI	221	Sternum	Yes	<i>Candida albicans</i>	–	No	Yes
10	2015	Lung	No	Yes	IP-SSI	104	Right and left chest wall	No	<i>Pseudomonas aeruginosa</i> <i>Serratia marcescens</i> <i>Candida albicans</i>	No Yes	No	No
11	2015	Heart	No	No	IP-SSI	150	Sternum	No	VRE <i>Enterobacter cloacae</i>	Yes	No	Yes
12	2015	Kidney	Yes	No	IP-SSI	96	Intra-abdominal abscess	–	–	–	No	Yes
13	2016	Lung	Yes	Yes	IP-SSI	147	Sternum	Yes	MRSA	–	No	Yes
14	2016	Lung	No	Yes	IP-SSI	99	Sternum	Yes	<i>Pseudomonas aeruginosa</i>	No	No	Yes
15	2016	Heart	No	No	IP-SSI	183	Sternum	Yes	<i>Pseudomonas aeruginosa</i>	No	No	Yes
16	2016	Heart	No	No	IP-SSI	126	Sternum	Yes	<i>Lactobacillus zeae</i>	–	No	Yes
17	2017	Lung	No	No	IP-SSI	110	Left clamshell incision	Yes	<i>Malassezia furfur</i>	–	No	Yes
18	2017	Lung	No	Yes	IP-SSI	297	Sternum	No	MSSA <i>Pseudomonas aeruginosa</i>	No	No	Yes
19	2017	Lung	No	Yes	IP-SSI	175	Left pleural cavity and chest wall	Yes	MSSA	–	Yes	Yes
20	2017	Lung	No	No	IP-SSI	262	Sternum	Yes	<i>Staphylococcus epidermidis</i>	–	No	Yes
21	2017	Heart	No	Yes	IP-SSI	244	Sternum and ascending aorta	No	<i>Candida albicans</i>	–	No	Yes
22	2018	Lung	No	Yes	IP-SSI	94	Right pleural cavity	No	Mixed anaerobes <i>Malassezia furfur</i> <i>Mycobacterium abscessus</i>	–	No	Yes
23	2018	Lung	No	Yes	IP-SSI	99	Right pleural cavity and chest wall	Yes	<i>Pseudomonas aeruginosa</i>	Yes	No	No

(Continued)

Table 1. (Continued)

Case	Year transplant	Organ transplant	Repeat transplant	Closure primary	SSI	Late SSI (days after transplant)	Area involved by late SSI	Mono-microbial SSI	Pathogen(s)	Gram negative MDR	Secondary bacteremia or fungemia	Return to the OR
24	2018	Lung	No	Yes	IP-SSI	101	Left chest wound	Yes	<i>Corynebacterium striatum</i>	–	Yes	Yes
25	2019	Lung	No	Yes	IP-SSI	209	Right pleural cavity	Yes	<i>Pseudomonas aeruginosa</i>	No	No	Yes
26	2019	Lung	No	Yes	IP-SSI	300	Right pleural cavity	No	<i>Granulicatella adiacens</i> <i>Candida albicans</i>	–	No	Yes
27	2019	Lung	No	Yes	IP-SSI	185	Lung parenchyma and left pleural cavity	Yes	<i>Mycobacterium abscessus</i>	–	No	Yes
28	2019	Lung	Yes	No	IP-SSI	137	Left pleural effusion	Yes	<i>Klebsiella pneumoniae</i>	No	No	No
29	2018	Lung Heart	No	No	IP-SSI	191	Sternum	No	<i>Staphylococcus epidermidis</i> <i>Staphylococcus lugdunensis</i>	– –	No	Yes
30	2019	Lung Liver	No	Yes	IP-SSI	165	Sternum	Yes	MRSA	–	No	Yes
31	2019	Heart	No	No	IP-SSI	113	Pericardium and bilateral pleural cavities	Yes	<i>Pseudomonas aeruginosa</i>	No	No	Yes
32	2019	Heart	No	Yes	IP-SSI	91	Mediastinum	Yes	MSSA	–	Yes	Yes

\*SIP: superficial infection primary. SIS: superficial infection secondary. IP-SSI: invasive primary surgical site infection. MRSA: methicillin-resistant *Staphylococcus aureus*. MSSA: methicillin-susceptible *Staphylococcus aureus*. VRE: vancomycin-resistant *Enterococcus*.

graft failure) associated with late IP-SSI. Secondary aims included: **i)** determining the cumulative rate of late SSI; and **ii)** comparing microbiology and clinical outcomes of late and early IP-SSI.

### 2.5. Statistical analysis

SSI rates were calculated based on the total number of SOT (denominator) and total number of SSI (numerator). Temporal trends were assessed by Mann-Kendall test. When clinical outcomes were evaluated, patients diagnosed with early SSI were excluded from the analysis. Log-rank test was used to estimate the equality of survival functions. A two-sided *P* value of <.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics (version 29.0; IBM, Armonk, New York).

## 3. Results

### 3.1. Late SSI rates

2073 SOT recipients were included in the study (Figure S1);<sup>6</sup> 32 late SSI, including 6 superficial SSI and 26 IP-SSI, were identified (Table S2). The rate of late IP-SSI did not vary significantly over time (Figure S2). Of the 26 late IP-SSI, 25 (96.2%) occurred among thoracic SOT recipients (Table 1).

### 3.2. Late SSI microbiology

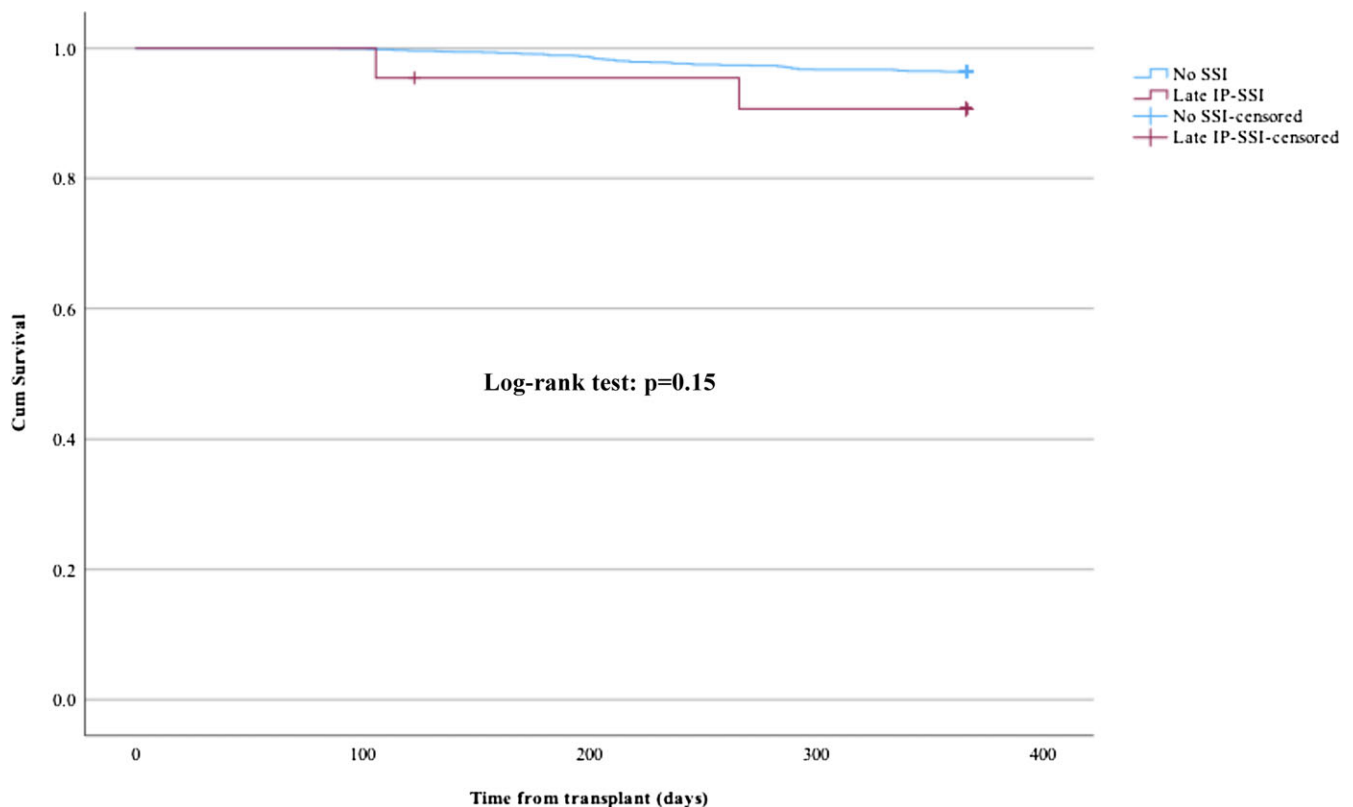
Microbiology of late SSI is detailed in Tables 1 and S3. Microbiology of late IP-SSI did not differ from the microbiology of early IP-SSI, as previously reported (Figure S4).<sup>6</sup>

### 3.3. Late SSI timing

Median time from transplant to late SSI was 148.5 (IQR 104.5–218.0) days. When only monomicrobial late IP-SSI were analyzed, time to IP-SSI differed based on the pathogen: yeast infections occurred later (232.5 days) than infections due to Gram positive (165.0 days) and Gram negative (125.0 days) bacteria (Figure S3). Only one monomicrobial non-tuberculosis mycobacterial late IP-SSI was diagnosed and this occurred 185 days after transplant.

### 3.4. Late SSI clinical outcomes

LOS during the index transplant admission was significantly longer for patients with late IP-SSI than for patients without SSI (39.0 days vs 15.0 days, *P* < .01) (Table S4). LOS did not differ among patients with late and early IP-SSI (Table S5). No significant differences in 1-year mortality and 1-year graft failure were documented among patients with late IP-SSI and patients without SSI (Table S6 and Figure 1). Finally, similar rates for 1-year



**Figure 1.** Survival curve in the first year after transplant for adult solid organ transplant recipients transplanted at Duke University Hospital in the period Jan 1, 2015–Dec 31, 2019 and diagnosed with late invasive primary surgical site infections (IP-SSI) versus those not diagnosed with surgical site infections (no-SSI) and alive at day 90.

mortality and 1-year graft failure were reported among patients with late and early IP-SSI (Table S7 and Figure S5).

#### 4. Discussion

Late IP-SSI have been rarely reported in the scientific literature,<sup>1–5</sup> perhaps driven by CDC-NHSN definitions and historical studies limiting surveillance to the early transplant period and excluding the evaluation of lung transplant surgeries. In our study, we identified 26 late IP-SSI over a 5-year period, suggesting that late IP-SSI are not uncommon and that surveillance for IP-SSI should be continued for up to 1-year post-transplant, particularly in the cardiothoracic transplant population. Notably, the 2021 CDC-NHSN definitions of SSI were revised in January 2024. The revised 2024 CDC-NHSN definitions of SSI recommend a 30-day surveillance period in the setting of solid organ transplant surgery (heart, kidney, and liver transplant surgery) and following thoracic surgery. Based on our data, median time from transplant surgery to late SSI diagnosis was 148.5 (IQR 104.5–218.0) days. Further, even early SSI were diagnosed > 30 days post-transplant, as shown by our prior publication.<sup>6</sup> Limiting surveillance and reporting to 30 days post-transplant would miss a substantial number of infections.

Surprisingly, the microbiology of late IP-SSI did not differ substantially from the microbiology of early IP-SSI.<sup>6</sup> Gram positive bacteria accounted for the majority of pathogens isolated in late IP-SSI, followed by Gram negative bacteria, and yeast. In this regard, it is worth noting that yeast infections tended to present later than bacterial infections, at a median of 232.5 days after transplant (Figure 1).<sup>9,10</sup>

When we assessed the clinical outcomes associated with late IP-SSI, we did not find a significant impact on 1-year all-cause mortality and 1-year graft failure, but we did find a significant association between late IP-SSI and longer index transplant hospital LOS.

This study has multiple limitations. Information bias may have affected data acquisition regarding late superficial SSI.<sup>6</sup> The external validity of this study is hampered by its single-center design. A detailed presentation of rate, microbiology, and clinical outcomes associated with early IP-SSI was previously published and thus out of scope for this manuscript.<sup>6</sup> Our assessment of the outcomes associated with late IP-SSI is hampered by the low number of late IP-SSI. Finally, evaluating risk factors for late IP-SSI was not among the aims of the present study. Future prospective studies are needed to identify factors leading to the development of late IP-SSI.

In conclusions, late IP-SSI occurring more than 3 months after transplant surgery were documented among 1.3% of transplant recipients. Careful surveillance for late IP-SSI should be maintained during the first year following surgery, especially for thoracic SOT recipients.

**Supplementary material.** To view supplementary material for this article, please visit <https://doi.org/10.1017/ice.2024.90>

**Data availability statement.** The data that support the findings of this study are available from the corresponding author upon reasonable request.

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