Archivos de Bronconeumologia

Impact of an improvised system on preserving oxygen supplies in patients with COVID-19.

--Borrador del manuscrito--

Número del manuscrito:	ARBR-D-20-00592R1
Tipo de artículo:	Carta científica / Scientific letter
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Respuesta a los revisores:	We are very grateful for the reviews provided by the Editors and each Reviewer of this manuscript. The comments are encouraging, and the Reviewers appear to share our judgement that this study and its results are clinically important. Please see below, in blue, our detailed point-to-point responses to all comments. All page numbers and lines refer to the revised manuscript file (clean version). Comments from the Editors: Given the reduced number of patientes recruited for the investigation we can offer the publication of a research letter, but not of an original research article. We encourage the authors to revise their manuscript according to the Journal's guidelines for research letters before the submission of a revised manuscript version. Authors' Response: As proposed, we revised our manuscript as a research letter (<1000 words, 1 figure or table, max 15 references) and added supplementary materials with your agreement. For the convenience of the reader, we would kindly ask to the Editors to consider adding the Figure explaining the DTM in the main text (currently e-figure 1) because this device is barely known and hard to visualize or understand at a first glance. We fully understand if it is not possible. Reviewer #1: 1.1. Reviewer comment: As minor comments, it would indicate a proposal for action to change from low-flow systems to double-trunk mask based on saturation levels and would comment on its role against non-invasive ventilation. Authors' Response: We added the following paragraph, keeping it short and prudent to meet the Editor's request (scientific letter): Page 6 Lines 80-84: "Although evaluation of its place relative to the non-rebreathing mask, high-flow oxygen therapy or non-invasive ventilation was not within the scope of this study, we believe the DTM could also be considered when SpO2 falls below the target value with standard LFOT systems. Consequently, the need for non-invasive respiratory support, which increases risks of generating aerosols, may possibly be avoided. 1.2. Reviewer comment: The manuscript should be reviewed by a native English

	speaker as some grammatical errors are observed Authors' Response: This new version was carefully revised by Mariana Andrade, Medical Writer. Reviewer #2: 2.1. Reviewer comment: Minor comments Table 1 includes the CRP. In isolation I am not sure what this provides I would weither omit or add a table of the inflammatory profile which would include a broader range of markers for covid hyperinflammatory syndrome including Ferritin, WCC and differential, fibrinogen/d-dimer, presence of other organ dysfunction, lipid profile. Authors' Response: In contrast, we believe that the CRP level in isolation already provides a fair estimation of the severity of the COVID-19 disease (Tan et al. J Med Virol 2020 ; Wang et al. Med Mal Infect 2020). Our retrospectively collected data also corroborate these findings: we have observed in our cohort that a high CRP is associated with a higher risk of mortality (manuscript submitted, under revision). Therefore, to keep the table (e-table 1) easy to follow, we would prefer to leave the description of the CRP level in isolation. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, et al. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol 2020;92:856-862. Wang L. C-reactive protein levels in the early stage of COVID-19. Med Mal Infect 2020;50:332-334. 2.2. Reviewer comment: The discussion should be expanded to make more detailed reference to the limitations of the duration of the trial and as such a longer term clinical trial as well as one including a broader range of O2 rates is required. Authors' Response: We agree with the Reviewer. Even if the modification of the format requested by the Editor requires a reduced number of words, we expanded our limitation section by insisting on the points highlighted by the Reviewer. The paragraph now reads: Page 6 Lines 92-95: "The main limitation was the pre-post intervention design of short duration. Moreover, the investigator who readjusted oxygen flow was not blinded in order to limit prolonged and multiple exposures of healthcare workers. Randomized controlled trials of longer duration involving a broader range of oxygen flows are required." 2.3. Reviewer comment: It would also be of interest to the reader to have an estimation of a potential effect on O2 consumption. The authors could estimate this by using proportion of patients admitted that met the inclusion criteria either from their own hospital, if known or from the literature. Authors' Response: We thank the Reviewer for this suggestion. We reviewed our database and found that 266 patients (on a total of 400 patients hospitalized because of the COVID-19 disease, that is 65%) were eligible at some point of their stay, which is consistent with the high proportion of patients who actually wore the DTM during at least one day in our hospital. Even if we are not able to give an accurate estimation of the DTM effect on O2 consumption because the patients' oxygen need was dynamic and we have not collected the O2 output day after day for each patient, we can provide an estimation of the O2 output spared in a day. Considering a mean of 5L/min of O2 use in our 266 potentially eligible patients during 1 day (thus, 1.915.200 liters) and an average O2 flow reduction of 50% with the DTM as found in this study, this system would spare 957.600 liters of O2 during these 24 hours. Accordingly, we added the following sentence: Page 6 Line 90-92: "The importance of our findings is emphasized by the large oxygen flow reduction under the DTM (56%) and the high proportion of our hospitalized patients who met the inclusion criteria at some point of their stay (266/412)."

Carta de presentación/Cover letter

UCL Université Catholique de Louvain
Secteur des Sciences de la Santé
Institut de Recherche Expérimentale & Clinique (IREC) – *Prof. JL Vanoverschelde*
Pôle Pneumologie, ORL et dermatologie **–** *Prof. Ch. Pilette*

Brussels, 17th July 2020

Dear Prof. Barreiro,

We are pleased to submit our revised manuscript for consideration for publication in *Archivos de Bronconeumología*. The manuscript is entitled "Impact of an improvised system on preserving oxygen supplies in patients with COVID-19." As proposed by the Editors, we modified the template of our manuscript from an original research to a scientific letter.

We confirm that neither the manuscript nor any part of its substance or figures have been or will be published or submitted to another scientific journal or are being considered for publication elsewhere.

Thank you for your consideration of our manuscript. We look forward to hearing from you in the near future.

Yours Sincerely,

For the authors, William Poncin, PT, PhD
Correspondence: william.poncin@uclouvain.be (+3227642832), Cliniques universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium

Impact of an improvised system on preserving oxygen supplies in patients with COVID-19.

Running title: DTM saves oxygen supply in COVID-19 **SCIENTIFIC LETTER**

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Declaration of Interest: None; **Sources of support:** None

Manuscript word count: 1000/1000; Reference count: 13/15; Figure: 1

Acknowledgements

We are grateful to Prof. Annie Robert for the statistical review of our analysis. We thank Mariana Andrade MD, who provided editorial assistance. Compensation but no commercial funding was received for this purpose. We also thank the interns (S. Brilot, S. Demartin, E. Lagneaux, R. Lattenist, J. Lux, G. Pierman, G. Vandercam, S. Wallemacq, M. Gagliardi) in the internal medicine and pneumology departments for their contributions.

Respuesta a los revisores (Response to reviewer) Click here to access/download;Respuesta a los revisores (Response to reviewer);Response Letter_ARBR-D-20-

Response letter – ARBR-D-20-00592

Impact of an improvised system on preserving oxygen supplies in patients with COVID-19.

We are very grateful for the reviews provided by the Editors and each Reviewer of this manuscript. The comments are encouraging, and the Reviewers appear to share our judgement that this study and its results are clinically important. Please see below, in blue, our detailed point-to-point responses to all comments. All page numbers and lines refer to the revised manuscript file (clean version).

Comments from the Editors: Given the reduced number of patientes recruited for the investigation we can offer the publication of a research letter, but not of an original research article. We encourage the authors to revise their manuscript according to the Journal's guidelines for research letters before the submission of a revised manuscript version.
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SCIENTIFIC LETTER

Impact of an improvised system on preserving oxygen supplies in patients with COVID-19.

Abbreviation list

COVID-19: Coronavirus Disease 2019

~~CT: Computed Tomography~~

DTM: Double-Trunk Mask

IQR: Interquartile Range

LFOT: Low-Flow Oxygen Therapy

~~NRM: Non-Rebreathing Mask~~

SaO2: Arterial Oxygen Saturation

~~SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2~~

SD: Standard Deviation

SpO2: Pulse Oxygen Saturation

Abstract (243/**250 words**)

Introduction: Patients with coronavirus disease (COVID-19) can develop severe hypoxemia. Meeting the soaring demands of oxygen may be a challenge. Our objective was to test the efficacy of an easily handmade system, the double-trunk mask (DTM), in reducing oxygen consumption while maintaining patient's oxygenation level.

Methods: Hospitalized adults with COVID-19 and hypoxemia treated with low-flow oxygen therapy we recruited. The standard oxygen delivery system was replaced by the DTM with nasal cannula for 30 minutes with an oxygen output adapted to maintain an identical oxygen saturation by pulse oximetry. The standard oxygen delivery system was then reinstated for 30 minutes. Primary outcome was the absolute change in oxygen flow between the standard delivery systems and the DTM.

Results: Eleven patients were analyzed (mean age 61 years; 27% were male). Compared with standard delivery systems, the oxygen output was significantly reduced with the DTM (median [IQR]: 5 [4-8] L/min vs 1.5 [1.5-4] L/min, respectively; p=0.003) when oxygen saturation and arterial oxygen tension remained stable. The DTM was also associated with a significant but slight increase in arterial carbon dioxide tension (36 vs 37 mmHg, p=0.006) and respiratory rate (26 vs 30 breaths/min, p=0.05). Other parameters were unaltered. The DTM was generally judged less comfortable than the baseline oxygen delivery system, especially in patients requiring low oxygen flow at baseline.

Conclusions: The DTM is a simple and efficient system to reduce oxygen consumption. This may have clinical implications in places where oxygen supplies are limited.

Keywords: Coronavirus Disease 2019; Severe Acute Respiratory Syndrome Coronavirus 2; Hypoxemia; Oxygen Therapy; Double-Trunk Mask

~~Introduction~~

~~Arterial hypoxemia~~Hypoxemia is a typical feature of the coronavirus disease 2019 (COVID-19~~) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. According to an early report, around 30% of patients required supplemental oxygen therapy at hospital admission[1]. Oxygen delivery in the context of the COVID-19 pandemic raises some specific challenges.~~). The rapid rise in the number of patients requiring oxygen therapy during the pandemic may cause a sharp increase in oxygen demands and potential threats of supply disruption~~. This is~~, particularly ~~true~~ in developing countries[1] or nursing homes. ~~Additionally~~Moreover, the use of elevated oxygen flows *via* nasal cannula raises concerns about exhaled air dispersion distance and the potential risk of generating aerosols[2-6]~~, both of which could be hazardous to health care workers, although this has not been confirmed to date.~~.

~~The Double Trunk Mask (DTM) is a modified Tusk mask developed in 1998 by Hnatiuk et al.[7] which was further modified into a patent free handmade system in the early 2000s[8]. A previous study showed that the addition of the DTM over nasal cannula increased PaO_2 by 50% in patients with acute respiratory failure without clinical impact on $PaCO_2$[9]. From another perspective, the DTM may be used to reduce the oxygen flow required to correct hypoxemia which, in addition to reducing side effects of prolonged dry oxygen administration[10-12], could have crucial implications in situations where medical gases are a rare commodity. The objective of this study was to assess the efficacy of the DTM for preserving oxygen consumption in patients with COVID-19.~~

Material and methods

Participants

The Double-Trunk Mask (DTM) (image and description in supplement) is a patent-free handmade system which, when placed over nasal cannula, increases the PaO_2 by 50% in patients with acute respiratory failure without clinical impact on $PaCO_2$[7]. From another perspective, the DTM may reduce the oxygen flow required to correct hypoxemia which, in addition to reducing side-effects of prolonged dry oxygen administration[8-10], could have crucial implications in situations where medical gases are a rare commodity. The study's objective was to assess the efficacy of the DTM in preserving oxygen consumption in patients with COVID-19.

All adult patients with laboratory-confirmed COVID-19 and hypoxemia requiring low-flow oxygen therapy (LFOT) ≤15L/min to maintain ~~pulse oxygen saturation (~~SpO_2~~)~~ between 92~~ and ~~96% and laboratory confirmed COVID-19 ~~%, who were consecutively hospitalized ~~in the COVID-19 ward~~ between April ~~9~~ and ~~1,~~ May 2020 ~~at Cliniques universitaires Saint-Luc, Brussels, Belgium~~in our hospital, were ~~invited~~asked to participate in ~~this trial~~the study.

This ClinicalTrials.gov registered study (NCT04346420) was conducted with the approval of the local ethics committee. All subjects signed informed consent. Exclusion criteria were chronic respiratory diseases, language barriers, confusion, altered consciousness (Glasgow Coma Scale ≤12), hypoxemia corrected with ~~an~~ oxygen flow ≤3L/min and any contra-indication ~~for performing~~to arterial ~~blood gas sampling~~puncture.

~~All included patients provided written informed consent to participate in the study. The study was approved by the local ethics committee (B4032020000004) and is registered in ClinicalTrials.gov (NCT04346420). All research procedures adhered to the tenets of the Declaration of Helsinki.~~

~~***Material***~~

~~The DTM is made up of a regular aerosol mask (Sidestream, Philips Respironics, New Jersey, USA) with two corrugated tubes (ISO 22) or "trunks", 15cm in length, inserted in the exhalation ports (Figure 1). This system is applied on the face of the patient, above the nasal cannula used for the delivery of oxygen therapy. By means of the tubing and the collector of the nebulizer, the DTM sequesters the amount of oxygen that is wasted during expiratory phases and restitutes it on subsequent inspiratory phases. Therefore, for a similar oxygen output, the DTM acts as a booster of the fraction of inspired oxygen.~~

~~***Study design***~~

~~The objective of this study was to assess the impact of the DTM in reducing oxygen consumption while maintaining patient's oxygenation level. The patients~~Patients were in a semi-recumbent position and received LFOT through their standard oxygen delivery method. The initial oxygen flow and ~~the baseline oxygen~~ delivery system were determined in accordance with our standard ~~of care~~practice. The baseline oxygen flow was titrated to achieve a target SpO_2 value of 94% at the lowest output. Oxygen flow requirements determined the baseline oxygen delivery system~~. Nasal cannulas were applied for flow up to 6 L/min, simple facemasks (oronasal masks) for oxygen flows between 7 and 10 L/min, and non-rebreathing masks (NRM) for flows between 11 and 15L/min. In circumstances where SpO_2 jumped from less than 92% with the oronasal mask at 10L/min to more than 96% with the NRM, one of the two one-way valves at the exhalation ports was removed in order to achieve the desired baseline target SpO_2 value.~~

~~The standard oxygen~~ (supplements). The baseline delivery system was then replaced by the DTM covering nasal cannula for 30 minutes. Oxygen output (primary outcome) was adjusted to achieve the same SpO_2 target as at baseline. ~~At the end of~~After this period, the DTM was withdrawn and the standard oxygen delivery system was reinstated for 30 minutes. Oxygen output was readjusted to achieve the baseline SpO_2 value. Patients received no instructions regarding nasal or mouth breathing during the whole process.

~~***Outcomes***~~

Arterial blood gases, vital parameters ~~(SpO_2, respiratory rate, heart rate, arterial blood pressure, temperature)~~ and oxygen output were measured at baseline (T_0) and at the end of the 30-min DTM period ~~under the DTM~~ (T_{30})~~. Blood gas sampling was performed by medical staff not involved in this study and analysed using the ABL90 FLEX blood gas analyser~~

~~(Radiometer, Denmark).~~ Vital parameters and oxygen output were measured again 30 minutes after the DTM was withdrawn (T_{60}). Comfort-discomfort level with each system was assessed at T_{30} and T_{60} (supplements).

~~At T_{30} and T_{60}, the patients were asked to note the comfort-discomfort level and preference using a 5-point Likert scale ranging from "strongly disagree" to "strongly agree". Questions were as follows: 1. "Is the oxygen delivering system comfortable?", 2. "is the oxygen delivering system more comfortable than the previous one?", 3. "is the oxygen delivering system inconvenient leading to a risk of its removal?".~~

~~Results of computed tomography (CT) performed at hospital admission as part of routine evaluation of patients suspected of COVID-19 were reviewed in patient medical records. The severity of pulmonary involvement was classified using the recent consensus statement on reporting of chest CT findings related to COVID-19[13].~~

~~Statistical analysis~~

~~The primary outcome was the change in oxygen flow generated by using the DTM. Assuming an α risk of .05 and a power of 90% in a two-sided test, a sample size of 11 subjects was needed to detect a mean difference of 2 L/min[14] with a standard deviation of paired difference 1.8 L/min (PASS 14, NCSS, LLC, Utah, USA). This conservative standard deviation was chosen because of the expected high variability of the fraction of delivered oxygen between patients with rapid breathing patterns receiving LFOT and between oxygen delivery systems[15,16].~~ Eleven subjects were needed to detect a mean difference of 2L/min[11] (SD, 1.8L/min) in oxygen output (α-risk, 0.05; power, 90%). Because SpO_2 may inaccurately reflect arterial oxygen saturation (SaO_2) and therefore interfere with our design, patients were retrospectively excluded from the analysis if ~~the~~SpO_2-SaO_2 mismatch ~~between both SpO_2 and SaO_2 measurements~~ exceeded

the expected error of 4%[17,18][12,13]. Data are presented as mean ±SD or median [interquartile range (IQR)] as appropriate. Pairwise comparisons were tested with paired t-test or Wilcoxon test. Ordinal paired data were compared with Wilcoxon test. P-values <0.5 were considered statistically significant.

~~Normality of data was verified with Shapiro-Wilk tests. Data are presented as mean ± standard deviation (SD) or median and interquartile range (IQR) as appropriate. Paired t-test and Wilcoxon test was applied for pairwise comparisons, as appropriate. Ordinal paired data were compared using the Wilcoxon test. Post hoc analysis for correlations were calculated by Spearman's rho coefficient. All tests were two-sided and p-values ≤.05 were considered significant. Statistical analyses were performed using SPSS version 25 (IBM, Armonk, New York).~~

~~Results~~

~~Participants~~

Of ~~the 13 consecutive eligible~~ 12 patients who ~~were asked to participate in this trial, 12 agreed to be enrolled and~~ completed the entire study procedure~~. One patient~~, one was excluded from the analysis because SpO_2 ~~and~~ -SaO_2 ~~measurements at T_0 were 93% and 97.3%, respectively (~~difference~~:~~ at T_0 was 4.3~~%).~~%. Final analyses were performed on ~~data collected from the remaining~~ 11 patients (~~study flowchart in Figure 2).~~

~~The mean age of patients was~~ 61 ~~years (SD,~~ ±14 years~~) and~~; 27% ~~were male. Most patients had moderate or severe pulmonary involvement on initial lung CT evaluation. The median oxygen flow value at baseline was 5 (4-8) L/min. Eight patients received LFOT via nasal cannulas, two received LFOT via a standard oronasal mask and the remaining patient received oxygen through the NRM but with one of the lateral one-way valves removed. The~~female). E-Table 1 details baseline characteristics~~ of patients are shown~~. Compared with standard delivery systems, the oxygen output was significantly reduced with the DTM (median [IQR], 5 [4-8]L/min vs 1.5 [1.5-4]L/min; p=0.003) when oxygen saturation and PaO_2 remained stable. The DTM was also associated with a significant but slight increase in $PaCO_2$ (median, 36 vs 37 mmHg, p=0.006), a decrease in pH (median, 7.48 vs 7.45, p=0.009) and an increase in respiratory rate (mean, 26 vs 30 breaths/min, p=0.05), Fig. 1, e-Table 2. Other parameters were unaltered. ~~table 1.~~

~~Primary outcome~~

~~Regardless of~~The DTM was generally considered less comfortable than the baseline oxygen delivery system, ~~for a similar SpO_2 level, the oxygen output systematically decreased from a~~

~~median value of 5 (4-8) L/min with the standard interface to a median value of 1.5 (1.5-4) L/min with the DTM (median difference, -3; [95%CI: -4 to -1.5]; p=0.003) (Table~~ especially in patients requiring low oxygen flow at baseline (e-Fig. 2~~; Figure 3).~~

~~**Secondary outcomes**~~

~~).~~ There were no ~~significant~~ differences between T_0 and T_{60} for any outcomes~~,~~ (e-Table 2), indicating that all values were reset when the standard ~~system for oxygen administration was reinstated (Table 2).~~

~~Between T_0 and T_{30}, there was a significant increase in $PaCO_2$ (median, 36 mmHg vs 37 mmHg, median difference, 1 [95%CI 0 to 2]; p=0.006) and a decrease in pH (median 7.48 vs 7.45; median difference, -0.02 [95%CI -0.02 to 0]; p=0.009) associated with the use of the DTM (Table 2; Figure 3). Mean respiratory rate significantly increased with the DTM (from 26 to 30 breaths/min; mean difference, 3 [95%CI 0 to 6]; p=0.05). Other vital parameters remained stable (Table 2).~~

~~The patients rated the standard oxygen delivery system as more comfortable than the DTM and preferred the former over the latter (median difference, 1 [95% CI 0 to 3]; p=0.016). However, there was no significant difference in the inconvenience generated by each system (p=0.13) (Table 3). Post-hoc analysis indicated that there was a negative association between oxygen flow at onset and a greater preference for the standard oxygen~~ delivery system ~~(rho = -0.75 [95% CI, -0.93 to -0.25], p=0.008) and a trend towards a negative correlation between baseline oxygen flow and greater comfort rating with the standard oxygen delivery system (rho = -0.57 [95% CI, -0.88 to 0.07], p=0.07), indicating that the DTM was more easily tolerated by patients receiving high oxygen flows (Figure 4).~~was reinstated.

~~Discussion~~

~~This pre-post intervention trial shows that DTM, an easily handmade patent-free oxygen delivery system, enables clinicians to safely treat severe hypoxemia while reducing the oxygen flow by more than half (mean oxygen flow ratio = 56%) that which would be required with conventional oxygen delivery systems (*i.e.* nasal cannula, simple oronasal mask and NRM). Indeed, stable PaO_2 and SaO_2 levels were maintained under the DTM while a slight increase of $PaCO_2$ and a decrease in pH were noted. These changes were of limited clinical significance because they did not translate into hypercapnia or acidosis. Instead, respiratory alkalosis was mitigated in this disease where hypocapnic hypoxemia is a typical feature[19]. By causing a shift in the oxyhaemoglobin dissociation curve to the left, arterial hypocapnia and alkalosis increase the oxygen affinity of haemoglobin thus increasing the SaO_2 for the same level of PaO_2. However, the DTM should not be viewed as an impediment to this adaptation mechanism since PaO_2 and SaO_2 remained stable despite its effects on $PaCO_2$ and pH. Furthermore, we calculated the oxygen tension when haemoglobin is 50% saturated with oxygen (p50) in our cohort based on the equation of Siggaard-Andersen[20], using temperature, SaO_2, PaO_2, $PaCO_2$ and pH and found no difference between pre- and post-intervention (mean, 23.24 mmHg vs 23.23 mmHg, respectively). Based on these findings, we believe the DTM may have a place in the management of hypoxemia in patients with COVID-19 but we recommend caution with its use in patients with chronic respiratory disease and ventilatory inefficiency. The safety and efficacy of the DTM in this latter population deserves further studies.~~

Treating hypoxemia is the cornerstone of COVID-19 patient management and this pre-post intervention trial shows that the DTM enables clinicians to safely treat severe hypoxemia while reducing the oxygen flow by more than half that required with conventional delivery systems.

Therefore, settings in which oxygen supplies are limited (*e.g.* nursing homes, healthcare centres in deprived medical areas, during patient transport) may benefit most from the DTM. Although evaluation of its place relative to the non-rebreathing mask, high-flow oxygen therapy or non-invasive ventilation was not within the scope of this study, we believe the DTM could also be considered when SpO_2 falls below the target value with standard LFOT systems[7,11]. Consequently, the need for non-invasive respiratory support, which increases risks of generating aerosols[6], may possibly be avoided.

The DTM ~~acts as a reservoir and stores the oxygen administered during the expiratory phase that would mainly be lost with the use of a nasal cannula or oronasal mask. Previous studies have shown that this system was able to increase the PaO_2 for a same oxygen output[8,14]. It should be noted that in our study the beneficial effect of DTM was manifest regardless of the baseline oxygen administration system, indicating that the effects were not linked to a correction in the mismatch between nasal oxygen administration and mouth breathing. The reduction of oxygen output with the DTM compared with the oronasal mask or the NRM is therefore likely due to the restitution of oxygen stored in the trunks during expiratory phases.~~

~~Different reasons may explain the limited $PaCO_2$ increase that was observed with use of the DTM. Although the total internal volume added by the system was 210 mL (including 60 ml per trunk)[9], the entirety of this volume cannot be considered as dynamic dead space. The proximity of the mouth with the inner parts of the trunks, the streaming effect of gas through the mask and the continuous oxygen flow beneath the DTM likely reduced dynamic dead space volume[21–23]. Furthermore, small amounts of exhaled gas may have leaked between the patient's face and the mask, thereby reducing CO_2 rebreathing. Finally, patients presumably~~

~~adapted to the added dynamic dead space volume by increasing their respiratory rate, as shown in our results.~~

~~Based on data showing increased mortality in acutely ill patients treated with liberal as compared to restrictive oxygen therapy[24], a SpO_2 target range of 92-96% has been suggested in the management of COVID-19 patients[25]. However, despite following restrictive oxygen therapy guidelines, hospitals dealing with the COVID-19 outbreak face a dramatic increase in oxygen demand. In our hospital for example, despite cancellation of all elective procedures and non-emergency care, the oxygen consumption during April 2020, at the peak of the outbreak in Belgium, was on average 10m^3 per hour higher than in April 2019 (+30%). Of note, the World Health Organization recently published guidance urging health facility administrators and decision makers to set up a surge oxygen delivery capacity[26]. Enabling physicians to deliver the required oxygen to patients is critical because management of hypoxemia is the cornerstone of COVID-19 patient management. By reducing oxygen consumption significantly with similar oxygenation outcomes, we believe the DTM deserves its place in the armamentarium of oxygen delivery systems for hypoxemic patients, especially in the current context of COVID-19 pandemic. Settings where oxygen supplies remain limited may benefit most from the DTM, such as in nursing homes, health care centres in deprived medical areas, or during patient transport. Beyond the current pandemic, the same reasoning may apply during extraordinary mass casualty events causing a sudden increase in oxygen demand.~~

~~As expected, the use of the DTM~~ was considered ~~to be~~ less comfortable than ~~standard~~ LFOT delivered through nasal cannulas~~. However, it should be noted that~~, yet patients who initially required high oxygen flow considered the DTM as equally comfortable~~, which~~. This might be

explained by ~~the use of~~using a ~~face mask~~facemask at baseline ~~for these patients~~ or the large absolute oxygen flow reduction with the DTM. ~~Although we did not estimate patient comfort for longer than 30 minutes with each system, the reduction of dry oxygen flow may also provide benefits over a longer period. Indeed, prolonged breathing of dry oxygen may cause nose and throat dryness, nose bleeds, and chest discomfort[27]. In addition, dry air breathing can alter the hydration level of the respiratory mucosa[11,28]. This may in turn reduce the mucociliary transport and increase the risk of coughing or sneezing which are important risk factors of viral transmission through generation of droplets and aerosols[29]. Therefore, reducing prolonged inhalation of dry oxygen are expected to yield indirect benefits, and further studies are warranted to evaluate this hypothesis.~~

~~We acknowledge that our study has several limitations. First of all, our study was not designed as a randomized controlled trial and the investigator in charge of readjusting oxygen flow between different systems was not blinded. In order to comply with the exceptional infection control procedures and to limit prolonged and multiple exposures of health care workers, blinding was not feasible. However, the large effect size observed in our primary outcome supports our conclusions. Secondly, although a decrease in oxygen flow was systematically observed regardless of the oxygen delivery system~~However, the low number of patients wearing oxygen facemasks at baseline precludes generalization of our conclusions with these systems. ~~Thirdly, we evaluated oxygen output requirements as primary outcome, and the extent to which DTM enables improved oxygenation for markedly hypoxemic patients was not within the scope of this study, although improved oxygenation at a same oxygen output has been previously demonstrated[8,9,30]. The clinical scenarios in which the DTM should be preferred outside a crisis context remains to be further determined. Evaluation of the long-term clinical impact of the DTM, including its relative efficacy compared to the NRM, will~~

~~enable clinicians to determine its precise place in the continuum of LFOT and high flow oxygen therapy.~~

~~Conclusion~~

The importance of our findings is emphasized by the large oxygen flow reduction under the DTM (56%) and the high proportion of hospitalized patients who met the inclusion criteria at some point of their stay (266/412). The main limitation was the pre-post intervention design of short duration. Moreover, the investigator who readjusted oxygen flow was not blinded in order to limit prolonged and multiple exposures of healthcare workers. Randomized controlled trials of longer duration involving a broader range of oxygen flows are required.

In conclusion, our study showed that the DTM is a useful oxygen delivery system that enables a safe reduction in oxygen output without hampering patient oxygenation. This finding is of particular interest in the current context of high and potentially overwhelming oxygen ~~demands~~demand.

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Figure legends

Figure 1. ~~**Illustration of the Double-Trunk Mask.**~~

~~The double-trunk mask consists of a regular aerosol mask with two corrugated tubes inserted in the lateral hole of the mask. The double-trunk mask is placed above the nasal cannula where the oxygen is delivered.~~

~~**Figure 2. Study flowchart.**~~

~~**Figure 3.**~~ **Change of oxygen output and blood gas outcomes.**

(a) Panel shows raw values of oxygen flow before (T0) and after (T30) wearing the double-trunk mask, as well as after reinstating the baseline oxygen delivery system (T60). Horizontal lines indicate median, 25th and 75th percentiles. The shape of each data point represents the baseline oxygen supply system: circles for nasal cannula, triangles for oronasal mask and square for the non-rebreathing mask. (b-d) Panels show respectively PaO_2, $PaCO_2$ and pH outcomes before (T0) and after (T30) wearing the double-trunk mask. The boxes indicate 25th and 75th percentiles; horizontal lines and "+" within boxes indicate median and mean, respectively; whiskers indicate the highest and lowest values within 1.5 × interquartile range; and points beyond the whiskers indicate outliers.

~~**Figure 4. Correlation between baseline oxygen flow and the difference of preference between each oxygen delivery system.**~~

~~Positive values indicate that participants preferred the standard oxygen delivery method over the double-trunk mask. Negative values indicate preference for the double-trunk mask over the standard oxygen delivery method.~~

Tables

Table 1: Baseline characteristics

Variables	n=11
Age, mean (SD), years	61 (14)
Sex, No. (%)	
- Male	9 (75)
- Female	3 (25)
BMI, mean (SD), kg/m^2	28.5 (4.0)
Oxygen flow, median (IQR), L/min	5 (4-8)
Oxygen delivery system, No. (%)	
- Nasal cannula	8 (73)
- Oronasal mask	2 (18)
- Non-rebreathing mask[a]	1 (9)
CT, severity of lesions, No. (%)	
- Mild (< 10%)	0 (0)
- Moderate (10-25%)	5 (45)
- Extensive (25-50%)	2 (18)
- Severe (50-75%)	4 (36)
- Critical (> 75%)	0 (0)
Interval between the study and CT, median (IQR), days	6 (2-18)
Interval between the study and onset of symptoms, median (IQR), days	10 (6-25)
CRP level at hospital admission, mean (SD), mg/L	112.49 (64.66)
CRP level the study day, mean (SD), mg/L	107.33 (72.27)
Setting, No (%)	
- Intensive care unit	1 (9)
- Medical wards	10 (91)

List of abbreviations: BMI, body mass index; CRP, C-reactive protein; CT, computed tomography.
[a] One of the two one-way valves on the front of the mask was withdrawn.

Table 2: Clinical outcomes at any time point of the study.

Outcomes	T_0 (Standard system)	T_{30} (Double-trunk mask)	T_{60} (Standard system)	Mean or Median change between time points, 95% CI, p-value: Change between Pre-Post intervention (T_{30}-T_0)	Change between Baseline and End of study (T_{60}-T_0)
Oxygen output, median (IQR), L/min	5 (4-8)	1.5 (1.5-4)	4 (3-8)	-3 (-4 to -1.5), p=0.003	0 (0 to 0), p=0.32
SpO_2, median (IQR), %	94 (94-95)	95 (94-95)	94 (94-95)	0 (0 to 2), p=0.19	0 (-1 to 1), p=0.71
SaO_2, median (IQR), %	95.5 (94.2-97.1)	95.7 (94.2-97.3)	/	0.2 (-0.6 to 1.5), p=0.24	n/a
PaO_2, median (IQR), mmHg	76 (65-82)	75 (69-86)	/	2 (-2 to 15), p=0.23	n/a
$PaCO_2$, median (IQR), mmHg	36 (34-39)	37 (35-41)	/	1 (0 to 2), p=0.006	n/a
pH, median (IQR)	7.48 (7.45-7.49)	7.45 (7.44-7.48)	/	-0.02 (-0.02 to 0), p=0.009	n/a
Temperature, mean (SD), °C	36.6 (0.55)	36.6 (0.58)	36.5 (0.55)	0.0 (-0.1 to 0.2), p=0.60	-0.1 (-0.3 to 0.1), p=0.31
Heart rate, mean (SD), beats/min	88.6 (17.9)	88.6 (17.3)	87.3 (17.2)	0.0 (-2.0 to 2.0), p>0.99	-1.3 (-3.5 to 0.9), p=0.23
Systolic blood pressure, median (IQR), mmHg	130 (120-143)	120 (110-143)	121 (110-135)	1 (-10 to 10), p=0.53	0 (-20 to 8), p=0.17
Diastolic blood pressure, median (IQR), mmHg	78 (70-83)	72 (70-83)	73 (70-80)	0 (-5 to 10), p=0.40	0 (-10 to 0), p=0.11
Respiratory rate, mean (SD), breaths/min	26 (4)	30 (7)	27 (5)	3 (0 to 7), p=0.054	1 (-1 to 3), p=0.45

List of abbreviations: SpO_2, pulse oxygen saturation; SaO_2, arterial oxygen saturation; PaO_2, arterial oxygen tension; $PaCO_2$, arterial carbon dioxide tension. T_0, baseline; T_{30}, 30 minutes after baseline, the double-trunk mask being worn 30 minutes; T_{60}, 60 minutes after baseline, the standard oxygen delivery system being worn 30 minutes between T_{30} and T_{60}.

Table 3. Comfort questions

Comfort questions, using scale 1-5*	Double-trunk mask	Standard system	p-value
Q1. Is the oxygen delivery system comfortable?	3 (2-4)	5 (4-5)	0.016
Q2. Is the oxygen delivery system more comfortable than the previous one?	3 (2-4)	5 (4-5)	0.016
Q3. Is the oxygen delivering system inconvenient leading to a risk of its removal?	4 (1-4)	1 (1-3)	0.13

Results are displayed as median (IQR)

* Comfort questions were assessed using 1-5 Likert scale. 1: strongly disagree, 2: disagree, 3: neutral, 4: agree, 5: strongly agree.

SCIENTIFIC LETTER

Impact of an improvised system on preserving oxygen supplies in patients with COVID-19.

Abbreviation list

COVID-19: Coronavirus Disease 2019

DTM: Double-Trunk Mask

IQR: Interquartile Range

LFOT: Low-Flow Oxygen Therapy

SaO2: Arterial Oxygen Saturation

SD: Standard Deviation

SpO2: Pulse Oxygen Saturation

Keywords: Coronavirus Disease 2019; Severe Acute Respiratory Syndrome Coronavirus 2; Hypoxemia; Oxygen Therapy; Double-Trunk Mask

Hypoxemia is a typical feature of the coronavirus disease 2019 (COVID-19). The rapid rise in the number of patients requiring oxygen therapy during the pandemic may cause a sharp increase in oxygen demands and potential threats of supply disruption, particularly in developing countries[1] or nursing homes. Moreover, the use of elevated oxygen flows *via* nasal cannula raises concerns about exhaled air dispersion distance and the potential risk of generating aerosols[2-6].

The Double-Trunk Mask (DTM) (image and description in supplement) is a patent-free handmade system which, when placed over nasal cannula, increases the PaO_2 by 50% in patients with acute respiratory failure without clinical impact on $PaCO_2$[7]. From another perspective, the DTM may reduce the oxygen flow required to correct hypoxemia which, in addition to reducing side-effects of prolonged dry oxygen administration[8-10], could have crucial implications in situations where medical gases are a rare commodity. The study's objective was to assess the efficacy of the DTM in preserving oxygen consumption in patients with COVID-19.

All adult patients with laboratory-confirmed COVID-19 and hypoxemia requiring low-flow oxygen therapy (LFOT) ≤15L/min to maintain SpO_2 between 92-96%, who were consecutively hospitalized between April and May 2020 in our hospital, were asked to participate in the study.

This ClinicalTrials.gov registered study (NCT04346420) was conducted with the approval of the local ethics committee. All subjects signed informed consent. Exclusion criteria were chronic respiratory diseases, language barriers, confusion, altered consciousness (Glasgow Coma Scale ≤12), hypoxemia corrected with oxygen flow ≤3L/min and any contra-indication to arterial puncture.

Patients were in a semi-recumbent position and received LFOT through their standard oxygen delivery method. The initial oxygen flow and delivery system were determined in accordance with our standard practice. The baseline oxygen flow was titrated to achieve a target SpO_2 value of 94% at the lowest output. Oxygen flow requirements determined the baseline oxygen delivery system (supplements). The baseline delivery system was then replaced by the DTM covering nasal cannula for 30 minutes. Oxygen output (primary outcome) was adjusted to achieve the same SpO_2 target as at baseline. After this period, the DTM was withdrawn and the standard oxygen delivery system was reinstated for 30 minutes. Oxygen output was readjusted to achieve the baseline SpO_2 value. Patients received no instructions regarding nasal or mouth breathing during the whole process. Arterial blood gases, vital parameters and oxygen output were measured at baseline (T_0) and at the end of the 30-min DTM period (T_{30}). Vital parameters and oxygen output were measured again 30 minutes after the DTM was withdrawn (T_{60}). Comfort-discomfort level with each system was assessed at T_{30} and T_{60} (supplements).

Eleven subjects were needed to detect a mean difference of 2L/min[11] (SD, 1.8L/min) in oxygen output (α-risk, 0.05; power, 90%). Because SpO_2 may inaccurately reflect arterial oxygen saturation (SaO_2) and therefore interfere with our design, patients were retrospectively excluded from the analysis if SpO_2-SaO_2 mismatch exceeded the expected error of 4%[12,13]. Data are presented as mean ±SD or median [interquartile range (IQR)] as appropriate. Pairwise comparisons were tested with paired t-test or Wilcoxon test. Ordinal paired data were compared with Wilcoxon test. P-values <0.5 were considered statistically significant.

Of 12 patients who completed the entire study procedure, one was excluded from the analysis because SpO_2-SaO_2 difference at T_0 was 4.3%. Final analyses were performed on 11 patients (61 ±14 years; 27% female). E-Table 1 details baseline characteristics. Compared with standard delivery systems, the oxygen output was significantly reduced with the DTM (median [IQR], 5 [4-8]L/min vs 1.5 [1.5-4]L/min; p=0.003) when oxygen saturation and PaO_2 remained stable. The DTM was also associated with a significant but slight increase in $PaCO_2$ (median, 36 vs 37 mmHg, p=0.006), a decrease in pH (median, 7.48 vs 7.45, p=0.009) and an increase in respiratory rate (mean, 26 vs 30 breaths/min, p=0.05), Fig. 1, e-Table 2. Other parameters were unaltered. The DTM was generally considered less comfortable than the baseline oxygen delivery system, especially in patients requiring low oxygen flow at baseline (e-Fig. 2). There were no differences between T_0 and T_{60} for any outcomes (e-Table 2), indicating that all values were reset when the standard delivery system was reinstated.

Treating hypoxemia is the cornerstone of COVID-19 patient management and this pre-post intervention trial shows that the DTM enables clinicians to safely treat severe hypoxemia while reducing the oxygen flow by more than half that required with conventional delivery systems. Therefore, settings in which oxygen supplies are limited (*e.g.* nursing homes, healthcare centres in deprived medical areas, during patient transport) may benefit most from the DTM. Although evaluation of its place relative to the non-rebreathing mask, high-flow oxygen therapy or non-invasive ventilation was not within the scope of this study, we believe the DTM could also be considered when SpO_2 falls below the target value with standard LFOT systems[7,11]. Consequently, the need for non-invasive respiratory support, which increases risks of generating aerosols[6], may possibly be avoided.

The DTM was considered less comfortable than LFOT delivered through nasal cannulas, yet patients who initially required high oxygen flow considered the DTM as equally comfortable. This might be explained by using a facemask at baseline or the large absolute oxygen flow reduction with the DTM. However, the low number of patients wearing oxygen facemasks at baseline precludes generalization of our conclusions with these systems.

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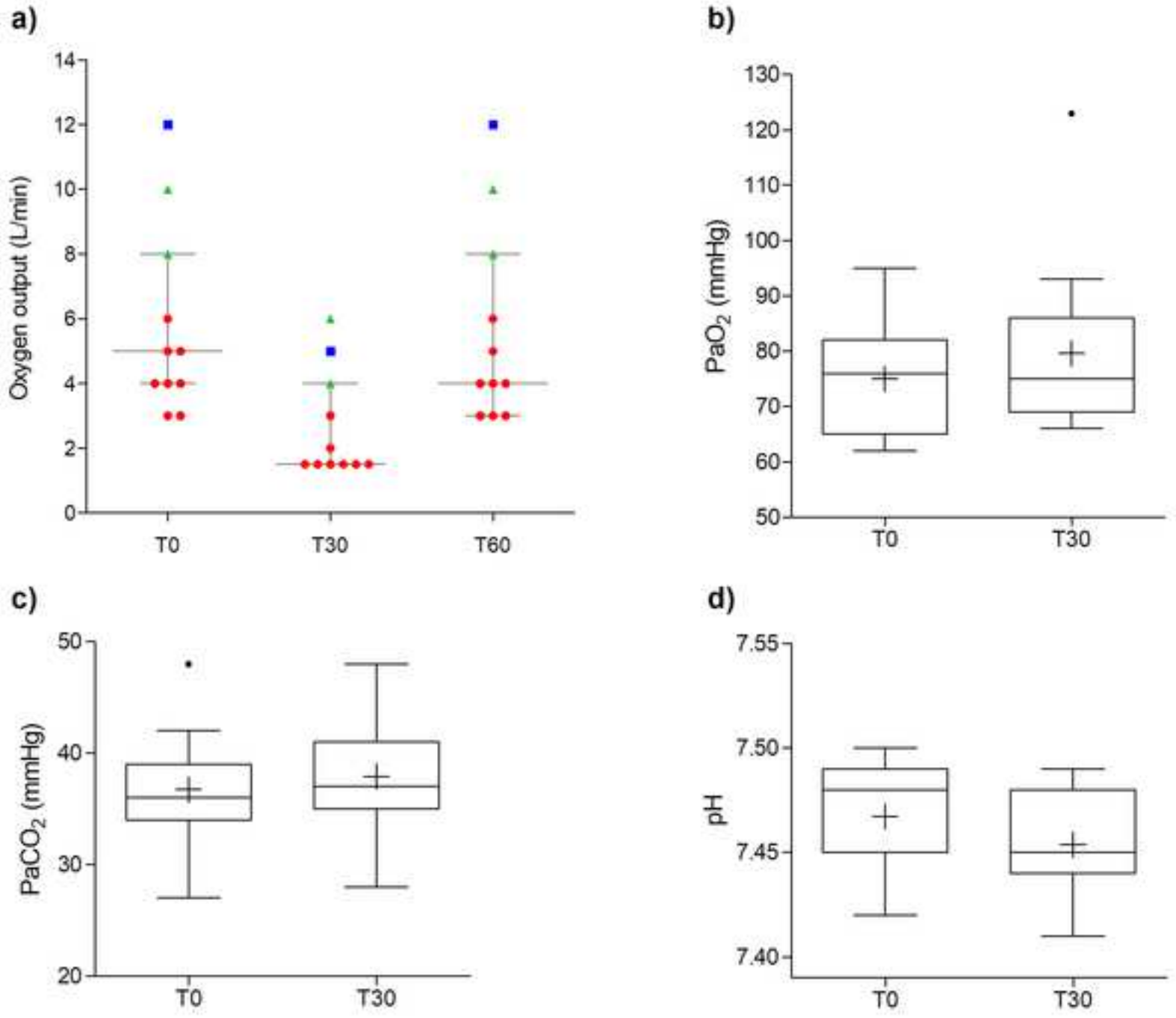
Figure legends

Figure 1. Change of oxygen output and blood gas outcomes.

(a) Panel shows raw values of oxygen flow before (T0) and after (T30) wearing the double-trunk mask, as well as after reinstating the baseline oxygen delivery system (T60). Horizontal lines indicate median, 25th and 75th percentiles. The shape of each data point represents the baseline oxygen supply system: circles for nasal cannula, triangles for oronasal mask and square for the non-rebreathing mask. (b-d) Panels show respectively PaO_2, $PaCO_2$ and pH outcomes before (T0) and after (T30) wearing the double-trunk mask. The boxes indicate 25th and 75th percentiles; horizontal lines and "+" within boxes indicate median and mean, respectively; whiskers indicate the highest and lowest values within 1.5 × interquartile range; and points beyond the whiskers indicate outliers.

Figure 1


a)
Oxygen output (L/min)
14
12
10
8
6
4
2
0
T0
T30
T60
b)
PaO2 (mmHg)
130
120
110
100
90
80
70
60
50
T0
T30
c)
PaCO2 (mmHg)
50
40
30
20
T0
T30
d)
pH
7.55
7.50
7.45
7.40
T0
T30

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Ethics in publishing

1. Does your research involve experimentation on animals?:
No

2. Does your study include human subjects?:
Yes

- If yes; please provide name of the ethical committee approving these experiments.:
Ethic Committee from Cliniques universitaires Saint-Luc and Université Catholique de Louvain in Brussels (B4032020000004)
- If yes; please confirm authors compliance with all relevant ethical regulations. :
Yes
- If yes; please confirm that written consent has been obtained from all patients. :
Yes

3. Does your study include a clinical trial?:
Yes

- If yes; please confirm that experiments have been conducted according to the CONSORT guidelines. :
Yes
- If yes; please provide clinical trial registration number from ClinicalTrials.gov.:
NCT04346420

4. Are all data shown in the figures and tables also shown in the text of the Results section and discussed in the Conclusions?:
Yes