#Response to Reviewer 1 Comments

Point 1: In Figure 1A, The IVC tumor thrombus was intrahepatic level, However, the authors misspelled it as infrahepatic level.

Response 1: Thank you for your recommendation and correction. We have removed the incorrect description. (See Figure 1 in 74773-Figures.pptx)

Point 2: The image is not clear and standard in Figure 2（Shoot freely with your mobile phone）.

Response 2: Thank you for your recommendation. Our anesthesia machine workstation can only record capnometry (the value of $EtCO_2$) instead of capnography (the figure of $EtCO_2$), which was just taken by a cell phone in order to document the finding as quickly as possible. We took 3 pictures at that time. In this revised version, we have replaced the clearest one. (See Figure 2 in 74773-Figures.pptx)

Point 3: In Figure 4, is the image of preoperative chest CT replaced by CT pulmonary angiogram more convincing? Preoperative accurate evaluation is very important.

Response 3: Thank you for your recommendation. There was no preoperative CT pulmonary angiogram due to no evidence of preoperative pulmonary embolism suspected. In Figure 4, we only wanted to demonstrate the diagnosis of pulmonary embolism by postoperative CT pulmonary angiogram, which showed filling defects in bilateral pulmonary arteries during the arterial phase. We did not attempt to compare preoperative and postoperative CT images. It is our fault. We have removed the misplanted Figure 4A. Thank you for your kind reminder. (See Figure 4 in 74773-Figures.pptx)

Point 4: The patient was hepatocellular carcinoma with renal tumor and inferior vena cava tumor thrombus is rarely suitable for surgical treatment.

Response 4: Thank you for your recommendation.

For this patient, his TNM tumor stage for hepatic cell carcinoma (HCC) is $T_1N_0M_1$, stage IVB. (Line 46) Though advanced stage, he had regular followed up at

out-patient department after hepatectomy and lung wedge resection for years and no evidence of disease until this newly found renal tumor. He got well functional compacity and strong desire of living.

“According to his history of stage IVB HCC, metastasis from previous HCC could not be excluded. Therefore, the origin of the tumor may come from clear cell type of renal cell carcinoma (RCC) or metastasize from previous HCC. There were two reasons which made us consider the tumor may be derived from clear cell type of RCC. First, HCC and RCC share similar MRI image features. Both of them have intracellular lipid that results in decreased signal on out-of-phase image as compared with in-phase images through the MRI. Second, the kidney is uncommon as a site for distant metastases of HCC[4]. However, there was no pathology report before surgery. Because of the abundant blood flow to the kidneys, preoperative biopsy may be complicated by massive bleeding. After discussing the benefits and complications with the patient, the patient declined preoperative biopsy and opted for direct surgery.” (Line 25-36)

References

4. D'Antonio, A.; Caleo, A.; Caleo, O.; Addesso, M.; Boscaino, A. Hepatocellular carcinoma metastatic to the kidney mimicking renal oncocytoma. *Hepatobiliary Pancreat Dis Int* **2010**, *9*, 550-552.

Point 5: Inferior vena cava embolism is a common cause of pulmonary embolism. Combined with the patient's medical history, inferior vena cava filter should be considered to prevent pulmonary embolism.

Response 5: Thank you for your recommendation. We have discussed in our manuscript (line 130-135).

“IVC filters are often used as a prophylactic treatment for patients with venous thrombosis to prevent pulmonary embolism[11]. It is not suitable for our patient to undergo implantation preoperatively as prophylaxis. In the process of IVC filter placement, the wire needs to bypass the tumor thrombus, which highly increases the risk of tumor thrombus rupture, leading to APE and distant metastasis from the tumor debrides [12].”

References

11. Piazza, G. Advanced Management of Intermediate- and High-Risk Pulmonary Embolism: JACC Focus Seminar. *J Am Coll Cardiol* **2020**, *76*, 2117-2127, doi:10.1016/j.jacc.2020.05.028.

12. Marron, R.M.; Rali, P.; Hountras, P.; Bull, T.M. Inferior Vena Cava Filters: Past, Present, and Future. *Chest* **2020**, *158*, 2579-2589, doi:10.1016/j.chest.2020.08.002.

Point 6: Although acute pulmonary embolism was confirmed by the transesophageal echocardiography during operation, it is not suitable for thrombolytic treatment (it is not a thrombus) because it is a cancer thrombus, and intraoperative thrombolysis also increase the risk of bleeding.

Response 6: Thank you for your recommendation. As we have discussed in our manuscript, tumor thrombus impairs the patency of IVC, leading to venous stasis, resulting in increased thromboembolic risks. (Line 123-124)
"According to Virchow's triad, endothelial injury and venous stasis increase the risk of thrombosis. During the course of treatment in our case, the emboli located in the right PA disappeared after thrombolysis, suggesting a thrombosis rather than tumor emboli. But left PA emboli still exist after thrombolysis, requiring percutaneous mechanical thrombectomy, suggesting that it should be tumor emboli. Based on the above reasons, IVC thrombus of this case seems to be composed of both tumor tissue and thrombus." (Line 124-130)

Intraoperative thrombolysis was not performed for this patient.

Although acute pulmonary embolism was confirmed by the transesophageal echocardiography intraoperatively, the thrombolytic therapy started hours after the surgery. At the end of the surgery, surgeon had well hemostasis, and there was no oozing at the wound. For thrombolytic therapy, recent major surgery does increase the risk of bleeding, but it is considered a relative rather than an absolute contraindication.

#Response to Reviewer 2 Comments

Point 1: For HCC patient, there is no TNM tumor stage and liver function evaluation (Child-Push grade). And has no PT (prothrombin time) and APTT(activated partial thromboplastin time).

Response 1: Thank you for your recommendation. The TNM stage of the patient's HCC was $T_1N_0M_1$, stage IVB, and the Child-Pugh classification was A. The prothrombin time (PT) was 10.0 seconds with an INR of 0.98, and the activated partial thromboplastin time (aPTT) was 26.8 seconds. Both PT and aPTT were within the normal limits. (Line 46-49)

Point 2: In the history of illness, "the origin of the tumor may come from clear cell type renal cell carcinoma (RCC)." Is there any pathology results? Why do you think it come from clear cell type renal cell?

Response 2-1: Thank you for your recommendation. There was no pathology report before surgery. Because of the abundant blood flow to the kidneys, preoperative biopsy may be complicated by massive bleeding. After discussing the benefits and complications with the patient, the patient declined preoperative biopsy and opted for direct surgery. (Line 33-36)

Response 2-2: Thank you for your recommendation. According to his history of stage IVB hepatic cell carcinoma (HCC), metastasis from previous HCC could not be excluded. Therefore, the origin of the tumor may come from clear cell type of renal cell carcinoma (RCC) or metastasize from previous HCC. There were two reasons which made us consider the tumor may be derived from clear cell type of RCC. First, HCC and RCC share similar MRI image features. Both of them have intracellular lipid that results in decreased signal on out-of-phase image as compared with in-phase images through the MRI. Second, the kidney is uncommon as a site for distant metastases of HCC[4]. (Line 25-32)

References

4. D'Antonio, A.; Caleo, A.; Caleo, O.; Addesso, M.; Boscaino, A. Hepatocellular carcinoma metastatic to the kidney mimicking renal oncocytoma. *Hepatobiliary Pancreat Dis Int* **2010**, *9*, 550-552.

Point 3: There is no way to identify inferior vena cava is the tumor emboli or thrombus, in the discussion should have some points to conduct.

Response 3: Thank you for your recommendation. It is difficult to determine before surgery whether the IVC thrombus consists of tumor tissue, thrombus, or a mixed type. As we discussed in the manuscript, tumors impair the patency of the IVC, leading to venous stasis. (Lines 122-124) "According to Virchow's triad, endothelial injury and venous stasis increase the risk of thrombosis. During the course of treatment in our case, the emboli located in the right PA disappeared after thrombolysis, suggesting a thrombosis rather than tumor emboli. But left PA emboli still exist after thrombolysis, requiring PMT, suggesting that it should be tumor emboli. Based on the above reasons, IVC thrombus of this case seems to be composed of both tumor tissue and thrombus." (Lines 124-130)

#Response to Reviewer 3 Comments

Point 1: Overall, manuscript was well-structured and no meaningful grammatical errors were found. Please discuss the limitations of the study.

Response 1: Thank you for your recommendation. We have discussed and stated limitations in the Discussion section. “Our study has two limitations. First, this is an observational case report. Our patient underwent surgery for HCC with distant metastases, which is not recommended in the current protocol. Prognosis of this case appears to show better outcomes compared to current life expectancy in advanced HCC. However, more evidence is needed to demonstrate the effectiveness of the treatment. Second, there is no standardized anesthesia protocol for IVC tumor thrombus surgery. APE during surgery in high-risk patients can lead to life-threatening conditions. We hope to see a comprehensive approach to anesthesia management in the future.” (Line 220-227)