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## Concise Communication

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

Manuela Carugati MD[1], Sana Arif MD[1], Debra Lynn Sudan MD[2], Bradley Henry Collins MD[2], John Carroll Haney MD[3], Jacob Niall Schroder MD[3], John Michael Reynolds MD[4], Sarah Lewis Stamps MD[1], Michael E. Yarrington MD[1], Rachel A. Miller MD[1] and Barbara D. Alexander MD[1]

[1]Department of Medicine, Division of Infectious Diseases, Duke University, Durham, USA, [2]Department of Surgery, Division of Abdominal Transplant Surgery, Duke University, Durham, USA, [3]Department of Surgery, Division of Cardiovascular and Thoracic Surgery, Duke University, Durham, USA and [4]Department of Medicine, Transplant Pulmonology, Duke University, Durham, USA

**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.[1–5] 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.[6]

### 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; and **ii)** 12-month post-transplant follow-up, unless death occurred before. Details on antimicrobial prophylaxis and immunosuppression protocols were previously described.[6]

### 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.[6] 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.[7] 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.[6,8]

### 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

**Corresponding author:** Manuela Carugati; Email: manuela.carugati@duke.edu
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**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 | *Mycobacterium chelonae* | – | 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 | *Pseudomonas aeruginosa* | 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 | *Staphylococcus epidermidis* | – | No | No |
| 8 | 2015 | Lung | No | Yes | IP-SSI | 317 | Left chest wall and sternum | Yes | *Candida albicans* | – | No | Yes |
| 9 | 2015 | Lung | No | Yes | IP-SSI | 221 | Sternum | Yes | *Candida albicans* | -<br>- | No | Yes |
| 10 | 2015 | Lung | No | Yes | IP-SSI | 104 | Right and left chest wall | No | *Pseudomonas aeruginosa*<br>*Serratia marcescens*<br>*Candida albicans* | No<br>Yes | No | No |
| 11 | 2015 | Heart | No | No | IP-SSI | 150 | Sternum | No | VRE *Enterobacter cloacae* | 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 | *Pseudomonas aeruginosa* | No | No | Yes |
| 15 | 2016 | Heart | No | No | IP-SSI | 183 | Sternum | Yes | *Pseudomonas aeruginosa* | No | No | Yes |
| 16 | 2016 | Heart | No | No | IP-SSI | 126 | Sternum | Yes | *Lactobacillus zeae* | – | No | Yes |
| 17 | 2017 | Lung | No | No | IP-SSI | 110 | Left clamshell incision | Yes | *Malassenzia furfur* | – | No | Yes |
| 18 | 2017 | Lung | No | Yes | IP-SSI | 297 | Sternum | No | MSSA<br>*Pseudomonas aeruginosa* | 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 | *Staphylococcus epidermidis* | – | No | Yes |
| 21 | 2017 | Heart | No | Yes | IP-SSI | 244 | Sternum and ascending aorta | No | *Candida albicans* | – | No | Yes |
| 22 | 2018 | Lung | No | Yes | IP-SSI | 94 | Right pleural cavity | No | Mixed anaerobes<br>*Malassenzia furfur*<br>*Mycobacterium abscessus* | – | No | Yes |
| 23 | 2018 | Lung | No | Yes | IP-SSI | 99 | Right pleural cavity and chest wall | Yes | *Pseudomonas aeruginosa* | Yes | No | No |

(*Continued*)

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**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 | *Corynebacterium striatum* | – | Yes | Yes |
| 25 | 2019 | Lung | No | Yes | IP-SSI | 209 | Right pleural cavity | Yes | *Pseudomonas aeruginosa* | No | No | Yes |
| 26 | 2019 | Lung | No | Yes | IP-SSI | 300 | Right pleural cavity | No | *Granulicatella adiacens Candida albicans* | – | No | Yes |
| 27 | 2019 | Lung | No | Yes | IP-SSI | 185 | Lung parenchyma and left pleural cavity | Yes | *Mycobacterium abscessus* | – | No | Yes |
| 28 | 2019 | Lung | Yes | No | IP-SSI | 137 | Left pleural effusion | Yes | *Klebsiella pneumoniae* | No | No | No |
| 29 | 2018 | Lung Heart | No | No | IP-SSI | 191 | Sternum | No | *Staphylococcus epidermidis Staphylococcus lugdunensis* | - - | 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 | *Pseudomonas aeruginosa* | 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);[6] 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).[6]

### 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

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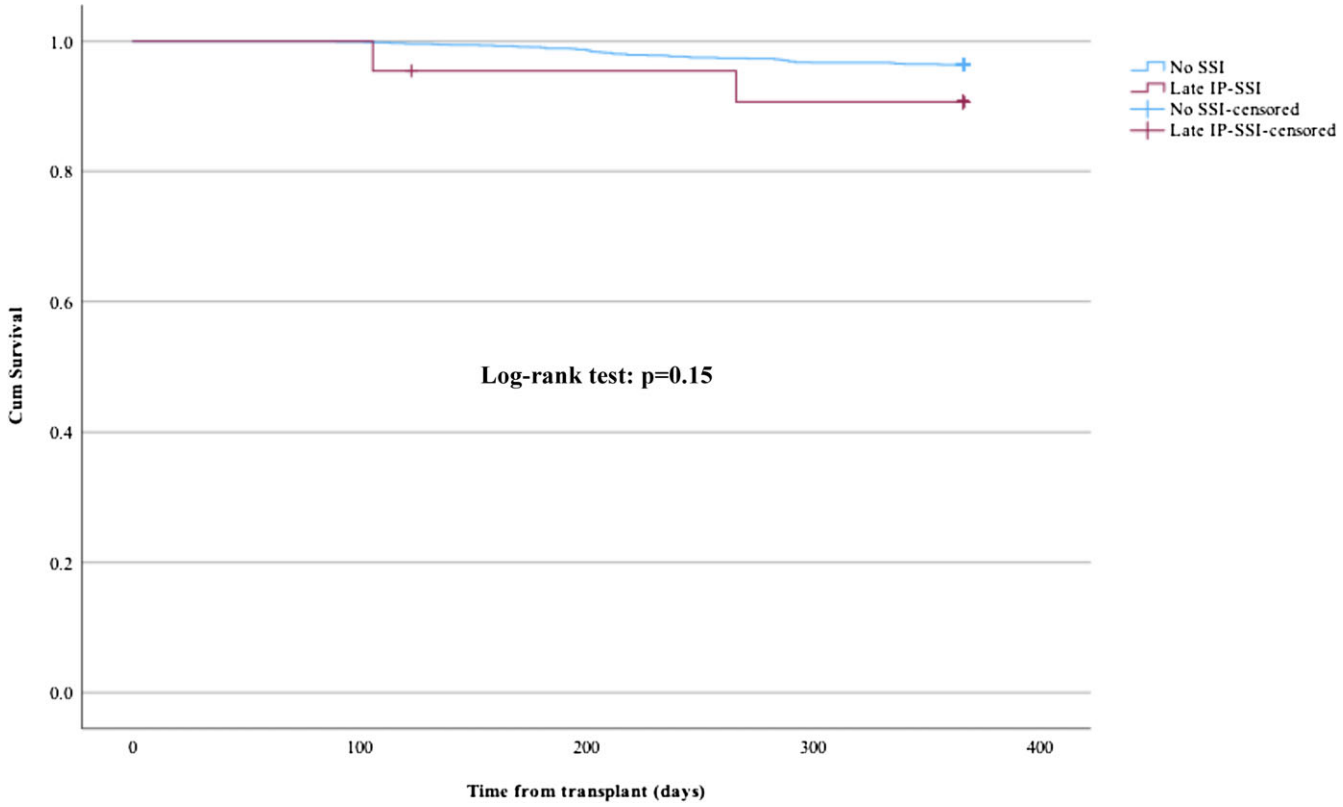


**Figure 1.** Survival curve in the first year after transplant for adult solid organ transplant recipients transplanted at Duke University Hospital in the period Jan 1, 2015–Dec 31, 2019 and diagnosed with late invasive primary surgical site infections (IP-SSI) versus those not diagnosed with surgical 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,[1–5] 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.[6] 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.[6] 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).[9,10]

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.[6] 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.[6] 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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