Reviewer 1

1	The authors evaluated SDC-1 in plasma samples of convalescent non-hospitalized patients with COVID-19, hospitalized patients with mild COVID-19 and control non-infected patients, observing elevated SDC-1 levels in both hospitalized and convalescent patients compared to control ones, thus supporting undergoing endothelial damage. Some points need to be clarified:	➔ We thank the reviewer for his good advice to improve the publication.
2	groups of patients need to be better described in terms of severity (refer to WHO grading scale) and potential selection biases in the group of non-hospitalized patients should be eventually discussed or, otherwise, it is advisable to state that no potential biases have been identified	➔ Thank you, this is a good point. The classification we used for COVID-19 inpatients (critical/severe/moderate) corresponds to the WHO classification (critical/severe/non severe). We adapted the classification we used to the WHO classification and added this in the methods section. **2. Methods** *2.1. Study Subjects and Samples* Samples were collected in the first 48 hours after hospital admission. Disease severity was defined using the World Health Organization (WHO) severity categorization as critical (requires life sustaining treatment, presence of acute respiratory distress syndrome (ARDS), sepsis, septic shock), severe (oxygen saturation <90% on room air, signs of pneumonia, signs of severe respiratory distress), or non-severe (absence of signs of severe or critical disease). ARDS

		was diagnosed according to the Berlin definition (bilateral opacities on chest radiograph, exclusion of other causes of respiratory failure) [13]. Thank you for this important aspect. All three groups studied (hospitalized COVID-19 patients, convalescent patients and healthy controls) are age and BMI matched. Compared with the healthy controls, more men were included in the convalescent and hospitalized patients. We added this as a limitation in the Methods section and Discussion. **3. Results** **3.1. Cohort Characteristics** The convalescent COVID-19 patients, hospitalized patients, and healthy controls showed no significant differences regarding patient age and body mass index (BMI). There was no difference in gender between hospitalized COVID-19 patients and convalescent patients; significantly more women were included in healthy controls (p=0.046). **4. Discussion** The overrepresentation of women in the healthy cohort must be considered as a limitation of our study. Compared with the collective of healthy controls of Karampoor et al., the control collective used in this study showed comparable mean syndecan-1 levels (Karampoor et al. 24 (23-32) ng/mL versus 31.6 (17.1–54.7) ng/mL in our study).
3	time of sampling of hospitalized patients (as time from symptoms onset) need to be reported: during hospitalization, at the beginning of the diseases or at the end of clinical course.	➔ Thank you, this is a good point. Blood sampling of hospitalized COVID-19 patients was performed in the first 48 hours after hospital admission. We have added this to the methods section. In median, blood collection

		occurred 6 days after symptom onset (IQR 2-17). We added this in the section 3.1 Cohort Characteristics. 2. Methods 2.1. Study Subjects and Samples Samples were collected in the first 48 hours after hospital admission. Disease severity was defined using the World Health Organization (WHO) severity categorization as critical (requires life sustaining treatment, presence of acute respiratory distress syndrome (ARDS), sepsis, septic shock), severe (oxygen saturation <90% on room air, signs of pneu-monia, signs of severe respiratory distress), or non-severe (absence of signs of severe or critical disease). **3. Results** **3.1. Cohort Characteristics** Blood sampling of hospitalized COVID-19 patients with non-severe course occurred a median of six days (IQR 2-17) after symptom onset.
4	if available, I would suggest to add D-dimer among biochemical markers	➔ Thank you for this note. Unfortunately, D-dimers were not determined. Citrate plasma for measurement is not available.
5	Overall, a comparison with severe patients and the absence of longitudinal sampling would have added much information regarding the potential clinical application of SDC-1 dosing in clinical practice, in terms of anticipating clinical deterioration or monitoring the course of the diseases. I would suggest to discuss these issues	➔ Thank you, this is a good point. We have expanded the discussion accordingly. **4. Discussion** Compared to healthy controls, hospitalized patients during acute disease showed significantly increased SDC-1 levels compared to healthy controls, but not when compared to convalescent patients. In the entire study cohort, correlation analysis provided evidence that higher inflammatory parameters (C-reactive protein, ferritin, interleukin-6) correlated significantly with elevated SDC-1 levels. These

		inflammatory parameters are established disease activity markers and predictors of worse outcomes in COVID-19 patients [18]. Elevated LDH levels [19], also an established marker of acute COVID-19, also correlated significantly with elevated SDC-1 levels. Our data are in line with data of Karampoor et al., who were able to demonstrate an increase of syndecan-1 levels in COVID-19 patients treated as inpatients, depending on the severity of the disease. Critically ill patients showed significantly increased syndecan-1 levels during the acute phase of the disease compared to moderately ill patients. It was shown that the determination of syndecan-1 on the day of admission is suitable for monitoring disease activity in addition to the determination of IL-6, IL-10, IL-18 and CRP [20]