

Abstract

Background: *C. difficile* infection (CDI) is an important infectious complication in solid organ transplant (txp). We sought to describe epidemiology and risk factors for CDI in lung txp.

Objectives: Primary objective was to evaluate epidemiology and describe incidence of CDI in lung transplant recipients. Secondary objective was to identify risk factors that predispose recipients to CDI.

Methods: Retrospective chart review (1/1/2008 to 12/31/2012) of index hospitalization for lung txp at a single institution. Demographics and risk factors including antibiotic (abx) exposure were evaluated. Impact of metronidazole for CDI prophylaxis was also examined. CDI was defined as positive EIA or PCR. Inclusion criteria were adult lung transplant recipients during index admission for transplant. No specific exclusion criteria were applied. Analytical techniques included univariate analysis, stepwise multivariate logistic regression analysis using SPSS 11.5 Software, Chicago, IL, USA.

Results: 529 lung txps (212 single, 312 bilateral, and 5 heart/lung) occurred over the 5 year period. Demographics included mean age 57±13 years, 66% male, and median hospital LOS 20 days (IQR 12-38). Overall incidence of CDI was 5% (25 cases) at 30 days and 7% (38 cases) at 90 days post-transplant. Incidence varied by year; 7% in 2008, 3% in 2009, 7% in 2010, 16% in 2011, and 5% in 2012 (p=0.002). Median time to CDI was 11 (IQR 6-37) days. Complications from CDI occurred in 6/38 cases; megacolon (n=3), perforation (n=1), ICU transfer (n=1) and hospital death (n=2). 43 patients (8%) received metronidazole 250 mg q8 hrs as CDI prophylaxis; 3/43 (7%) developed CDI at 30 days and 5/43 (12%) developed CDI at 90 days. Metronidazole prophylaxis was not associated with a lower CDI incidence at either time point. Cases of CDI at 30 days were compared to controls to evaluate risk factors. The only independent risk factors for CDI were IV abx use > 14 days (OR 2.96, 95% CI 1.17-7.48, p=0.022) and 3rd & 4th gen cephalosporin use (OR 2.84, 95% CI 1.19-6.8, p=0.019). Hospital mortality was 16% (4/25) in CDI cases vs 6% (29/504) in controls, p=0.062.

Conclusion: In the first 90 days post-txp, CDI occurred in 7% of patients, with about half of cases occurring within 10 days of txp. Abx exposure, especially 3rd & 4th gen cephalosporins and longer durations were independent risk factors for CDI. Judicious selection and duration of abx is paramount to preventing CDI in lung txp.

Background

- Prior studies have demonstrated significant morbidity and mortality associated with CDI in lung transplant recipients
- Patients at the Cleveland Clinic may receive metronidazole 250mg every eight hours as prophylaxis for CDI, although this practice is not supported by IDSA/SHEA guidelines
- The incidence and risk factors for CDI development after lung transplantation are not clear

Results

Table 1: Demographics	Total (N=529)
Age (years), mean ± SD	57±13
Gender (male), n (%)	349 (66)
Hospital LOS*, median (IQR)	20 days (12-38)
ICU [†] LOS, median (IQR)	6 (4-15)
Type of Transplant	
Unilateral transplant, n (%)	212 (40)
Bilateral transplant, n (%)	312 (59)
Heart-lung transplant, n (%)	5 (0.9)

* LOS = Length of Stay
[†] ICU = Intensive Care Unit

Table 2: Overall incidence of CDI	N = 529
30 days post-transplant n (%)	25 (5)
90 days post-transplant n (%)	38 (7)
CDI complications*	6/38 (16)

*Complications included: megacolon (3), perforation (1), ICU transfer (1), hospital death (2)

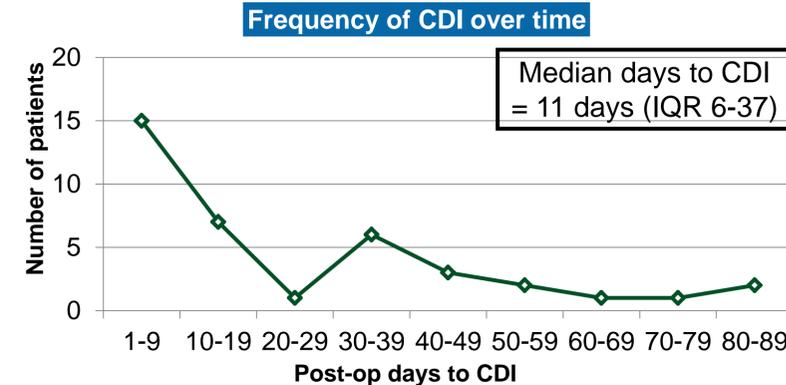
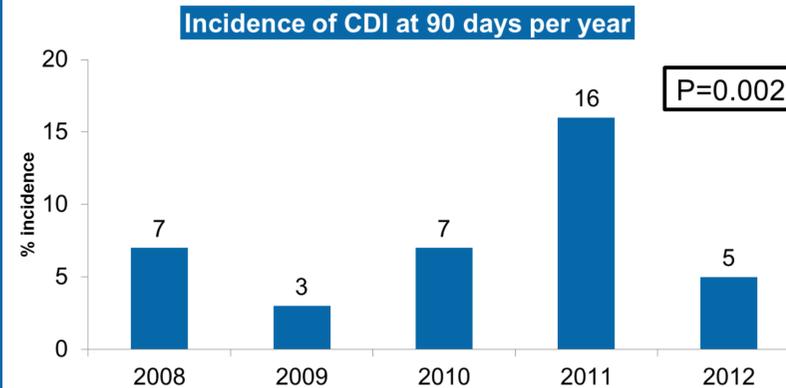


Table 3: Risk Factors for CDI at 30 days

Variable	Case N=25	Control N=504	P-Value
Hospital LOS, median (IQR)	28 (18-59)	20 (12-37)	0.024
ICU LOS >14 days n (%)	10 (40)	122 (24)	0.095
Acute rejection n (%)	2 (8)	40 (8)	1.00
Hospital stay prior to transplant n (%)	8 (32)	97 (19)	0.126
Intravenous abx >14 days n (%)	18 (72)	204 (41)	0.018
High risk abx ^{†‡} n (%)	18 (72)	293 (58)	0.213
Carbapenem use n (%)	13 (52)	149 (30)	0.025
3 rd , 4 th gen ceph use n (%)	10 (40)	73 (15)	0.002
PPI use >7 days n (%)	19 (76)	357 (71)	0.658
Hospital mortality n (%)	4 (16)	29 (6)	0.062

[†] High-risk antibiotics (abx) = fluoroquinolone (FQ), clindamycin (CL), a carbapenem or 3rd or 4th generation cephalosporin used during index admission
[‡] FQ and CL use were not significantly different between groups

Table 4: CDI Incidence with Metronidazole Prophylaxis

	Prophylaxis N=43	No Prophylaxis N=486	P-Value
CDI at 30 days n (%)	3 (7)	25 (5)	0.446
CDI at 90 days n (%)	5 (12)	38 (8)	0.222

Results

Table 5: Multivariate Analysis of Risk Factors for CDI at 30 days*

Variable	Adjusted OR (95% CI)	P-Value
IV antibiotic use > 14 days	2.96 (1.17-7.48)	0.022
3 rd , 4 th gen cephalosporin use	2.84 (1.19-6.8)	0.019

* Factors entered into the model included IV antibiotic use > 14 days, hospital stay prior to transplant, ICU LOS, carbapenem use, and use of a 3rd or 4th generation cephalosporin. Only independent predictors of the outcome are presented in the table.

Discussion

- We sought to characterize epidemiology and risk factors for contracting CDI in lung transplant recipients at Cleveland Clinic
- The overall incidence of CDI was comparable to previous studies
- The median time to CDI was 11 days and about half of cases occurred within the first ten days post-transplant
- Hospital mortality was more frequent in CDI cases, but this difference was not statistically significant
- Metronidazole prophylaxis was not associated with a lower CDI incidence at either time point
- The only independent risk factors for CDI were IV abx >14 days and 3rd and 4th generation cephalosporin use
- Limitations included the retrospective nature of the study and that evaluation at a single institution may limit external validity

Conclusions

- CDI occurred in 7% of recipients within the first 90 days post-transplant with about half occurring within the first 10 days
- Antibiotic exposure, especially 3rd & 4th generation cephalosporins and longer durations were independent risk factors for CDI
- Judicious selection and duration of antibiotics is paramount to preventing CDI in lung transplants recipients

References

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