EP0173
ePoster Session
Clostridium difficile: news on clinical epidemiology and novel approaches to therapy

Distinguishing C. difficile recurrence from reinfection – poor performance of current recommendations

Ana Durovic[1], Andreas F. Widmer[2], Reno Frei[3], Sarah Tschudin-Sutter*[4]

[1]*University Hospital Basel, Basel, Switzerland*

[2]*University Hospital Basel, DIV. of Infectious Diseases & Hospital Epidemiology, Basel, Switzerland*

[3]*University Hospital Basel, Department of Laboratory Medicine, Division of Clinical Microbiology, Basel, Switzerland*

[4]*., Basel, Switzerland*

Background: Guidelines on *Clostridium difficile* infection (CDI) suggest defining recurrence as re-appearing CDI within 8 weeks after the onset of a previous episode - providing resolution of prior symptoms. CDI diagnosed after 8 weeks from initial diagnosis is considered as reinfection. To date, this timeframe has not been validated for its ability to distinguish recurrence of infection with the same strain of *C. difficile* as identified during initial diagnosis from reinfection with a new strain. Our objective is to validate the proposed eight-week timeframe for distinguishing recurrent CDI from reinfection and to compare respective patient characteristics.

Material/methods: From 01/2004 to 12/2013 a cohort of all inpatients diagnosed with CDI at the University Hospital Basel, Switzerland was established and toxigenic *C. difficile* strains were prospectively collected. CDI was defined according to standard criteria endorsed by the European Society for Clinical Microbiology and Infectious Diseases (ESCMID). In patients diagnosed with a second episode of CDI, both respective *C. difficile* strains were submitted to PCR-ribotyping using high-resolution capillary gel-based electrophoresis. The standard definition of recurrence (i.e. occurrence of a second episode of CDI within an 8-week period after initial diagnosis) was evaluated for its performance to predict microbiologically confirmed recurrence, defined as identification of the same strain of *C. difficile* in both CDI episodes, and reinfection, defined as identification of two different strains of *C. difficile* in both episodes.

Results: Among 750 patients diagnosed with CDI, 130 (17.3%) were diagnosed with either recurrence or reinfection. Strains from both episodes of CDI were available from 106 patients, of which 47 (6.5%, 47/726) were considered as recurrence based on the standard definition and 59 (8.1%, 59/726) as reinfection. Identical strains were identified during both episodes of CDI in 36 patients with recurrence (36/47) and 27 patients with reinfection (27/59). Sensitivity, specificity, negative and positive predictive value of the standard criteria were 57.1%, 74.4%, 76.6%, and 54.2%, respectively. Time from initial diagnosis of CDI to second episode was associated with reinfection with a different strain (OR 1.31 95%CI 1.09-1.56, p=0.003 per week) with the receiver operating characteristic curve having an area under the curve of 0.666). Patients with a second episode of CDI caused by the same strain as initially detected, were older than patients with reinfection caused by a different strain, while other baseline characteristics and exposures did not differ (table).

Conclusions: The 8-week cut-off for distinguishing recurrent CDI from reinfection shows poor overall performance characteristics and time between the first and the second CDI-episode shows low

measures of discrimination for episodes of CDI caused by identical or different strains. Our results question the utility of this broadly used standard definition of recurrence for determining this important outcome measure in studies of CDI.

Table

	Patients with CDI recurrence (n=63)		Patients with *C. difficile* reinfection (n=43)		p-value
	n/median	**%/IQR**	**n/median**	**%/IQR**	
Demographics					
Age (years)	68	59-77	61	49-69	**0.012**
Male gender	38	60.3	22	51.2	0.350
Hospital onset CDI	45	71.4	33	76.7	0.542
Hospital days after diagnosis of CDI	15	8-30	11	6-26	0.499
Comorbidities					
McCabe Score					0.730
Nonfatal disease	26	41.3	20	46.5	
Ultimately fatal disease	28	44.4	19	44.2	
Rapidly fatal disease	9	14.3	4	9.3	
Charlson Comorbidity Index	3	2-5	3	2-5	0.633
Bone marrow transplant	3	4.8	5	11.6	0.265
Solid organ transplant	5	7.9	6	14.0	0.347
Exposures					
Antibiotics within the last 8 weeks	55	87.3	39	90.7	0.758
Steroids within prior 7 days	12	19.1	9	20.9	0.809
Other immunosuppressants within prior 7 days	10	15.9	12	27.9	0.150
Antacids within prior 7 days	45	71.4	29	67.4	0.661
Chemotherapy within prior 3 Months	17	27.0	11	25.6	0.872
CDI severity					0.708
Severe CDI	15	23.8	13	30.2	
Severe/complicated CDI	1	1.6	0	0.0	
Treatment of initial episode					
Metronidazole	56	88.9	40	93.0	0.737
Vancomycin	7	11.1	3	7.0	0.737
Surgery	0	0.0	0	0.0	-
Death during hospital stay	3	4.8	2	4.7	1.000