IBD and CDI: The contrasting views of international clinical professionals

Stallmach A[1], Anttila VJ[2], Hell M[3], Gwynn S[4], Merino-Amador P[5],Petrosillo N[6], Ráčil Z[7], Warren T[4], Wenisch C[8], Wilcox M[9]

[1]Universitätsklinikum Jena, Germany, [2]Helsinki University Hospital, Helsinki, Finland, [3]Zentrum für Krankenhaushygiene und Infektionskontrolle, Salzburg, Austria, [4]Triducive Ltd, UK, [5]Hospital Clinico San Carlos, Madrid, Spain, [6]National Institute for Infectious Diseases "L. Spallanzani", Rome Italy, [7]LF Masarykovy univerzity a Fakultní nemocnice Brno, Czech Republic, [8]Süd Kaiser Franz Josef Spital, Vienna, Austria, [9]Institute of Biomedical and Clinical Sciences, Leeds, UK

Background

C. difficile infection (CDI) varies in severity in different patient groups. In patients with inflammatory bowel disease (IBD), CDI is a risk factor for both morbidity and mortality[1]. Interaction between the two disease processes may result in more severe colitis[2] than either condition alone. Currently there are a paucity of data concerning outcomes in patients with IBD who also have CDI, meaning that the appropriate choice of treatment strategy may be unclear. Guidance on best practice in the treatment of CDI in patients with IBD is therefore needed urgently.

Objectives

This consensus project examines the issues impacting clinical professionals working with IBD and CDI. It aims to understand the perceptions and attitudes of key stakeholders regarding best practice in the management of CDI in patients with IBD. Areas of controversy can thus be identified and addressed in order to improve patient outcomes.

Methodology

A multidisciplinary group of clinicians who treat patients with IBD and CDI met in May 2015 to discuss and clarify the management of these patients. Six key themes were identified and following further discussion, 27 consensus statements (Table 1.) were developed and submitted to respondents from around the world by questionnaire at conferences and congresses. Statements were grouped into six themes as shown in Table 1.

Respondents were asked to rate their agreement with each statement using a 4-point Likert scale. A modified Delphi methodology[3] was used to review responses. In accordance with Best Practice[4,5], a level of 75% agreement was defined as a threshold for consensus for each statement.

Results

423 respondents completed questionnaires, distributed across the professional roles shown in table 2. 361 respondents were from Europe.

Table 1. Individual Statements and Overall Scores (% agreement)

Statement:	%
CDI outcomes	
1. The 'severity of disease' is different to the 'severity of outcomes' in CDI	**74.3**
2. 30-day outcome (mortality, recurrence, colectomy) is a more important measure of success than initial clinical response	**83.6**
3. The risk factors that predict a poor 30-day outcome are clear and easily recognisable	**46.4**
4. Risk factors associated with poor outcome (e.g. mortality, recurrence, colectomy) should be determined early	**92.6**
5. Patients with non-specific markers suggestive of severe disease such as fever, pain and disorientation should be managed more closely than those without such markers	**88.3**
6. Severity of the disease should be considered alongside patient clinical background when predicting severity of outcome	**94.7**
7. I feel confident that I am able to recognise risk factors of severe disease and patient characteristics that predict a poor 30-day outcome in CDI	**76.0**
8. Patients with risk factors for poor outcomes should be evaluated more frequently and more aggressive management used earlier than patients without such risk factors	**93.1**
Defining recurrence of CDI	
9. There is an accepted definition of recurrent CDI	**70.8**
10. Recurrence of CDI should include both relapse and reinfection	**83.2**
11. The definition of recurrent CDI should be tailored to the individual patient background	**62.2**
12. Testing is required as part of a diagnosis of recurrent CDI	**86.4**
13. Prevention of recurrence is a major therapeutic goal	**96.1**
Diagnosis of CDI and IBD	
14. IBD is an independent risk factor for CDI	**84.1**
15. The testing strategy for CDI in patients with IBD should be the same as for those without IBD	**70.8**
16. The interpretation of CDI test results in patients with IBD may differ from those without IBD	**65.2**
Guidelines for CDI in IBD patient management and testing	
17. Current guidance on CDI testing and management is evidence-based but lacks robustness (strength of evidence)	**78.3**
18. A two-stage diagnosis is required for all patients (e.g. including IBD patients) being tested for CDI	**76.4**
19. A daily assessment is required for all inpatients to measure response to therapy	**76.1**
20. Higher quality evidence is required to inform future CDI guidelines	**93.0**
21. I feel confident to recognise when to change specific anti-CDI therapy in a failing patient	**74.4**
Treatment choice in patients with CDI and IBD	
22. CDI outcomes in patients with IBD are worse than in the general CDI population	**84.3**
23. The most efficacious treatment option recommended for CDI should be administered to IBD patients with CDI	**83.8**
24. Immunosuppressants should not be reduced when treating CDI in patients with IBD	**62.0**
25. If patients with IBD do not respond to CDI treatment, the level of immunosuppression should be increased	**37.9**
Faecal microbiota transplantation (FMT) in IBD	
26. Faecal microbiota transplantation reduces recurrence of CDI in patients with IBD	**83.3**
27. Faecal microbiota transplantation should be routinely offered to IBD patients with recurrent CDI	**57.6**

Figure 1. Plot of Total Agreement Scores

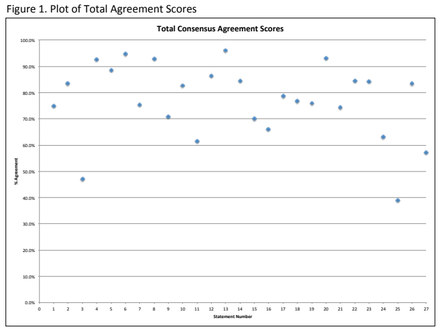


Table 2. Respondents by Specialty

Specialty:	n:
Infectious Diseases	104
Microbiology	95
Unknown	78
Gastroenterology	63
Intensive medicine	38
Consultant Physician (Unknown Specialty)	17
Internal Medicine	16
Pharmacist	5
General Practitioner	4
Nurse	3
Total:	**423**

The largest single group of respondents was Infectious Disease specialists (n=104), followed by microbiologists (n=95). 17 of the 27 statements (62.9%) achieved consensus with agreement scores of 75% or greater (Figure 1.). Responses were received from 23 countries (Table 3.). Some difference was seen between respondents from various countries with most of the responses from Germany being from gastroenterologists.

Table 3. Respondents by Country

Country:	n:
Other countries including Asia and Far East	52
USA	10
Europe (total)	361
Germany only	90
Spain only	54
Greece only	34
Italy only	24
United Kingdom only	22
Total:	**423**

Discussion

Differences were observed between the perceptions of microbiologists and gastroenterologists as well as among countries (Figures 2 and 3). It was observed that unprompted recognition of risk factors is low amongst clinicians and a model for scoring symptom severity is required. In addition, clarity regarding clinical definitions of recurrent CDI is needed. Responses from other countries included a broader mix of specialties. This may explain relatively low levels of agreement from the German respondent group to statements 3 and 25.

Figure 2. Plot of Comparison of Consensus Scores Between Countries

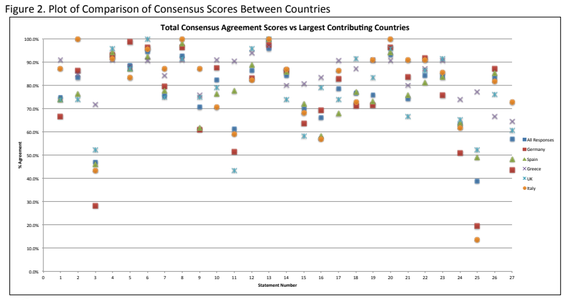
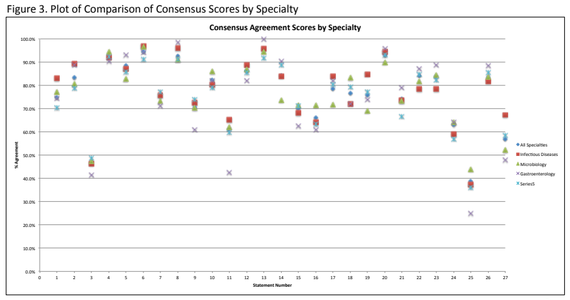


Figure 3. Plot of Comparison of Consensus Scores by Specialty



Conclusion

This research suggests that physicians consider that treatment strategy for CDI in IBD should be driven by risk factors for poor outcome rather than being solely defined by severity of disease. In addition, a uniformly accepted definition for recurrent CDI is needed for patients with IBD. A common approach to CDI in IBD would reduce variance in clinical practice between specialties and to achieve this, clinicians should be familiar with the role responsibilities of other specialties in managing CDI in IBD. Higher quality evidence is required to inform future CDI guidelines, including clarity regarding the adjustment of immunosuppression in patients with IBD. More data are required to define the place for faecal microbiota transplantation in CDI patients with IBD.

1. Takahashi M et al. Multi-institution case–control and cohort study of risk factors for the development and mortality of Clostridium difficile infections in Japan. BMJ Open 2014;4:e005665 doi:10.1136/bmjopen-2014-005665
2. Nizan O et al. Clostridium difficile and inflammatory bowel disease: Role in pathogenesis and implications in treatment. World J Gastroenterol. 2013 Nov 21; 19(43): 7577–7585.
3. Norman Dalkey, Olaf Helmer (1963) An Experimental Application of the Delphi Method to the use of experts. Management Science, 9(3), Apr 1963, pp 458-467
4. Von der Gracht H. Consensus measurement in delphi studies. Review and implications for future quality assurance. Technological Forecasting and Social Change. 79 (2012) 1525-1536
5. Murphy MK et al. Consensus development methods, and their use in clinical guideline development. Health Technology Assessment 1998; Vol 2: No 3

FDX/15/0064/EU(1)a Date of Preparation March 2016

This project and poster has been initiated and funded by Astellas EMEA and supported by Triducive Ltd.