The American Journal of Surgery 219 (2020) 513–514

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Discussion on: The morbidity of *C. difficile* in necrotizing pancreatitis☆

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DR. PAUL C. KUO (Tampa, Florida): In this paper, Tom and his colleagues report a retrospective review of prospective institutional database analysis. They examined all patients with necrotizing pancreatitis treated during the period 2005–2018. And the search generated a total of 704 patients. 10% of these patients developed CDI approximately 78 days after the onset of necrotizing pancreatitis.

I have a number of questions, and they are as follows: Was there any association of CDI with a specific antibiotic regimen? Was the presentation of CDI in the setting of necrotizing pancreatitis any different from the standard textbook description of CDI? Were any of the CDI patients initially on Flagyl for any other reason? And did this alter their presentation, your treatment strategy and/or their outcomes?

Now specifically within the methods, the patient population that you describe included two time periods during which your diagnostic methodology for CDI changed from an enzyme immunoassay to PCR. Did the change in diagnostic testing create two different study populations? Was there any difference between the two study populations?

And now having completed your study, and I think this is really the take-home message certainly for me and many in the audience, what is your current institutional protocol to the management not only of CDI, but how do you approach the patient with necrotizing pancreatitis for which the senior resident, chief resident or attending gets the call that Mr. and Mrs. Jones developed diarrhea last night? What do you do?

DR. MAATMAN: Thank you, Dr. Kuo, for your thorough review of our paper and lot of really important questions that are definitely take-home points. To answer your first question regarding the association of antibiotics, this was definitely one of the aims of the study, however, when we attempted to analyze specific antibiotics in the development of CDI, we were unable to really thoroughly do this because a significant number, about 80%, of our patients are transferred to our institution after about a week or several weeks of treatment at an outside facility. The data that we got from these hospitals in their transfer paperwork was very limited and often just included whether or not patients were given antibiotics but not the type.

Another really important question that you bring up that's another take-home point, is the second question you asked, evaluating the presentation of C. diff infection in the setting of necrotizing pancreatitis. And I think that it's important to keep in mind that the presentation is going to be masked by the symptoms from necrotizing pancreatitis, as most patients will have abdominal pain, abdominal distention, and may or may not have recently been initiated on tube feeds, which can contribute to diarrhea.

We did attempt to evaluate patients on whether or not they received Flagyl prior to development of necrotizing pancreatitis but, again, it was difficult to find antibiotics they were given at the outside facilities. We do know that in the 67 patients that developed CDI, none of them were on Flagyl at the time of diagnosis.

Regarding the question you asked about the two study groups that were identified from the change in diagnostic methods, we actually appreciate getting this question in advance. It gave us the opportunity to go back and look at the two study groups and compare them. We found no differences in demographic data, incidence of CDI, or outcomes between the two study groups.

Finally, as you mentioned, one of the key take-home points in the management of CDI in the setting of necrotizing pancreatitis that we discussed is to have a low threshold for diagnostic testing. I think in the patient that develops any diarrhea in the setting of necrotizing pancreatitis would be beneficial to test given the high incidence and their risk factors. Then as I showed in one of the graphs, the majority, about half of patients resolved with just oral Flagyl alone. So as long as the patient has enteral access and you're confident that the antibiotics are going to be absorbed enterally, I think that oral Metronidazole is appropriate.

DR. MARSHALL BAKER (Chicago, Illinois): Tom, this represents a tremendous amount of work on your part, and you should be congratulated for that. It's a huge series, and I hope you continue to kind of bang away at it, because I think you're going to teach us a lot about how to manage pancreatitis.

I have a couple questions for you. One of the things that I think you see a lot of in Indiana that we don't see maybe as much in other parts of the country for whatever reason is disconnected duct syndrome and really severe pancreatitis that ends up requiring a lot of operative intervention.

Did you notice that there were variations in rates of C. diff

DOI of original article: https://doi.org/10.1016/j.amjsurg.2019.08.006.

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https://doi.org/10.1016/j.amjsurg.2020.02.004

infection and how to manage those with the pattern of pancreatitis that you were seeing? The second thing is, I feel like during this study time period, our approach these folks got changed dramatically, you know, the step-up approach coming out from the Dutch group and that sort of thing. So can you comment on how that is being managed at IU and whether or not that is something you saw a relationship to C. diff rates?

DR. MAATMAN: One thing that we didn't analyze is the severity or the distribution of necrosis in association with C. diff. We just wanted to really evaluate the incidence, but we know that organ failure as a surrogate marker of severity is a risk factor for CDI. We didn't specifically analyze the types of intervention and the timing of the development of CDI in correlation to surgery if it was performed.

I agree there has been a significant change in the last ten years providing the treatment of necrotizing pancreatitis including everything from operative management but nutrition. We did not evaluate the effect of tube feeds and enteral nutrition on the rates of CDI compared to those patients that received TPN, but I think that would be interesting to go back and look at. I think our practices at our institution is early enteral feeding, so I think looking back I think it would be important to look at to see if that decreases the rates. I think in some literature it shows that that's protective.

DR. HEATHER DOLMAN (Detroit, Michigan): On that same vantage I just had a question, have you looked at any other risk factors besides oral nutrition such as immunocompromised or people who are on PPI at the same time that would cause your rates of C. diff to increase?

DR. MAATMAN: That's a great question, and that's something we haven't done. But I think it would be worth going back to make that addition to the manuscript. So hopefully we can do that.

DR. WILLIAM C. CIROCCO (Phoenix, Arizona): As far as institution protocol, there's a current trend to abandon PO Flagyl for PO Vancomycin as first line. And also, is fecal transplant available at your institution? And then, thirdly, these two cases that died that typically we see organ failure, which leads to a downward spiral, so do you think there was maybe perhaps a failure to intervene more quickly surgically in those two patients?

DR. MAATMAN: Thank you for those questions. I think they are some good points. I will answer your last question first. Going back to one of the key take-home points is that the symptoms from necrotizing pancreatitis can mask CDI and even its severity. Organ failure is often present, and so I think it's possible for patients to develop CDI and not really understand the severity of it. It's hard to tell if these patients were treated swiftly enough retrospectively. To answer your question regarding fecal transplant, it is available at our institution. None of these patients required it. I think either oral Flagyl or oral Vancomycin is appropriate, whatever the trends in the treatment are, keeping in mind the availability of enteral access in these patients. (Applause)