American Journal of Ophthalmology Case Reports 16 (2019) 100569

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.elsevier.com/locate/ajoc

Case report

Bilateral central retinal/ophthalmic artery occlusion and near-complete ophthalmoplegia after bilateral lung transplant

Nadine Rady[a], Ashwini Kini[b], Jonathan A. Go[c], Bayan Al Othman[b], Andrew G. Lee[a,b,d,e,f,g,h,*]

[a] School of Medicine, National University of Ireland, Galway, Ireland
[b] Department of Ophthalmology, Blanton Eye Institute, Houston Methodist Hospital, 6550 Fannin St, Houston, TX, 77030, USA
[c] Baylor College of Medicine, One Baylor Plaza, Houston, TX, 77030, USA
[d] Department of Ophthalmology, Neurology and Neurosurgery, Weill Cornell Medicine, 1305 York Ave, New York, NY, 10021, USA
[e] Department of Ophthalmology, University of Texas Medical Branch, 700 University Blvd, Galveston, TX, 77555, USA
[f] University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX, 77030, USA
[g] Texas A and M College of Medicine, 8447 Bryan Rd, Bryan, TX, 77807, USA
[h] Department of Ophthalmology, The University of Iowa Hospitals and Clinics, 200 Hawkins Drive, Iowa City, IA, 52242, USA

ARTICLE INFO

Keywords:
Cardiopulmonary bypass
Central retinal artery occlusion
Ophthalmoplegia
Idiopathic
Non-arteritic anterior ischemic optic neuropathy

ABSTRACT

Purpose: Recognize a rare yet existing risk of severe visual loss as a postoperative complication of bilateral lung transplant.

Observations: A 62-year-old male had undergone bilateral lung transplant for end-stage idiopathic pulmonary fibrosis and emphysema overlap syndrome. The operation was initially off-pump; however, during the left lung transplantation, cardiopulmonary bypass conversion was necessary to maintain intraoperative hemodynamic stability. On post-operative day 4, shortly after extubation and full recovery from sedation, the patient reported bilateral no light perception vision. There were no other associated neurologic symptoms. A computed tomographic (CT) of the head, cranial magnetic resonance (MR) scan of the head, MR angiogram of the circle of Willis and neck were negative. Neuro-ophthalmologic examination revealed no light perception vision in both eyes (OU). The pupils were non-reactive to light (amaurotic pupils). The intraocular pressure measured 18 mm Hg OU, and complete bilateral ophthalmoplegia was present. The fundus exam showed bilateral pallid optic disc edema, cherry red spots, with arteriolar attenuation, and mildly dilated and tortuous veins. Stroke work up was negative.

Conclusions and importance: A case of post-operative visual loss and ophthalmoplegia carrying significant and permanent quality of life implications. It questions the role disruption of homeostasis during cardiopulmonary bypass contributes for this outcome.

1. Case presentation

A 62-year-old male underwent a scheduled bilateral lung transplant for end-stage lung disease secondary to pulmonary fibrosis and emphysema overlap syndrome. Apart from lung disease, the patient has a background history of well-controlled hypertension and type 2 diabetes mellitus. He was on treatment with prednisone, budesonide, furosemide, arformoterol and metformin.

On arrival to the operative room, his pre-operative hemoglobin was 7.8 gm/dl and hematocrit was low at 29.1% (normal range 41–51%). The right lung was transplanted off-cardiopulmonary bypass (CPB), however, intraoperative pulmonary hypertension prompted surgeons to convert to CPB for the left lung transplant. During CPB, mean arterial pressure was maintained between 50 and 60 mm Hg. The patient was successfully weaned off CPB but the estimated blood loss during the surgery was 3000ml and he was transfused with 8 units packed red blood cells intraoperatively, 2 units of fresh frozen plasma, and 2 units of platelets. Post–operatively his mean arterial pressure was maintained with milrinone and later with dobutamine.

On postoperative day 4 after full recovery from sedation, the patient reported bilateral blindness. There were no other associated neurologic symptoms. On examination, the patient was no light perception (NLP) in both eyes (OU). The pupils were 5 mm OU and were non-reactive to light (i.e., amauroutic pupils). There is exotropia OS at primary position. Extraocular motility showed near-complete ophthalmoplegia OU; with the exception of mildly preserved abduction and elevation OS

* Corresponding author. Blanton Eye Institute, Houston Methodist Hospital, 6560 Fannin Street Suite 450, Houston, TX, 77030, USA.
E-mail address: aglee@houstonmethodist.org (A.G. Lee).

https://doi.org/10.1016/j.ajoc.2019.100569
Received 29 April 2019; Received in revised form 18 September 2019; Accepted 4 November 2019
Available online 11 November 2019

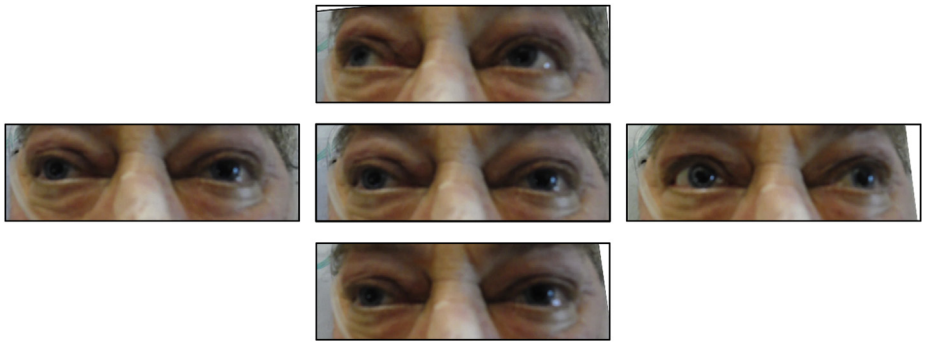

Fig. 1. Extraocular motility showed near-complete ophthalmoplegia bilaterally, however, the eyes remained straight in primary position.

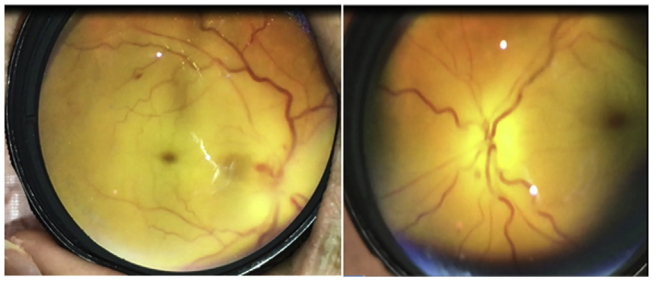

Fig. 2. Fundus photos at bedside show with pale edematous disc, dilated veins, pale retina with cherry red spot of a Central retinal artery occlusion (Taken at bedside in non-ambulatory patient).

(Fig. 1). The intraocular pressure was 18 mm Hg OU. External exam was otherwise unremarkable, with no ptosis. Anterior segment exam was normal OU. The fundus exam showed bilateral retinal opacification and edema with a "cherry red spot" in the macula and pallid optic disc edema OU. (Fig. 2). A bilateral embolic ophthalmic artery occlusion was suspected based upon bilateral central retinal artery occlusion (CRAO), concomitant pallid edema from anterior ischemic optic neuropathy (AION) OU, and bilateral lid sparing ophthalmoplegia OU. Compute tomographic (CT) and magnetic resonance (MR) scans of the head (including diffusion weighted imaging (DWI) MR) were within normal limits.

The patient was started on empiric brimonidine tartrate and latanaprost drops. Two months post-operatively the vision remained NLP OU with non-reactive (amaurotic) pupils and improvement in the global ophthamoplegia OU. Optical coherence tomography (OCT) of the disc showed diffuse thinning of retinal nerve fibre layers in all sectons and OCT macula showed diffuse thinning of both inner and outer retinal layers OU (Fig. 3). Fundus fluorescein angiogram showed reestablished posterior segment circulation and timing.

On follow up, fundus exam at 6 months showed pigmentation around the right eye optic disc consistent with RPE disruption further strengthening our hypothesis of an ophthalmic artery occlusion.

2. Discussion

Postoperative visual loss from CRAO or AION or posterior ION (PION) is a well-recognized complication of non-ocular surgery (especially cardiac surgery and spine surgery). We present a unique case of complete bilateral loss of vision with a presumed ophthalmic artery occlusion OU (with a cherry red spot, pallid optic disc edema, and near-complete ophthalmoplegia OU) status post-bilateral lung transplant with intraoperative conversion to cardiopulmonary bypass.

Significant hemodynamic changes occur during cardiopulmonary bypass (CPB). Fluctuations in vascular resistance, hypothermia, changes in metabolic demand, autonomic neuronal tone, catecholamine levels, and PaO_2 and PCO_2 levels all occur during CPB.[1] In addition, hemodilution decreases hemoglobin concentration and blood oxygen carrying capacity.[2] Metabolic acidosis, electrolyte disturbances, and blood viscosity are additional hemodynamic parameters which can cause hypoperfusion to vital organs.[1]

Sweeney et al. reported cases of unilateral (7 cases) and bilateral (3 cases) ischemic optic neuropathy as a complication of CPB surgery in 10 of 7685 consecutive on-pump cardiac procedures.[3] The ischemic infarction of the optic nerve disc was attributed to hypotension, hypothermia and activation of complement factors by the bypass procedure.[3] Lieberman et al. and Portnoy et al. presented cases of visible retinal emboli associated with AION and choroidal nonperfusion, as observed by fluorescein angiography, with emboli seen histopathologically in a short posterior ciliary artery supplying an infarcted optic disc.[4,5] PION as a post-operative complication of cardiac and spine surgery has also been reported[6,7] as well as juxtapapillary nerve fiber infarction and retinal nerve fiber layer loss in cardiac transplant recipients.[8,9]

In a large retrospective study of 27,915 patients who underwent CPB, ION was identified in 17 patients (0.06%, 12 NAION, 5 PION) with no improvement on follow up.[10] Advanced age, lower post-operative hemoglobin concentrations, hypertension, prolonged hypotension, history of clinically severe vascular disease, pre-operative angiogram within 48 hours of CPB, prolonged pump time, surgical disruption of particulate matter, RBC transfusions and use of non-RBC blood components were among the identified risk factors.[10,11]

Some of the etiological mechanisms incriminated in neurological damage post-surgery involving CPB include macroembolization, from air in the perfusion system, dislodgement of atheromatous debris from the aorta, or release of left ventricular thrombus during cardiac manipulation, and/or microembolisms of fat, air, platelet aggregates, fibrin or silicone.[12] During CPB, large numbers of microemboli circulate in the blood.[13] Emboli of platelets, of fat, and of "crystalline" material have been identified at necropsy in the brain and other organs of patients after surgery involving CPB.[14]

Orbital infarction syndrome is characterized by ischemia of the whole orbit due to occlusion of the ophthalmic artery and its branches. It is a rare occurrence due to the rich anastomotic vascularization of the orbit. It manifests with orbital pain, total ophthalmoplegia, and acute blindness. Unilateral orbital infarction has been reported in context of acute perfusion failure,[15] mucormycosis,[15] systemic or orbital vasculitis,[15] cocaine,[16] and surgical clipping of aneurysms[17] causing ischemia to all the intra orbital and intra ocular structures, while bilateral orbital infarction has been reported after a bifrontal craniotomy.[18] Orbital pain, present in 40% of cases, and ptosis are two features of OIS that were not present in our patient.

Rainio et al. in a prospective randomized study indicated a decreased frequency in retinal infarcts following off-pump CPB compared to on-pump (OP) CPB.[19] Systemic embolization and circulatory disturbances are also a recognized hazard of CPB. The authors suggested limiting or avoiding aortic manipulation during OP CPB to reduce retinal microvascular damage and systemic embolization.[20] A meta-

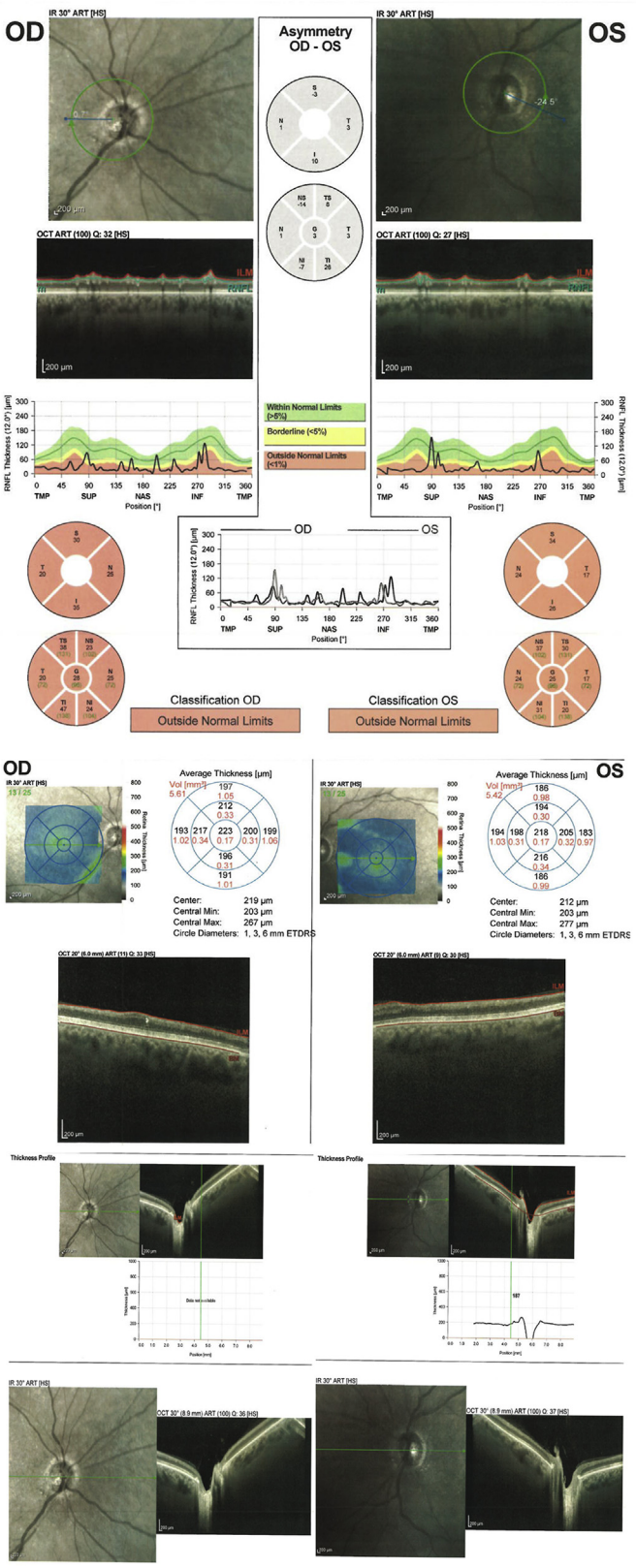

Fig. 3. OCT of optic nerve showed cup disc ratio of 0.7 OD and 0.6 OS showing diffuse atrophy of all sectors. OCT macula showed diffuse thinning of both inner and outer retinal layers OU suggesting ophthalmic level occlusion.

analysis of pooled data from 37 randomized trials (3369 patients) who underwent off-pump CPB showed a non-significant reduction in stroke.[21]

Rapid advances in technique have increased the number of bilateral lung transplants (BLT) performed in the United States. The indications for BLT versus single lung transplant (SLT) are controversial and the decision for BLT or SLT is dependent upon primary pulmonary surgical indication, the age of recipient, donor lung quality and patient disease severity.[22] SLT is associated with decreased operative times, less hemodynamic perturbations, and subsequently lower perioperative mortality in high-risk lung recipients.[23] In contrast, BLT requires a larger incision with associated worse pulmonary mechanics. This, coupled with the increased need for CPB and other more complex and longer duration operative factors may lead to increased perioperative mortality in BLT compared with SLT.[22]

The risk-benefit for utilizing CPB in BLT remains debatable. A meta-analysis of 14 retrospective observational studies of BLT with and without CPB revealed six papers with significantly worse outcomes with CPB; six papers found no difference; and two gave mixed results depending on the specific postoperative outcomes assessed.[24]

CPB does offer several advantages in BLT including: exposure through a median sternotomy incision is greatly facilitated and expedites the pneumonectomy, and implantation of donor lungs; improved control of hemodynamics and reperfusion; avoidance of dependence after initial SLT ventilation from the freshly implanted lung while the contralateral lung is being implanted in BLT.[25] A meta-analysis of 11 studies found that the incidence of primary early graft failure was significantly higher with CPB as compared to off-pump (32.3% vs. 24.7%).[26] In other studies, CPB was shown to be associated with higher mortality, delayed chest closure, more radiographic infiltrates, worse immediate graft function and longer (endotracheal) intubation, despite comparable 30-day mortality and one-year survival.[27,28]

Central nervous system complications after lung transplantation are common. A retrospective cohort review of the Mayo Clinic Lung Transplant Registry (1988–2008) revealed that up to 92% of patients within 10 years were affected, being severe in 31% of cases most commonly being stroke and encephalopathy.[29] Age, history of coronary artery disease, prolonged use of CPB,[30] and bilateral[29] (as opposed to unilateral) lung transplant among the risk factors for CNS complications.

Some authors report that any use of CPB may be detrimental to patient outcome[31] and that CPB for SLT/BLT should be reserved for decompensated cases whereas others feel that outcomes are comparable regardless of whether or not CPB is utilized.[32] A notable limitation of published reports comparing on-pump CPB and off-pump lung transplants is having grouped “off-pump cases, which required emergent conversion to CPB” with the “on-pump” CPB group.[27,28,32] Mohite et al. showed that despite segregation of unplanned CPB conversion cases from elective on-pump cases, patients with comparable preoperative demographic and risk profiles demonstrated better early postoperative outcomes and a possible better early survival with an off-pump strategy.[32] In contrast, off-pump BLT/SLT has other risks. One study showed that patients undergoing off-pump BLT were at higher risk of profound intraoperative hypothermia despite multimodal preventive therapy. Off-pump SLT had a similar time trend for their body temperature but the extent of the decrease was much smaller than that in off-pump BLT patients.[33]

Tarabishy et al. found that the most common ocular abnormality following lung transplant was posterior subcapsular cataract, followed by infectious ocular complications.[34] High levels of immunosuppression, advanced age, drug-specific side effects, underlying comorbidities such as diabetes mellitus, have been suggested to play a role in pathogensis.[35] Although visual loss from CPB has been reported previously, to our knowledge there are no prior reports of ophthalmic artery level ischemia presenting with CRAO, AION, and bilateral ophthalmoloplegia in the English language ophthalmic literature.

In conclusion, this case highlighted a rare complication of non-ophthalmic surgery. Bilateral blindness post-lung transplant on cardiopulmonary bypass is most likely attributed to preexisting

vasculopathic risk factors with hemodynamic changes in intra and post-operative period causing hypoperfusion and failure of autoregulatory control in addition to embolic phenomena to the ophthalmic arteries arising from maneuvers on major vessels during the surgical procedure itself. Whether this devastating and permanent complication can be prevented in the future by more off-pump surgeries remains uncertain.

Patient consent

Written consent obtained to publish case details.

Funding

None.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures: Rady N, A Go, J, Kini A, Al Othman B, G. Lee A.

Acknowledgement

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2019.100569.

References

1. Nenekidis I, Pournaras CJ, Tsironi E, Tsilimingas N. Vision impairment during cardiac surgery and extracorporeal circulation: current understanding and the need for further investigation. *Acta Ophthalmol.* 2012;90:e168–e172.
2. Roth S. The effects of isovolumic hemodilution on ocular blood flow. *Exp Eye Res.* 1992;55:59–63.
3. Sweeney PJ, Breuer AC, Selhorst JB, et al. Ischemic optic neuropathy: a complication of cardiopulmonary bypass surgery. *Neurology.* 1982;32:560–562.
4. Lieberman MF, Shahi A, Green WR. Embolic ischemic optic neuropathy. *Am J Ophthalmol.* 1978;86:206–210.
5. Portnoy SL, Beer PM, Packer AJ, Van Dyk HJ. Embolic anterior ischemic optic neuropathy. *J Clin Neuro Ophthalmol.* 1989;9:21–25.
6. Moster ML. Visual loss after coronary artery bypass surgery. *Surv Ophthalmol.* 1998;42:453–457.
7. Buono LM, Foroozan R. Perioperative posterior ischemic optic neuropathy: review of the literature. *Surv Ophthalmol.* 2005;50:15–26.
8. Jarrell III RL, Jones WL. Juxtapapillary nerve fiber layer infarction as a complication of coronary artery bypass surgery. *J Am Optom Assoc.* 1998;69:759–765.
9. Pires CS, Remigio MC, Aguiar MI, Tenório D, Moraes CR, Cavalcanti HD. Ophthalmologic findings in cardiac transplant recipients. *Arq Bras Oftalmol.* 2007;70:767–770.
10. Nuttall GA, Garrity JA. Risk factors for ischaemic optic neuropathy after cardiopulmonary bypass: a matched case/control study. *Anesth Analg.* 2001;93:1410–1416.
11. Lee LA, Roth S, Posner KL, Cheney FW, Newman NJ, Domino KB. The American society of anaesthesiologists postoperative visual loss Registry. *Anaesthesiology.* 2006;105:652–659. https://doi.org/10.1097/00000542-200610000-00007.
12. Shaw PJ, Bates D, Cartlidge NE, et al. Neuro-ophthalmological complications of coronary artery bypass graft surgery. *Acta Neurol Scand.* 1987;76:1–7.
13. Ditzel J. Intravascular changes in the retina during open-heart surgery. *Lancet.* 1971;2:984.
14. Williams IM. Intravascular changes in the retina during open-heart surgery. *Lancet.* 1971;2:1260.
15. Borruat FX Bogousslavsky J, Uffer S, Klainguti G, Schatz NJ. Orbital infarction syndrome. *Ophthalmology.* 1993:100562–100568.
16. Van Stavern GP, Gorman M. Orbital infarction after cocaine use. *Neurology.* 2002:59642–59643.
17. Zimmerman CF, Van Patten PD, Golnik KC, Kopitnik Jr TA, Anand R. Orbital infarction syndrome after surgery for intracranial aneurysms. *Ophthalmology.* 1995:102594–102598.
18. Maier P, Feltgen N, Lagrèze WA. Bilateral orbital infarction syndrome after bifrontal craniotomy. *Arch Ophthalmol.* 2007;125(3):422–423.
19. Rainio A, Hautala N, Pelkonen O, et al. Risk of retinal microembolism after off-pump and on-pump coronary artery bypass surgery. *J Cardiovasc Surg.* 2007;48:773–779.
20. Ascione R, Ghosh A, Reeves BC, et al. Retinal and cerebral microembolization during coronary artery bypass surgery: a randomized, controlled trial. *Circulation.* 2005;112:3833–3838.
21. Cheng DC, Bainbridge D, Martin JE, Novick RJ. The Evidence-based Perioperative Clinical Outcomes Research Group. Does off-pump coronary artery bypass reduce mortality, morbidity, and resource utilization when compared with conventional coronary artery bypass? A meta-analysis of randomized trials. *Anesthesiology.* 2005;102:188–203.
22. Subramanian M, Meyers B. Bilateral versus single lung transplantation: are two lungs better than one? *J Thorac Dis.* 2018;10(7):4588–4601.
23. Aigner C, Klepetko W. Bilateral lung transplantation. *Oper Tech Thorac Cardiovasc Surg.* 2012;17:181–193.
24. Nagendran M, Maruthappu M, Sugand K. Should double lung transplant be performed with or without cardiopulmonary bypass? *Interact Cardiovasc Thorac Surg.* 2011;12(5):799–804.
25. Bates M, Factor M, Parrino PE, et al. Lung transplantation and the routine use of cardiopulmonary bypass and median sternotomy: experience at the ochsner multi-organ transplant institute. *Ochsner J.* 2017;17(1):38–41 Spring.
26. Liu Y, Liu Y, Su L, Jiang S. Recipient-related clinical risk factors for primary graft dysfunction after lung transplantation: a systematic review and meta-analysis. *PLoS One.* 2014;9(3):e92773.
27. Aeba R, Griffith B, Kormos R, et al. Effect of cardiopulmonary bypass on early graft dysfunction in clinical lung transplantation. *Ann Thorac Surg.* 1994;57(3):715–722.
28. Gammie J, Lee J, Pham S, et al. Cardiopulmonary bypass is associated with early allograft dysfunction but not death after double-lung transplantation. *J Thorac Cardiovasc Surg.* 1998;115(5):990–997.
29. Mateen F, Dierkhising R, Rabinstein A, van de Beek D, Wijdicks E. Neurological complications following adult lung transplantation. *Am J Transplant.* 2010;10(4):908–914.
30. Shigemura N, Sclabassi R, Bhama J, et al. Early major neurologic complications after lung transplantation. *Transplant J.* 2013;95(6):866–871.
31. Shennib H, Noirclerc M, Ernst P, et al. Double-lung transplantation for cystic fibrosis. *Ann Thorac Surg.* 1992;54(1):27–32.
32. Mohite P, Sabashnikov A, Patil N, et al. The role of cardiopulmonary bypass in lung transplantation. *Clin Transplant.* 2016;30(3):202–209.
33. Dong L, Mizota T, Tanaka T, Chen-Yoshikawa T, Date H, Fukuda K. Off-pump bilateral cadaveric lung transplantation is associated with profound intraoperative hypothermia. *J Cardiothorac Vasc Anesth.* 2016;30(4):924–929.
34. Tarabishy A, Khatib O, Nocero J, Budev M, Kaiser P. Ocular complications in patients with lung transplants. *Br J Ophthalmol.* 2010;95(9):1295–1298.
35. Dhal U, Singh A, Mehta A. "For your eyes only": ophthalmic complications following lung transplantation. *J Thorac Dis.* 2018;10(11):6285–6297.