It has been reported that bile acid reflux promotes the growth of esophageal epithelium via COX-2 and leads to esophageal carcinogenesis, and that Barrett's esophagus is the basis of its development (1-3). Hashimoto reported the experimental study, entitled as “Bile acids (taurocholic acid, taurodeoxycholic acid, taurochenodeoxycholic acid, tauroursodeoxycholic acid) develop esophageal cancer in a rat model of duodenoesophageal anastomosis after total gastrectomy” in the XX issue of AOE (Ann Esophagus 2020 http://dx.doi.org/10.21037/aoe-20-47). In this article, he examined whether reflux of duodenal juice to the esophagus was involved in esophageal carcinogenesis by using rat model of the esophagoduodenal anastomosis (EDA) with total gastrectomy. Then, they conclude that reflux of duodenal contents, especially bile acids, caused oxidative stress, subsequently induce COX-2, and induced esophageal carcinogenesis in EDA rat model. His findings are very interesting in the point that bile acid reflux would induce esophageal carcinogenesis as was shown by our molecular experimental study (4), but there could be several concerns to directly interpret this result to human esophageal carcinogenesis.

As well known, standing position is totally different between rat and human. Carcinogenesis of the thoracic esophagus, not of the abdominal esophagus, may be due to the use of rats, which are not upright animals like humans. Furthermore, histological and anatomical structure of esophagus and forestomach is different between rats and humans. Should the rat esophagus and stomach be considered physiologically synonymous? In this concern, regarding the method of collecting bile acid in rats, it was collected directly from the common bile duct using a thin tube in his study. The concentration of bile acid should be changed depending on the collection site of the common bile duct. The same concern can be said for the collection of bile acids in the esophagus. Bile acid concentration in the esophagus should have been higher than that of the duodenum depending on the part of the esophagus. About the cause of Barrett's esophagus, there could be two answers such as the direct effect by gastrectomy or the bile acid related development. How many years does the 40-week period set by the author correspond to in humans? The exposure time of bile acids in each rat is all 40 weeks. Why is it 40 weeks? If these are clarified, it will be applied to the medical treatment of esophageal carcinogenesis in humans.

In addition, although this is a model for developing both squamous cell carcinoma and adenocarcinoma of the esophagus, the mechanism of occurrence of these two different types of cancer is not considered to be the same, and molecular biological studies in this area are for future work. Even considering the above concerns, it is of great significance in the pathophysiological examination of how bile acid reflux affects esophageal carcinogenesis after gastrectomy. In the future, studying how drugs (5,6) that modify bile acid metabolism and enterohepatic circulation affect this mechanism may lead to the establishment of new preventive or therapeutic strategies for esophageal cancer.
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**Footnote**

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**References**


