



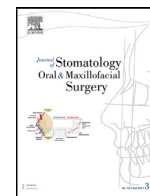
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Original Article

Prolonged viral shedding identified from external splints and intranasal packings in immediately cured COVID-19 patients with nasal fractures: A retrospective study



Poramate Pitak-Arnnp^{a,*}, Chatpong Tangmanee^b, Jean-Paul Meningaud^{c,1}, Andreas Neff^{a,1}

^a Department of Oral and Craniomaxillofacial Plastic Surgery, University Hospital of Giessen and Marburg, UKGM GmbH, Campus Marburg, Faculty of Medicine, Philipps-University of Marburg, Marburg, Germany

^b Department of Statistics, Chulalongkorn Business School, Bangkok, Thailand

^c Department of Plastic, Reconstructive, Aesthetic and Maxillofacial Surgery, Henri Mondor University Hospital, AP-HP, Faculty of Medicine, University Paris-Est Créteil Val de Marne (Paris XII), Créteil, France

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ABSTRACT

Background: Our aim was to measure and compare prolonged viral shedding (PVS) identified from external splints (ES) and intranasal packings (IP) for isolated nasal fracture (INF) repair in immediately cured asymptomatic vs. mildly symptomatic COVID-19 patients (AS-COVID vs. MS-COVID).

Methods: We designed a retrospective cohort study and enrolled a sample of post-AS-COVID and post-MS-COVID patients, whose INF were treated at a German level 1 trauma centre. The primary predictor variable was COVID severity presurgery (AS-COVID vs. MS-COVID). The main outcome variable was PVS detected in ES/IP. Other study variables were separated into demographic, clinical, and operative. Descriptive, bi- and multivariate statistics were computed, and statistical significance was set at $P \leq 0.05$.

Results: The study sample comprised 15 INF patients (53.3% females; 46.7% post-AS-COVID) with a mean age of 42.2 ± 22.7 years (range, 18–85). 13.3% ES and 53.3% IP were contaminated with SARS-CoV-2. However, only IP-contamination between the two cohorts reached statistical significance ($P = 0.01$; odds ratio, 0.02; 95% confidence interval, 0 to 0.47; Pearson's $r = 0.73$; *post hoc* power = 87.4%). Multiple linear regression models refuted the associations between PVS and the other parameters (i.e. age, gender, time to treatment, length of hospital stay, lengths of ES/IP placement).

Conclusions: Despite a relative low sample size, our findings suggest PVS via endonasal materials removed from cured COVID-19 patients, especially those healed from MS-COVID. This PVS may trigger re-infection and surgical site infections and/or transmission to other humans, and thereby, requires further investigations.

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1. Introduction

Our recent meta-narrative review and prospective study documented that the nasal and oral cavities and ocular surfaces are

Abbreviations: AS-COVID, Asymptomatic COVID-19 patients; CI, Confidence interval; CMFT, Craniomaxillofacial trauma; COVID-19, Coronavirus disease 2019; CR-INBF, Closed reduction of isolated nasal bone fractures; ES/IP, External splints and intranasal packings; INBF, Isolated nasal bone fractures; IP/IS, Intranasal packs and/or splints; LOS, Length of hospital stay; MS-COVID, Mildly symptomatic COVID-19 patients; NAAT, Nucleic acid amplification test; NAAT, Nucleic acid amplification test; NAAT, Nucleic acid amplification test; OR, Odds ratio; PVS, Prolonged viral (i.e. SARS-CoV-2) shedding; RAT, Rapid antigen test; RKI, German Robert Koch Institute for Disease Control and Prevention; RT-PCR, Real-time reverse transcription polymerase chain reaction; SARS-CoV-2, Severe acute respiratory syndrome coronavirus-2; STROBE, The STrengthening the Reporting of OBServational studies in Epidemiology statement

* Corresponding author. Dr. Poramate Pitak-Arnnp (c/o Fr. Jutta Kundendorf), Klinik für MKG-Chirurgie, Universitätsklinikum Marburg, UKGM, Baldingerstr., 35043 Marburg, Germany.

¹ Equal contribution

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reservoirs of the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1–2]. Despite decreased craniomaxillofacial trauma (CMFT) cases during the coronavirus disease 2019 (COVID-19) pandemic (e.g. due to lockdowns), many COVID-19 patients with CMFT required immediate treatments, such as those with retrobulbar haematoma or polytrauma [2]. Conversely, treatments for isolated nasal bone fractures (INBF) may be postponed until posttraumatic swelling subsides and the COVID-19 heals, especially in asymptomatic/mildly symptomatic COVID-19 (AS/MS-COVID) patients [2]. Prolonged viral shedding (PVS) in INBF patients post-symptom has never been studied before.

The purpose of this study was to answer the following clinical question: “amongst immediately cured COVID-19 patients undergoing closed reduction of INBF (CR-INBF), is contamination of external splints and intranasal packings (ES/IP) by SARS-CoV-2 different between post-AS-COVID vs. post-MS-COVID groups?”. The investigators’ null hypothesis was that there would be no different PVS

Table 1
Severity grades and epidemiology of COVID-19 (in Germany; $n > 1.7$ Millions) [3], and meta-analytic data with respect to viral shedding [8].

Grade	Definition ²	Distribution (%) [3]	(Average) duration of illness (days) [3]	Pooled mean viral shedding time (days; 95% CI) [8]
Asymptomatic (AS-COVID)	No reported symptoms corresponding to COVID-19, or no information on clinical manifestations	42	14	10.9 (8.3–14.3)
Mildly symptomatic (MS-COVID)	General signs of illness, sore throat, runny nose, disturbance of smell or taste, diarrhoea are present	25	14	19.7 (17.2–22.7)
Moderately symptomatic	As MS-COVID “PLUS” fever, cough, or pneumonia	27	14	22.8 (16.4–32.0)
Severely symptomatic	Requiring hospitalisation (but not in an intensive care unit)	5	21	24.3 (18.9–31.1).
Very severely/ critically symptomatic	Requiring intensive medical care	< 1	32	Not reported

Note: 95% CI – 95% confidence interval.

following the COVID-19 course between these two patient groups. Our specific aims were to 1) measure PVS in immediately cured AS/MS-COVID subjects apt to CR-INBF, 2) compare PVS between the two groups, and 3) discuss PVS and its possible relevance. At the end of this study, we supposed to reach the Oxford Centre for Evidence-Based Medicine’s Level of Evidence 2c.

2. Materials and methods

2.1. Ethical considerations

The study was approved by the institutional review board, and followed the Helsinki Declaration and the STrengthening the Reporting of OBServational studies in Epidemiology (STROBE) statement. All patients gave written consent for their anonymous data usage.

2.2. Study design and sample description

A retrospective double cohort study was designed and implemented enrolling two patient samples derived from the immediately cured AS/MS-COVID patient populations who had undergone CR-INBF at a German level 1 trauma centre of a regional hospital group comprising seven hospitals in six “hot-spot” locations (over 65,000 confirmed cases during the study period) during a 12-month interval.

Subjects eligible for study were age ≥ 18 years, immediately cured from AS/MS-COVID (i.e. treated on the day of the COVID-19 end or one day later), and who had suffered from breathing difficulty due to displaced or mildly comminuted INBF with/without septal deviation and received CR-INBF under general anaesthesia. As indicated by the German Robert Koch Institute (RKI) for Disease Control and Prevention and the hospital’s guideline, the “cured” AS/MS-COVID patients were 1) isolated (and treated) for ≥ 14 days since the first laboratory diagnosis of SARS-CoV-2 infection (at the time of this study; currently [since January 2022], the RKI has suggested the cut-off of 10 days with no further tests), 2) asymptomatic, and 3) tested negative twice for the virus by a rapid antigen test (RAT) and a nucleic acid amplification test (NAAT) using real-time reverse transcription polymerase chain reaction (RT-PCR) [2]. The total amount of intravenous dexamethasone 16 mg was provided for both cohorts when parenteral anaesthetic induction was begun and before the surgery ended (i.e. 8 mg twice).

Subjects were excluded if they did not satisfy the inclusion criteria, or had other procedures for treating INBF, or had an underlying disease that affects wound healing and/or microbial accumulation, such as diabetes mellitus, chronic rhinosinusitis.

2.3. Study variables

The primary predictor variable was COVID-19 symptoms before surgery (Table 1) [3], which were recorded as binary (AS-COVID vs. MS-COVID).

The main outcome variable was PVS detected in ES/IP (i.e. the inner side of ES in contact with the nasal alar skin, and both sides of IP) removed from the patients (Fig. 1), using an NAAT/RT-PCR. This variable was categorical (positive vs. negative on ES/IP). Viral RNA was extracted from the swabs using our previously described method [2]. The primary author (P.P.) performed every surgery (including fracture repair, IP insertion, and ES application), which conformed to suggestions by the AO CMF (<https://surgeryreference.aofoundation.org/>) and lasted 10–20 min. Intraoperatively, the patients including their mouth, were covered by disposable draping materials (Raucodrape® Abdecktücher, Lohmann & Rauscher GmbH & Co. KG, Rengsdorf, Germany), and the eyelids were closed and held together with 12 mm-wide 3M™ Steri-Strip™ (3 M Deutschland GmbH, Neuss, Germany). After fracture repair, we packed the nares with Merocel® nasal sponge (Medtronic GmbH, Meerbusch, Germany), soaked in the 50/50 mixture of 0.1% oxymetazoline and 2% lidocaine, for a few days, and used an external splint made of Biplatrix® rapid plaster bandage (BSN Medical, Hamburg, Germany) for 7–14 days.

The other variables were demographic (gender; age), clinical (time to treatment between the COVID-19 cure [please see the three indications of the COVID-19 cure in the section “Study Design and Sample Description”] and operative treatment [days]; length of hospital stay from surgery to discharge [LOS, days]), and operative (lengths of NS/IP [days]) groups.

2.4. Data management and statistical analyses

After collecting data from the hospital database, de-identified data were exported to Microsoft Excel 2007 (Microsoft Corp., Redmond, WA, USA). We performed descriptive, bi- and multivariate statistics using MedCalc® (MedCalc Software Ltd., Ostend/Belgium) and the *post hoc* power analysis with G Power 3 for Windows (Düsseldorf, Germany). The level of statistical significance for all analyses was set at a $P \leq 0.05$.

3. Results

15 patients were included. Table 2 presents descriptive statistics and bivariate analyses. There was no significant difference on demographic, clinical, and operative parameters between the two cohorts (AS/COVID vs. MS/COVID). ES/IP was used in all cases. 13.3% ES and 53.3% IP were contaminated, but only IP-contamination significantly differed between the two cohorts ($P=0.01$; odds ratio [OR]: 0.02; 95% confidence interval [CI]: 0 to 0.47; Pearson’s $r=0.73$ [i.e. moderate



Fig. 1. Clinical photograph showing postoperative closed reduction of isolated nasal bone fracture with external nasal splint made of gypsum (yellow star) and intranasal Merocel® packings (red stars).

Table 2
Cohort characteristics grouped by severity grade of COVID-19 symptoms before the surgery, and bivariate analyses.

Parameters	Overall	AS/COVID	MS/COVID	P value (OR; 95% CI)
Demographic				
Sample size	15 (100)	7 (46.7)	8 (53.3)	N/A
Female gender	8 (53.3)	5 (62.5)	3 (37.5)	0.31 (4.17; 0.47 to 36.74)
Age at surgery (years)	42.2 ± 22.7 (18–85)	41.4 ± 19.8 (19–69)	46.6 ± 27.2 (18–85)	0.68 (N/A; –32.13 to 21.73)
Age at surgery ≥ 46 years§	8 (53.3)	4 (50)	4 (50)	1.0 (1.33; 0.17 to 10.25)
Clinical				
Time to treatment (days)†	0.7 ± 0.5 (0–1)	0.7 ± 0.5 (0–1)	0.6 ± 0.5 (0–1)	0.74 (N/A; –0.47 to 0.65)
Length of hospital stay (days)*	2.6 ± 1.1 (2–5)	2.3 ± 0.5 (2–3)	2.9 ± 1.4 (2–5)	0.3 (N/A; –1.76 to 0.58)
Operative				
Length of external splinting (days)	8.9 ± 2.6 (7–14)	8.7 ± 2.2 (7–13)	9.1 ± 3.2 (7–14)	0.78 (N/A; –3.52 to 2.7)
Length of intranasal packing (days)	1.7 ± 0.6 (1–3)	1.7 ± 0.5 (1–2)	1.8 ± 0.7 (1–3)	0.91 (N/A; –0.72 to 0.65)
Outcome: PVS identified from				
External splint (inner side in contact with nasal alar skin)	2 (13.3)	0	2 (100)	0.47 (0; 0 to NaN)
Intranasal packing (both sides)	8 (53.3)	1 (14.3)	7 (87.5)	0.01 (0.02; 0 to 0.47)

Note: OR – odds ratio; 95% CI – 95% confidence interval; N/A – not applicable; NAN – undefined. Continuous data are listed as mean ± SD (range); § – median.
 †“Time to treatment” means the duration between the COVID-19 cure (which were justified using 3 indications: 1) isolated for ≥ 14 days since the first laboratory diagnosis of SARS-CoV-2 infection, 2) no symptom, and 3) tested negative twice for the virus by an RAT and an NAAT/RT-PCR) and surgical repair of the nasal bone.
 *In general, patients with closed nasal reduction require a one-night hospital stay; however, the patients in this cohort underwent delayed treatment and a longer antibiotic prophylaxis.
 Categorical data are presented as number (percentage). Statistically significant P-values are indicated in **bold** typeface.

positive correlation]; *post hoc* power = 87.4%). Patients with contaminated SP reported multiple hand contacts.

Multiple linear regression models rejected the associations between the other parameters (age, gender, time to treatment and LOS, lengths of ES/IP), and PVS on ES ($P=0.21$; $r^2=0.42$) and on IP ($P=0.6$; $r^2=0.22$).

In general, CR-INBF patients require a one-night hospital stay in order to observe postoperative bleeding, which is a common cause of readmission amongst “ambulatory” CR-INBF patients [4]. However, the patients in this cohort underwent delayed treatment and a longer antibiotic prophylaxis, i.e. 5 days, (none had penicillin allergy). LOS in this study was, therefore, longer than usual.

4. Discussion

The purpose of the present study was to measure PVS on ES/IP in immediately cured AS/MS-COVID patients with INBF. We hypothesised that there would be no SARS-CoV-2 detection on the ES/IP used for CR-INBF. Our results dismantle the hypothesis: i.e. 46.7% (or 7 of 15) patients presented with PVS, and the presence of MS-COVID is associated with an increased frequency of PVS after CR-INBF.

Several investigators paid attention to bacterial profiles in relation to IP/intranasal splints (IP/IS) [5–7], while we looked at SARS-CoV-2 shedding post-symptom in INBF patients. 40–87% of IP/IS are found to be contaminated, for example, with *Staphylococcus aureus*, and *Enterobacteriaceae* sp., and linked to serious complications, such as toxic shock syndrome, endocarditis, meningitis, and cavernous sinus thrombosis [5–7]. We prescribed a course of antibiotics for our patients because of delayed treatment with re-fracturing, subsequent mucosal breakdown, and nasal packing for 24–72 h, in agreement with other authors [5–7]. However, routine systemic antibiotic prophylaxis is “not” recommended (because of adverse drug reactions, e.g. emergence of resistant bacterial strains, anaphylaxis, or gastrointestinal disturbances), cost-effective, and evidence-based [5–8]. Meroce[®] porosity could increase biofilm formation [6,7], and antibiotic impregnation does not reduce microbial growth [5].

SARS-CoV-2 shedding after symptomatic relief and two negative tests has been sporadically reported in the literature (pooled mean PVS: 16.8 days [95% CI, 14.8 to 19.4]) [9,10], and increases with patients’ symptoms (Table 1) [9]. However, a case series revealed the mean PVS of 53.5 days (IQR: 47.75 to 60.5) and the longest PVS of 83 days [10]. It can be implied that PVS occurs in a similar manner to bacterial contamination of IP/IS. Because ocular surfaces were not swabbed, PVS in our study may be due to viral inoculation and spread from the oculo-nasolacrimal system amidst viral clearance via nasal mucosal capillaries and colonisation in postoperative blood clot [1,2]. Moreover, dexamethasone for anaesthetic induction and an anti-inflammatory/swelling measure given to all patients might exaggerate intensive microbial growth, and extend SARS-CoV-2 shedding time to the mean of 28.3 days (95% CI: 25.6 to 31.2) [9].

The strengths of this study include a relatively generalisable sample with demographics (e.g. a wide age range in both genders), and the absence of confounding factors related to different practice patterns, clinical skill levels, and triaging protocols, as limited to one surgeon. Weaknesses of our study were the retrospective design (i.e. data might have been missed, lost, or inaccurate), a small sample size (despite high power), and the probability that our findings were false-negative cases (whose IgM titre chemiluminescent immunoassay showed a superior diagnostic value over the dual RAT and RT-PCR [10]). However, a recent Cochrane review revealed that pooled sensitivity of RAT and RT-PCR tests were 0.69 and 0.95 [11]. The false negative rate of the combined RAT and RT-PCR could therefore be 0.0155. In other words, there would not be a false-negative case (0.2325/15) in our cohort. Moreover, this study’s *post hoc* power is 87.4%, depicting high likelihood of the results’ real effect.

5. Conclusions

This is the first study to examine PVS identified from ES/IP in immediately cured AS/MS-COVID patients. Our findings could be attributed to increased awareness of endonasal materials removed from cured COVID-19 patients, which may trigger re-infection and surgical site infections after CMFT (as of our still unpublished data) and/or transmission to other humans (i.e. strict intra-/postoperative protection, and patient discharge after the negative PCR results of “IP” are mandatory). In other words, the strict protective measures during IP/ES removal during this COVID-19 pandemic should be applied, regardless of the presence of SARS-CoV-2 infection. Future studies should be directed towards investigating mechanism and clinical relevance of PVS in this patient population.

5.1. Take-Home messages

- The nasal and oral cavities and ocular surfaces are reservoirs of SARS-CoV-2.
- Craniomaxillofacial trauma patients with COVID-19 may be treated after the COVID-19 heals.
- PVS on intranasal packings could be found in “immediately cured” (i.e., 1) being isolated/quarantined for ≥ 14 days, 2) no clinical symptoms, and 3) two negative test results), asymptomatic or mildly symptomatic COVID-19 patients with isolated nasal bone fractures.
- PVS appears to be high, if the patient was COVID-19-symptomatic.
- The abovementioned criteria in confirming the COVID-19 cure might be inappropriate and require a revision.
- IP/ES removal during this COVID-19 pandemic requires strict protective measures, regardless of the presence of SARS-CoV-2 infection (i.e. “universal precaution”).

5.2. Availability of data and material

Deidentified individual participant data are not available. The datasets generated and analysed during this study are available from the first author (P.P.) upon reasonable request.

5.3. Disclosure of potential conflicts of interest

Prof. Jean-Paul Meningaud is the Immediate Past President of the European Association for Cranio-Maxillo-Facial Surgery (EACMFS). Prof. Andreas Neff is the Head of the TMJ Section of the Strasbourg Osteosynthesis Research Group (S.O.R.G) and the Immediate Past President of the European Society of TMJ Surgeons (ESTMJS), as well as has received remunerations as a design surgeon for Medartis (Basel, Switzerland) for the development of midfacial and mandibular osteosynthesis systems.

All of the authors indicate full freedom of investigation and manuscript preparation without potential conflict of interest as regards this study.

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Conception and study design: P.P., C.T., J.-P.M., A.N.
Acquisition of (blinded) data: P.P., C.T.
Statistical analysis and interpretation: P.P., C.T., J.-P.M., A.N.
Drafting the work: P.P., C.T., J.-P.M., A.N.

Final approval and agreement of all aspects of the work: P.P., C.T., J.-P.M., A.N.

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