THE LANCET
Respiratory Medicine

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Ceulemans LJ, Van Slambrouck J, De Leyn P, et al. Successful double-lung transplantation from a donor previously infected with SARS-CoV-2. *Lancet Respir Med* 2020; published online Dec 1. http://dx.doi.org/10.1016/S2213-2600(20)30524-5.

Appendix

Chronological overview of the SARS-CoV-2 related history of the donor.

- Month - 4: Later donor and husband were vaccinated for influenza and pneumococcal disease.
- Day - 8: Husband had mild symptoms, presented at the emergency room, was tested positive for SARS-CoV-2 (nasopharyngeal swab, PCR) and send home to stay in quarantine with his wife (the later donor).
- Day 0: Later donor contacted her general practitioner by phone for mild COVID-19 related symptoms (fever, cough, general weakness and muscle pain). As specified in the case report, she had not been tested for SARS-CoV-2 at that time due to the limited testing capacity in our country and the national lock-down during which tele-consultations were advised.
- Day 11: Husband admitted to the hospital and referred immediately to ICU due to serious COVID-19 related respiratory failure where he passed away one day later. He had severe co-morbidities (cardiovascular, dialysis, 82-years of age) for which it was decided not to intubate or resuscitate (Do Not Resuscitate-policy).
- Day 12: Tele-consultation between later donor and general practitioner for persistent mild COVID-19 related symptoms. Since symptoms were not worsening, the patient was asked to continue the quarantine.
- Day 96: Later donor was admitted to the emergency room with cerebral hemorrhage.
- Day 96: First nasopharyngeal swab for SARS-CoV-2 PCR was negative.
- Day 104: SARS-CoV-2 IgG was positive.
- Day 105: Second nasopharyngeal swab for SARS-CoV-2 PCR was negative. Donation

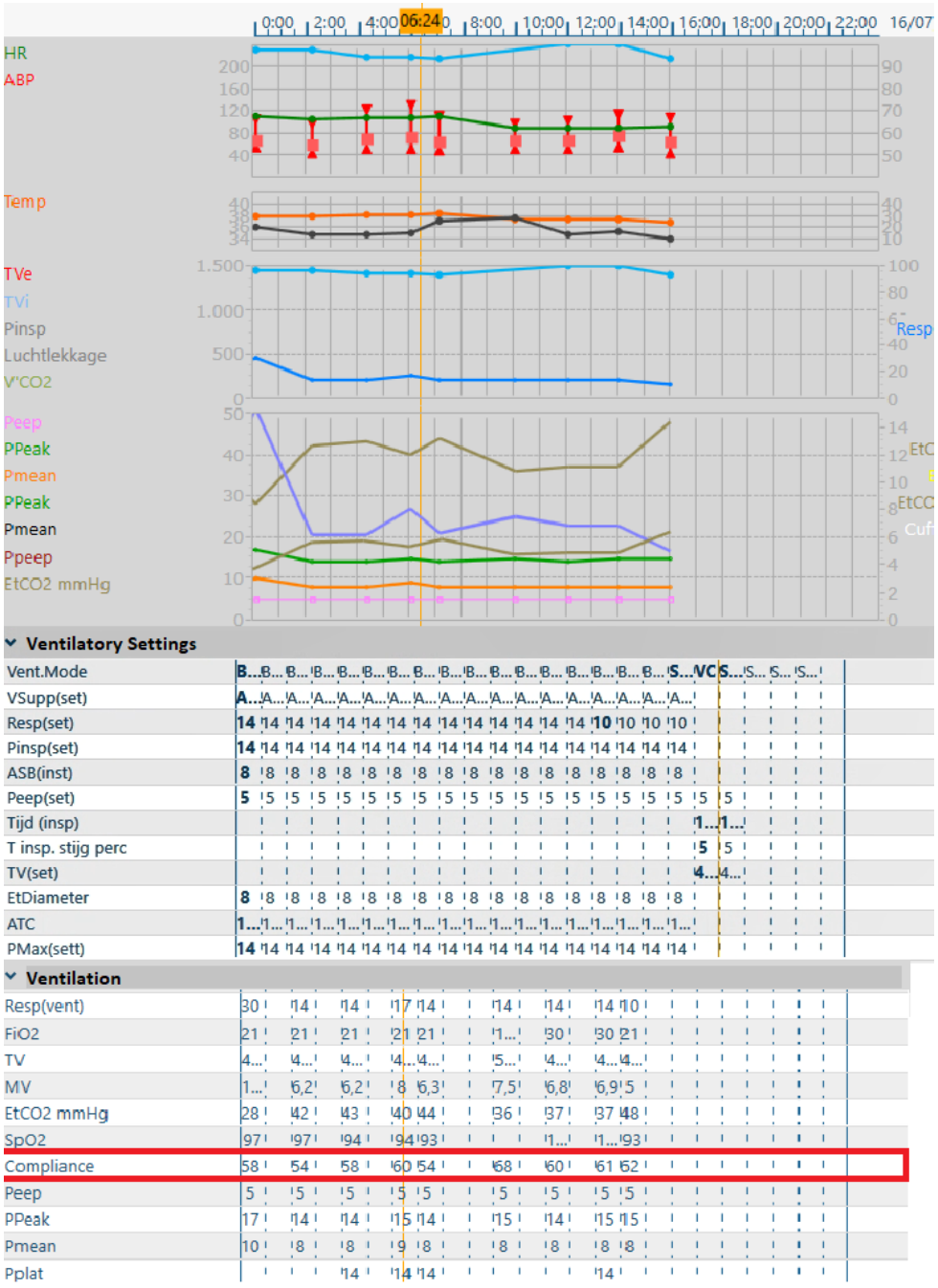
SARS-CoV-2 antibodies were found to be positive, exactly 104 days after onset of COVID-19 related symptoms. These antibodies prove that the donor has been exposed to SARS-CoV-2.

The exact dates of this chronological information is confidential according to the Belgian law.

Liver and kidney function of the donor.

Aspartate aminotransferase (ASAT)	30 U/L
Gamma-glutamyl transferase (gamma-GT)	12 U/L
Total bilirubin	0·24 mg/dL
Ureum	37 mg/dL
Creatinine	0·48 mg/dL

Ventilatory settings (BiPAP modus, ventilator Dräger XL) and dynamic compliance values (ml/cm H_2O) before donation.



Clarification of the Belgian law regarding patient rights and organ donation.

According to article 8 § 2 of the Belgian law on patient rights, the patient has to be informed in advance about the purpose, the nature, the grade of urgency, the possible contra-indications as well as potential complications and risks of the proposed procedure. In case of transplantation, our transplant candidates sign an informed consent at the moment that they are listed, in which it is specifically stated that the decision to accept and transplant an organ is a medical decision by the physicians of the transplant team, who accept or decline the offered organ based on their expertise and best clinical judgement. In Belgium, no specific consent is required regarding organ transplantation from extended criteria donors (e.g. donation after circulatory death, donor CMV status, donor HCV status, etc…). The same is true for a donor with a history of previous COVID-19.

In this specific case of a donor with a history of COVID-19, the decision to accept and transplant the organs was made after multidisciplinary consultation between the transplanting surgeon, pulmonologist as well as the virologist-expert in SARS-CoV-2. The decision was also in accordance with the ISHLT consensus guideline revised version of July 10 and August 19, 2020, stating that: ´´a donor with former COVID-19 following complete clinical recovery, at least 28 days from symptom onset, and two negative PCR tests 24-48 hours apart may carefully be assessed for donation and ultimately be considered eligible for donation if no permanent end-organ damage resulted from COVID-19 and appropriate donor organ function is confirmed.´´ (*https://ishlt.org/ishlt/media/documents/SARS-CoV-2_-Guidance-for-Cardiothoracic-Transplant-and-VAD-centers.pdf*)

In addition and according article 4bis of the Belgian law on organ transplantation, it is strictly forbidden to communicate any donor information that could reveal directly or indirectly the identity of the donor to the recipient. Therefore, in a small country like Belgium, we are obliged to limit any donor-related information to the recipient at the moment of transplantation.

However, since it was an exceptional case and when we were sure at one month post-transplant that the recipient could not retrace the donor identity based on the COVID-19 information, we have explained to the recipient the need for close and long-term follow-up.

This text was assisted by professor Herman Nys from the Interfaculty Centre for Biomedical Ethics and Law at the KU Leuven, Belgium (herman.nys@kuleuven.be) (https://gbiomed.kuleuven.be/english/research/50000687/50000697/pcbmer/00015339)

Methodology on SARS-CoV-2 Polymerase Chain Reaction (PCR) and viral culture.

Real-time reverse transcription polymerase chain reaction (qRT-PCR)
qRT-PCR was performed on nasopharyngeal swabs, lung biopsies and BAL fluids. Briefly, qRT-PCR was performed using the 2019-nCoV CDC EUA Kit (IDT - Integrated DNA Technologies, Leuven, Belgium) targeting the N1 and N2 genes on a QuantStudio 7 Real-time PCR system (Applied Biosystems, The Netherlands).

SARS-CoV-2 cell culture
Homogenized material from lung biopsies or BAL fluid was used to inoculate Vero E6 (CRL-1586, Epithelial monkey kidney cells, ATCC, USA) and Huh7 (human epithelial hepatocyte derived cellular carcinoma, ThermoFisher, Merelbeke, Belgium) cells. Flasks were monitored daily for the development of SARS-CoV-2 cytopathic effect. Viral load was assessed by qRT-PCR every 72 hours.

Summary of all operative timings related to procurement and transplantation.

DONOR:
Switch off: 18:29
Cardio-circulatory arrest (start ischemic time): 18:52
Total agonal phase in the donor: 23 min

Declaration of death and incision: 18:57
Perfusion: 18:59
Total warm ischemic phase in the donor: 7 min

Arrival donor organs in the transplant center: 22:08

RECIPIENT:
Start incision: 22:29 *(delay due to the fact that the lead surgeon was performing an urgent revision for bleeding in another lung transplant patient)*
Reperfusion right lung: 00:48
Total ischemic time right lung: 357 minutes

Reperfusion left lung: 03:30
Total ischemic time left lung: 518 minutes

End of operation: 04:25
Total operative time: 356 minutes

Lung transplantation protocol, drug regimen.

Induction:
- Solumedrol® (methylprednisolone): 500 mg IV per-operatively before reperfusion (day 0).
- rATG 3 mg/kg/d IV for 3 days (day 1-3).

Maintenance:
- Solumedrol® /Medrol® (methylprednisolone): Day 1 3x125 mg/d IV, as of day 2-14 0.4 mg/kg/d po or IV, later gradual tapering depending on clinical situation to 0.2 mg/kg/d and finally 4 mg/d after 1 year.
- Prograft® (Tacrolimus, FK506): 0.05 - 0.3 mg/kg po (start day 1), target through level 13 à 15 ng/mL during first 2 months.
- Cellcept® (Mycophenolate Mofetil): 2 x 1-1.5 g/d po or IV (start day 0), first dose is started per-operatively before reperfusion.
- Azithromycin 250 mg/d for first 5 days post-transplant, thereafter 250 mg 3x/week (start day 1).
- Nystatin 100 000 U/mL, 4*5 mL/day po (start day 1).
- Aspergillus prophylaxis:

  On ICU (while intubated): Abelcet® (amphotericine B lipid complex) 15 mg in NaCL 0.9% in aerosol 1x/day (start day 1).

  After extubation: Abelcet® (amphotericine B lipid complex) 50 mg in NaCL 0.9% + 5 drops Ventolin in aerosol, 2x/week, stop if no suture necrosis at discharge, continued if suture necrosis/dehiscence/positive aspergillus culture in total 3 months.
- Herpes prophylaxis if CMV Donor (D) - / Recipient (R) - (if D+ or R+: CMV prophylaxis):

  Acyclovir 3 x 5 mg/kg/d IV for at least 2 weeks post-LTx, thereafter Acyclovir 3x 800 mg/d (if >50 kg) or 3x 400 mg/d (if <50 kg) po in total 3 months post-LTx (start day 1).
- CMV prophylaxis if D+ or R+ CMV IgG positive (if D-/R-: Herpes prophylaxis):

  * D+/R-: Ganciclovir 2 x 5 mg/kg/d I.V. for at least 2 weeks post-LTx (if eGFR 10-50 mL/min: 2 x 2.5 mg/kg/d IV), thereafter Valganciclovir 900 mg/d (2x450 mg) po in total 6 months post-LTx.

  * D-/R+ or D+/R+: Ganciclovir 1 x 5 mg/kg/d I.V. for at least 2 weeks post-LTx (if eGFR 10-50 mL/min: 1 x 2.5 mg/kg/d IV), thereafter Valganciclovir 900 mg/d (2x450 mg OD) po in total 6 months post-LTx.
- Pneumocystis prophylaxis:

  Sulfamethoxazole–trimethoprim 2*160 mg 2x/week (if >50 kg), 2*80 mg 2x/week (if <50 kg), initially IV, later po (start week 2).