Comparison of Pulsed-Field Gel Electrophoresis and Whole Genome Sequencing in Clostridium difficile Typing


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Background
Clostridium difficile (C. difficile) causes healthcare-associated diarrhea and is a major cause of morbidity and mortality in hospitalized patients. Effective infection control and outbreak management require accurate typing methods.

Pulsed-field gel electrophoresis (PFGE) is a common typing method for Clostridium difficile (C. difficile).

Methods

• 467 C. difficile isolates were collected in a cohort study on host and pathogen factors of C. difficile infection, in 2006-2007
• Each isolate originated from a unique patient (colonized or infected)

Typing

• PFGE was performed at time of study using standard methods
  • Patterns were categorized using 80% similarity as determined by dendrogram analysis using Dice coefficients (BioNumerics)
  • Strain relatedness was assessed using Tenover’s criteria
  • Four possible categories: indistinguishable, closely related, possibly related, or different

• WGS was performed in 2015 using the Illumina HiSeq 2500 platform
  • Reads were mapped to reference genome CD630 using Stampy
  • Single nucleotide variants (SNVs) between isolates were identified using Samtools, after quality filtering

Comparison

Numbers of SNVs across all possible pairs were compared with PFGE categories

Adjusted Wallace coefficient2 was calculated to assess congruence between the methods

Simpson’s index was calculated to assess discriminatory power

Results

Table 1. Numbers of SNVs among PFGE categories

Table 2. Simpson’s index of diversity

Table 3. Adjusted Wallace coefficient (95% CI)

Discussion

• C. difficile strain relatedness assessment correlated between PFGE and WGS, but the higher resolution of WGS showed that PFGE classified a significant portion of genotypically distinct isolates as related.

• The Simpson’s index shows that WGS has higher discriminatory power, with 2 strains chosen at random having 97.3% probability of belonging to 2 different types.

• WGS can further refine molecular links in the epidemiology of C. difficile infection transmission.

Conclusion

References