Peer Review File

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Reviewer #1

In this case report, Martens et al described the technique of direct open aortic cannulation under a normothermic circulatory arrest in conjunction with retrograde cerebral perfusion (RCP). This technique was used in the case of acute type A aortic dissection with intramural thrombus. The authors suggested that RCP could avoid the air, debris, and thromboembolic materials going into the arch vessels.
It was an interesting technique, and thank you for submitting an intraoperative video.

Comment 1: My major critique is as follows; you spent more than 3 minutes until you restore the antegrade flow to the aorta. During that time, the brain was only perfused by RCP under normothermia. I have a strong concern for brain ischemia with this technique. Is there any evidence that showed safety of RCP under normothermia? Did you monitor INVOS or cerebral oximeter? I feel like a direct aortic cannulation through the thrombosed false lumen could even be safer than your technique.

Response 1: We thank the reviewer for the valuable comments.

We have made the experience that in patients with the need for a fast direct aortic cannulation, cerebral embolization is an important issue, especially if the cannulation is being performed through a thrombosed false lumen or accidentally into the false lumen. Hence, we decided to perform direct open cannulation under direct visual control in these specific cases as described in this case report. Our method is based on the published experience of other groups, that successfully use direct open cannulation during normothermic circulatory arrest, but have not described the use of RCP as an additional protective adjunct.

We strongly believe that a short period (<=5min) of normothermic circulatory arrest with RCP (the blood is already being cooled at this stage) poses a smaller risk for cerebral injury, than an “uncontrolled” direct aortic cannulation. NIRS is used in all of these cases. During temporary RCP, rSPO2 typically remains constant or indeed increases over baseline values. In the presented case, sPO2 remained at baseline throughout the cannulation and RCP period. (NIRS shortly before establishing antegrade flow to the aorta: Right rSPO2 = 63% and Left rSPO2 = 61%).

We have yet to publish our series of patients treated with this approach. However, our preliminary experience in approximately 15-20 cases suggests, that cerebral event rates are lower with this technique than with direct aortic cannulation under “unsafe” conditions. This notion notwithstanding, this technique is only used in bailout situations.

We have added the information to the manuscript.

Comment 2: Why did you cut off the RCP pressure at 40 mmHg? Was there any literature that showed RCP pressure > 40 mmHg would cause cerebral edema?

Response 2: Literature from the 90's suggests that RCP pressures of approximately 25mmHg are the best compromise between hypoperfusion and hyperperfusion. Higher perfusion pressures, especially over longer perfusion periods, are feared to result in cerebral edema (Usui A, Abe T, Murase M. Early clinical results of retrograde cerebral perfusion for aortic arch operations in Japan. Ann Thorac Surg. 1996;62(1):94-103; discussion -4.).

However, some clinical studies reported that perfusion pressures of up to 40mmHg seem to be safe. RCP pressure of 40mmHg resulted in a oxygen desaturation of only 0.4%/min. Signs of cerebral edema were not seen. (Ganzel BL, Edmonds HL, Jr., Pank JR, Goldsmith LJ. Neurophysiologic monitoring to assure delivery of retrograde cerebral perfusion. J Thorac Cardiovasc Surg. 1997;113(4):748-55; discussion 55-7). These data is in line with our experience that rSPO2 values typically remain at baseline during flush RCP.

Most groups that currently use RCP on a regular basis, suggest perfusion pressures of up to 25-30mmHg with a relative low flow of 100-300cc/min (Pochettino A, Brinkman WT, Moeller P, Szeto WY, Moser W, Cornelius K, Bowen FW, Woo YJ, Bavaria JE. Antegrade thoracic stent grafting during repair of acute DeBakey I dissection prevents development of thoracoabdominal aortic aneurysms. Ann Thorac Surg. 2009;88(2):482-9; discussion 9-90.)

Since we use RCP during cannulation for a short period of time and with the specific aim to "flush" debris and air from the cerebral arteries, we decided to use RCP pressures of up to 40mmHg. This results in flow rates of 500-1500cc/min, depending on body size and whether the azygos vein is included in the retrograde perfusion.

We have added the information to the discussion.

Comment 3: The dissection of right subclavian artery was not clear in Figure 1.

Response 3: The contrast filling of the RSA was suboptimal in the CT scan. However, the dissection is clearly visible in the high resolution version of Figure 1 (arrows). Unfortunately, PDF conversion has reduced the quality of the picture.

Comment 4: Did you replace all the neck vessels with entire arch? I could not tell it with the postoperative CT scan.

Response 4: Yes, the patient underwent complete aortic arch repair with a branched forozen elephant trunk graft (Thoraflex Hybrid).

Comment 5: Reference 15 was written in German. Please exclude it.

Response 5: We have removed this reference.

Reviewer #2

Interesting idea and technique from Hannover to facilitate central aortic cannulation. For this particular case, I would go to the PA side of aorta directly without using this technique based on CT scan. Authors' technique seems more useful in case of more severe circumferential dissection. Nice pictures and videos.
Some technical questions.

Comment 1: How about putting a purse string suture in advance? Because I don't think this technique needs a precise determination of cannulation site after circulatory arrest.

Response 1: We thank the reviewer for the valuable comments.
Putting a purse string suture in advance is certainly a valid option. We prefer not to determine the cannulation site before we have visualized from within the aorta.

Comment 2: In Figure 2C, it is unclear this arterial tubing is a "Y-shape" or separate pump, as was a venous circuit of RCP. It would be great if authors could mention about CPB circuits a little bit more.

Response 2: Indeed the SVC cannula is connected to the main arterial line via a Y-connector. We have added this information to the manuscript.

Comment 3: In Figure 3D, there is a big bubble in the tubing. In Video, it looks like a lot of air went through the aortic cannula. Personally I think the tubing part should be filled without air. One of the benefits of RCP is a retrograde flow through the neck vessels for de-airing. The way of de-airing inside the aortic is one of the technical challenges of this technique.

Response 3: Correct observation. However, the cannula cannot be filled completely at this stage without closing it at the tip within the aorta. Therefore the arterial line is filled as fare as possible and the remaining air within the tubing and cannula is flushed out through the open aortic arch under continued RCP. Thereby, air embolization into the head vessels cannot occur. Figure 4 A shows the already filled cannula while the aortic arch is still open und the RCP running. We have clarified the fact in the manuscript (Figure legend, Figure 4).

Comment 4: One of the concerns using this technique is a proximal or mid arch tear with IMH. The chance of migrating thrombus into the arch through the tear is not negligible when applying a cross-clamp. On Video, removing thrombus during warm ischemia seems time consuming. Any thoughts?

Response 4: We agree that the embolic risk is high in cases of IMH and that an ascending aorta with IMH should not be clamped routinely. We prefer subclavian cannulation and non-clamping of the aorta in AADA IMH cases. However, despite showing no pericardial effusion in the external CT scan, this specific patient developed pericardial tamponade by the time she had arrived in our OR. After removing the tamponade, we decided to proceed with the open aortic cannulation technique. As you suggested in Comment 7, we could have established left subclavian artery cannulation after removing the tamponade. However, we considered this option too time consuming at this stage and decided to use the open cannulation approach together with thrombus removal at the clamp site. We have added our thoughts on IMH to the manuscript.

Comment 5: The pressure of RCP up to 40 mmHg seems a little bit high side. I understand this was performed normothermia so probably needs a higher flow than that of RCP during hypothermia. Any monitoring of cerebral circulation during RCP such as the cerebral saturation monitor?

Response 5: Please see or Response 2 of Reviewer #1.

Comment 6: Do authors use retrograde cardioplegia? I guess retrograde CP definitely minimizes warm ischemic time of the heart. I don't use ice routinely but should put ice on the heart before starting Vfib to minimize ischemic damage? Would be informative for readers if authors could add how long the warm ischemic time was (from Vfib to antegrade cardiopegia).

Response 6: Very good suggestion. In our center retrograde cardioplegia is rarely used. Certainly, it could reduce cardiac ischemia time in these cases. However, it must be established through a closed right atrium alongside a two stage cannula, which might not be straightforward in some cases. Using bicaval venous cannulation and opening the right atrium for retrograde cardioplegia might add

critical time before one can address the aorta for cannulation. In addition, one has to switch the SVC cannula from drainage to perfusion and vice versa using this technique. Personally, I have used retrograde cardioplegia through a closed RA too rarely to combine it in these cases.

Comment 7: How about using the left axillary artery ("subclavian artery" in Europe) cannulation in this case? If there is no malperfusion of R arm, dissected R axillary or innominate artery is not contraindication for using right axillary artery, as authors know.1,2

Ref

1. Ohira S, et al. Direct Axillary Artery Cannulation for Type A Dissection and Impact of Dissected Innominate Artery. Ann Thorac Surg. 2021 May 27;S0003-4975(21)00905-X.
2. Rylski B, et al. Is right axillary artery cannulation safe in type A aortic dissection with involvement of the innominate artery? J Thorac Cardiovasc Surg. 2016;152:801-807.e1.

Response 7: Although not perfectly visible in Figure 1, in this case the RSA was dissected and could not be used for cannulation. In addition the patient became unstable during anesthesia because of tamponade and emergency sternotomy was performed. As discussed in Response 4, we could have established LSA cannulation at that stage but decided against it for the sake of time. It is certainly an option. Due to our good results with the open direct aortic cannulation technique, we more reluctantly use subclavian cannulation in these cases.