Author's response to reviews

Title: Left ventricular apical thrombus after systemic thrombolysis with recombinant tissue plasminogen activator in a patient with acute ischemic stroke

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Author's response to reviews: see over
Dear Editor-in-Chief,

Thank you very much for your efforts regarding our manuscript entitled “Left ventricular apical thrombus after systemic thrombolysis with recombinant tissue plasminogen activator in a patient with acute ischemic stroke.”

We tried to address all reviewers comments in our manuscript. Below you will find our detailed remarks.

With kind regards
Sincerely
Florian Doepp
Comments to the first reviewer:

- We discussed the study of Kono et al. (1) regarding the hypothesis of an acute neurogenic myocardial stunning in our patient. Furthermore, we screened the literature on this topic. Acute neurogenic myocardial stunning seems very unlikely but can not definitively be ruled out: Our patient had a reversible left ventricular dysfunction with abnormal left ventricular wall motion and reduced ejection fraction but no elevation of cardiac enzymes. However, acute neurogenic myocardial stunning has so far been described as a cardiac complication after subarachnoid hemorrhage (1-4), in an isolated case of subdural hematoma (5) and a Guillain-Barré syndrome (6), only. We found no evidence in the literature for acute neurogenic myocardial stunning after stroke. In addition, our patient suffered from coronary artery disease whereas the syndrome of acute neurogenic myocardial stunning describes reversible left ventricular dysfunction in patients without cardiac disease. The cardiac failure in our patient occurred on the 3rd day after stroke unlike neurogenic stunned myocardium described as a more acute complication (1, 4, 5). As recommended by the reviewer, we added an extra paragraph to the discussion (page 5 line 20 – page 6 line 4). However, as this differential diagnosis seems very unlikely it is questionable, if the extra paragraph should remain in the manuscript.
- We added the potential value of close echocardiographic monitoring in rt-PA treated patients with stroke into our conclusion.

5. Ohtsuka et al. **Neurogenic stunned myocardium.** *Circulation* 2000, **101:**2122-2124.


**Comments to the second reviewer:**

In the section “case presentation” the clinical picture is now described on more detail:
- The ultrasound exam of the brain supplying arteries is mentioned (point 2).
- The patient got no outpatient medical treatment before admission (point 5).
- Further risk factors for cardiac events are added (point 8)
- The hemorrhagic transformation of the ischemic lesion did not worsen the neurological state and did probably not influence the left ventricular function: As described, the hemorrhagic transformation was confirmed 24 hours after admission on CT scan, whereas the cardiac failure occurred on the 3rd day (point 6). In addition the alternative hypothesis of an acute neurogenic stunned myocardium is discussed in the section “discussion” on page 6.
- A phrase was added regarding the closed monitoring of the fluid balance (point 7)

In the section “discussion” we do not argue against the hypothesis of an acute coronary syndrome (point 1). See page 4 last break: “We postulate, that he developed an acute coronary syndrome (dyspnea and tachycardia) on the basis of the pre-existing cardiac disease with kinetic disturbance which subsequently enabled the formation of a ventricular thrombus – promoted by the risk factors hypercoagulability, atrial fibrillation and previous myocardial infarction”. Therefore we agree with the reviewers comment that the rapid worsening of the left ventricular function is caused by a transient cardiac ischemia.

The increased D-Dimer concentration as a marker of hypercoagulability is discussed. Further markers however, as e.g. thrombin-antithrombin–III-complex and plasminogen activator inhibitor-1 were not evaluated during the acute state in our patient.
The recalled recent guidelines regarding early stroke management and coronary risk evaluation are now mentioned (point 4 and 8)

We followed all minor comments of both reviewers