**Dear Author(s)**

Our publication policy requires the return of your revised manuscript within **one week from** the date of receipt of this message.

When you submit a revised manuscript for further consideration, please make sure that all the suggested changes are incorporated into the manuscript. Also, Also, color any changes made throughout the text in yellow for ease of reference. Moreover, show the sentence that was removed from the article.

The final decision will be taken after the nature of your response letter and revision.

Authors should ensure that their article has been carefully checked for language, grammar, and style (where appropriate). This is in your interest as it will substantially reduce the time taken for the publication of your article.

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**Response letter must be based on the following pattern:**

**Reviewer Comments:**

**Reviewer A/**

**Problem 1:**

**Response 1:**

**Reviewer B/**

**Problem 1:**

**Response 1:**

**FOR EXAMPLE**

Reviewer Comments:

**REVIEWER A/Problem 1**  
**Comments:**

**Problem 1** Excelent initial Research is mandatory to confirm these Results in a Big Trial to use this method for the coronary patients  
**Reply 1:** Dear reviewer, thank you so much for your nice comments regarding our article.

We believe your concerns about our relatively small population, indeed we expressed this in limitation section, May be in the future we perform this study with a large population.

We added sentence to limitation section as’’ *Further prospective studies with larger participant are required for better determining the relationship between CD31 and coronary collateral development’’.*

**REVIEWER B/Problem 2**  
**Comments:**Title: Exploring the Role of CD31 in Coronary Collateral Development: A Critical Review Introduction: The paper delves into the intriguing realm of coronary collateral development, an area pivotal in understanding myocardial function in patients with coronary artery disease (CAD). It aims to elucidate the role of CD31, an angiogenesis marker, in this process. The introduction aptly contextualizes the significance of collateral arteries and highlights the existing gap in understanding their evolution. Methodological Rigor: The study design, a cross-sectional case-control approach, aligns with the research objective. However, several methodological considerations warrant attention.

*Dear reviewer, thank you so much for your nice comments regarding our article*.

**Problem 1**Firstly, the relatively small sample size and single-center nature diminish the generalizability of findings. *Dear reviewer, thank you so much for your comments.*

**Reply 1** We added sentence to limitation section follow as: **‘’**The relatively small number of patients included in the study and the single-center nature of the study limits the meaning of the study. Further prospective studies with larger participant are required for better determining the relationship between CD31 and coronary collateral development’’

**Problem 2** Secondly, the evaluation of collateral circulation solely through coronary angiography may overlook subtle nuances, necessitating complementary imaging modalities for comprehensive assessment. Furthermore, the absence of longitudinal follow-up limits insights into the dynamic nature of collateral development.

**Reply 2:** *Dear reviewer, thank you so much for your suggest. You are certainly right*.

We added this sentences to limitation section. *’’Detailed evaluation and long-term follow-up of collateral flow with more advanced imaging methods such as cardiac CT angiography could have increased the value of our study’’.*

**Problem 3** Results Interpretation: The study reports a significant elevation in CD31 levels among CAD patients compared to controls, corroborating existing literature on its association with vascular pathology. Additionally, the correlation between CD31 and collateral quality underscores its potential relevance in CAD management. However, the discussion of results lacks depth in addressing potential confounders and alternative hypotheses, detracting from the robustness of conclusions drawn.

**Reply 3** Atherosclerosis is a chronic inflammatory disease. Chronic inflammation is one of the conditions that trigger angiogenesis. Stimulation of angiogenesis is the physiological response of a tissue to ischemia. Compared to a single occluded coronary artery, the presence of an atherosclerotic process in other coronary vessels may have affected the CD31 level.

We added this sentence to discussion section ‘*’Including patients with only one occluded coronary artery and normal other coronary arteries could better show the effect of CD31 level on the collateral in patients’’.*

**Problem 4** Discussion and Implications: The discussion adeptly synthesizes findings within the broader context of collateral development and angiogenesis regulation. However, the paper falls short in addressing certain critical aspects.

Firstly, the discussion on metabolic factors influencing collateral formation lacks nuance, overlooking conflicting evidence and failing to integrate findings into a cohesive framework.

**Reply 4** *Dear reviewer, thank you so much for your suggest.*

We added this paragraph to discussion section. Follow as ‘’*One of the other metabolic conditions is renal dysfunction. Previous studies have shown that it is associated with good collateral in patients with low eGFR. In renal dysfunction, there may be ischemia and inflammation resulting from accelerated atherosclerosis’’.*

**Problem 5** Secondly, the extrapolation of CD31 as a therapeutic target warrants caution, necessitating further validation through robust clinical trials before clinical implementation.

**Reply 5** *Dear reviewer, thank you so much for your suggest. You are certainly right*.

Large-scale prospective randomized studies are required before CD31 can be used as a therapeutic target. We removed these sentences in the discussion and the conclusion section. ‘*In this context, it has the potential to be a therapeutic target in vascular permeability disorders and atherosclerosis.’ ‘If the results of this study are confirmed by more randomized large clinical trials, CD31 can be used as a therapeutic target in the appropriate patient population.’*

**Problem 6** Conclusion and Recommendations: The study presents intriguing insights into the role of CD31 in coronary collateral development, albeit with certain limitations. To enhance the rigor and clinical relevance of future research, adopting a multi-modal approach for collateral assessment, increasing sample size, and incorporating longitudinal follow-up are imperative. Moreover, elucidating the mechanistic underpinnings of CD31-mediated angiogenesis through experimental models would enrich our understanding and pave the way for targeted therapeutic interventions. Overall Assessment: While the study represents a commendable endeavor in unraveling the complexities of coronary collateral biology, it falls short in certain methodological and interpretative aspects. Addressing these limitations and embracing a more comprehensive approach would augment the scientific rigor and translational potential of future investigations in this domain  
**Reply 6**

*Dear reviewer,* thank you so much for your nice comments regarding our article.

The corrections and changes have been marked with yellow color in the manuscript.