Dear Editors:

We have revised the manuscript as suggested by the reviewers. We have also revised some parts of the Introduction and Conclusion sections to include reviewers' suggestions.

We thank all referees for their critical and supportive comments, which we believe improved the manuscript substantially.

Thank you very much for the careful review of our manuscript.

Sincerely,

Junichi Iwamoto

Reviewer #1:
Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing)
Conclusion: Minor revision
Specific Comments to Authors: I think that the manuscript is well written. I ask the authors to read my suggestions and to include a few important facts in the introductory part of the paper. I wrote in which direction to discuss. After that the paper could be accepted for publication. What are the new hypotheses that this study proposed? What are the new phenomena that were found through experiments in this study? What are the unique insights that this study presented? What are the questions that this study prompts for the authors to do next? How might this publication impact basic science and/or clinical practice?

Replies to the comments from reviewer1

RESPONSE: Thank you for your suggestion.
We have added the sentences about the new hypotheses , new phenomena, unique insights and etc. as below in the 4th paragraph of Introduction part.

“Dysbiosis has been reported in several gastrointestinal diseases, especially a reduced *Clostridium* subcluster XIVa (XIVa). Since XIVa is thought to be the main bacterial cluster that metabolizes BAs in the human intestine[22,23], we have a new hypothesis that the BA profile in feces and in serum could be a convenient biomarker for intestinal XIVa activity. We have demonstrated the new facts that fecal and serum DCA/(DCA+CA) could be useful surrogate markers for the intestinal proportion of XIVa, including the inflammatory bowel diseases(IBD) and *Clostridium difficile* infection (CDI) [24,25]. The unique insight of this review is that this review focused on the studies using the BA calculated product/(product+substrate) ratio, which is not discussed enough in previous reviews. We believe these results are useful in clinical practice, and it is necessary to investigate various diseases in the future studies. ”

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: In this manuscript, the authors systematically summarize the relevant studies on serum and fecal bile acid profiles to evaluate intestinal dysbiosis and conclude that the DCA/(DCA+CA) ratio in stool and serum is a valuable marker for detecting intestinal microbiota imbalance without enterobacterial genetic analysis. However, the conclusions of this paper are not very accurate. It is necessary to systematically analyze a variety of intestinal flora and metabolic disorders related diseases, and analyze the metabolic system of bacteria related to previous diseases to ensure the accuracy of the conclusions.

Replies to the comments from reviewer2

RESPONSE: Thank you for your comment.

Although we searched the literature, we could not search and add the previous studies investigating the relationship between BA calculated product/(product+substrate) ratio such as DCA/(DCA+CA) ratio and variety of intestinal flora other than the shown studies in Table2. We have demonstrated that decreased *Clostridium* subcluster XIVa

(XIVa) exhibits a strong correlation with reduced intestinal BA metabolism and fecal and serum DCA/(DCA+CA) could be useful surrogate markers for the intestinal proportion of XIVa. We modified the sentence in the conclusion section as below because the DCA/(DCA+CA) ratio in feces and serum can serve as a surrogate marker of the intestinal dysbiosis caused by decreased XIVa.

“ Therefore, the DCA/(DCA+CA) ratio in feces and serum is a valuable marker for detecting dysbiosis caused by decreased XIVa without genetic analysis of enterobacteria. ”