

Reviewer #1:

In the manuscript entitled "Nutritional supplement drink reduces inflammation and postoperative depression in patients who have undergone off-pump coronary artery bypass surgery", the authors investigated the effect of daily intake of an herbal medicine-containing drink for rehabilitation in patients after coronary artery bypass surgery. I have only one minor comment for your consideration. Except the control and the YKR groups, additional placebo group (patients in the control group underwent the regular post-cardiac surgery course and consumed the placebo drink) is strongly recommended.

Response to Reviewer #1:

We appreciate on your precious suggestion. We did consider a placebo drink during the design of the study. The company informed us, however, that it would be difficult to provide a placebo drink as, due to the unique taste of the nutritional supplement drink, a consumer would be easily aware the difference. In addition, as this nutritional supplement drink is popular and commercially available at grocery stores in Japan, patients may be familiar with its packaging and taste. As you suggested, a placebo control is important since one of the main results of the study was the reduction of anxiety and depression after surgery, which might be come from the behavior itself of "taking a special drink" . In contrast, we also found other effects on the attenuation of inflammation, which might come from the herbal medicine contained in the drink. Instead of having a placebo control, we set the "control group" as normal treatment after surgery without taking any drink. Moreover, we randomly assigned patients to the control group to minimize bias.