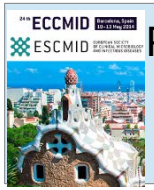

Population dynamics of *Staphylococcus aureus* recovered from the airways of cystic fibrosis patients during a longitudinal prospective observational multicenter study

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Introduction

Cystic fibrosis patients suffer from chronic recurrent bacterial infections of the airways, which lead to lung insufficiency and early death (1). *Staphylococcus aureus* is not only the first but also one of the most prevalent and persistent pathogens cultured from the airways of CF-patients (2). The aim of this prospective longitudinal multicenter study was to dissect colonization from infection in patients with *S. aureus* cultured from the airways by determining a variety of host- and pathogen specific parameters.

Materials and Methods

Inclusion criteria: confirmed CF-diagnosis; >6 years to be able to perform lung function tests; persistent *S. aureus* cultures from airway specimens within the year before recruitment.

Exclusion criteria: persistent *P. aeruginosa* and/or *Burkholderia cepacia* infection one year prior recruitment or during the study period of 21 months.

Microbiology: Specimens were processed at the central study laboratory in Muenster according to CF microbiology requirements (3). *S. aureus* isolates from primary cultures were distinguished by phenotypical appearance (hemolysis, pigmentation, size). All isolates were analyzed by *spa* sequence typing (4).

Participating centers

The study was registered: ClinicalTrials govIdentifier: NCT00669760

Results

Data were collected for 195 patients from 16 centers in Germany and 1 center in Austria. 75 female (38.5%) with a mean age of 15.7 years (range 5 to 41 y) were recruited; 49% patients were ΔF508 homozygous.

Data from 1359 visits were evaluated (mean visits/ patient: 7). 1381 of 1897 specimen (73%) were positive for *S. aureus*. 3963 Isolates of 191 patients were analyzed. The isolates were assigned to 269 different *spa* types. Eleven isolates were non *spa* typable.

spa types per patient

spa types	# of patients	%
1	33	17
2	59	31
3	33	17
4	22	11
5	15	8
6	14	7
7	5	3
8	3	2
10	2	1
11	2	1
12	1	0

spa types per center

spa types	centers	%
179	1	66
46	2	17
18	3	7
5	4	2
4	5	1
6	6	2
1	7	0,4
3	8	1
3	9	1
1	10	0,4
1	12	0.4
1	14	0,4
1	16	0,4

Most prevalent *spa* types

centers	# of patients	*spa* type
16	32	t084
14	27	t091
12	18	t015
10	18	t008
9	16	t002
9	14	t056
9	12	t056
8	15	t012
8	10	t005
8	10	t065

Clones with mutations in a single patient

spa type	1	2	3	4	5	6	repeats	mutation
t002	x	x	x	x	x		26-23-17-34-17-20-17-12-17-16	
t2164						x	26-23-17-34-17-82-17-12-17-16	pm
t3012				x			26-23-23-17-34-20-17-12-17-16	pm
t509	x	x				x	26-23-17-20-17-12-17-16	del
t5685	x						26-17-20-17-12-17-16-17-12-17-16	del+dupl
t5686		x					26-23-17-20-17-12	del
t6376			x				26-23-17-34-17-17-34-12-17-16	del+dupl
t686					x		26-23-17-34-17-20-17-12-17-17	pm

Clones during visits

C	P	*spa* type	1	2	3	4	5	6	7	8	9
14	24	t021	x	x	x	x	x	x	x	x	x
1	4	t050	x	x	x	x	x	x	x	X	
		t295					x				
		t024						x			
		t008						x		x	
		t6172						x			

C= center; P= patient;
numbers are visits during the observation period

Conclusions

- Most patients were infected by their individual clone, while 4 clones were present in many CF centers and in many patients. Such distribution indicates that CF patients acquire not only special but also clones, which are prevalent in the community.
- In most patients one clone persisted, while several other clones could be isolates sporadically.
- Most clones with mutations in the *spa* repeat region were only isolated once indicating that such mutations were not superior compared to the original clone

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