

## ELECTIVE SURGICAL PROCEDURES IN ONCOLOGICAL PATIENTS DURING THE COVID-19 OUTBREAK. THE COVID-FREE TRIAL

Alfonso Recordare<sup>1</sup>, Giovanni Pirozzolo<sup>1</sup>, Rubina Palumbo<sup>1</sup>, Lucrezia D'Alimonte<sup>1</sup>, Alice Albanese<sup>1</sup>, Andrea Barelli<sup>2</sup>, Sandro Panese<sup>2</sup>, Maurizio Rizzo<sup>1</sup>

<sup>1</sup>Department of Surgery, <sup>2</sup>Department of Infectious Diseases - Ospedale dell'Angelo, Venezia-Mestre

Contact person: Alfonso Recordare, arecordare@ulss.tv.it

### Resume

The rapid spread of COVID-19 in Europe and in the rest of the world has put a strain on healthcare facilities. From the beginning of epidemic, hospitals have become the epicentre of both treatment and dissemination of the virus (1-3). Healthcare personnel, as well as patients, developed the infection inside the hospitals, and this particular circumstance reopened the debate: how can we take action to control the paradoxical intrinsic dangerousness of health centres, for both patients and healthcare workers (4)?

The Covid-free area is an innovative concept. Currently, hospital is divided into "Covid" and "no-Covid" areas. But the so called "no-Covid" areas are uncertain: the presence or absence of infected patient and healthcare personnel is not clearly determined, so it is not possible to consider them as "Covid Free". Our aim is to create totally clean areas, named "COVID FREE" accessible only to authorized healthcare personnel (through a filter zone) and only to patients after quarantine. Accordingly, Covid Free operating theatres should be prepared. All these areas should have dedicated and safe elevators and paths. Trained operators will guarantee patients isolation during all the steps.

To continue surgical activities is essential even during the current pandemic. To establish a clear surgical strategy during the Covid-19 pandemic would help to increase the resilience of the Sanitary System and to guarantee the best therapy throughout the continuum of care.

**Key words:** COVID-19, "Covid" and "no-Covid" areas, Covid Free areas, Covid-free trial

### BACKGROUND

The rapid spread of COVID-19 in Europe and in the rest of the world has put a strain on healthcare facilities. From the beginning of epidemic, hospitals have become the epicentre of both treatment and dissemination of the virus (1-3). Healthcare personnel, as well as patients, developed the infection inside the hospitals, and this particular circumstance reopened the debate: how can we take action to control the paradoxical intrinsic dangerousness of health centres, for both patients and healthcare workers (4)?

At the same time, Intensive Care Units have reached a saturation point, which means there is an insufficient supply of beds to monitor patients in the postoperative period. That is why in most cases elective surgical procedures have been reduced or, at worst, cancelled (5-13). On the other hand, surgical procedures, both diagnostic and therapeutic, have been cut off to avoid the contamination of operating theatres and the infection of the healthcare personnel, due to the high probability of respiratory transmission. It is also widely known that the risk of spreading is higher in operative theatres, because the microbiological status of the patient is unknown in many instances, there is a large number of operators involved and mechanical ventilation is often needed.

However, outcome of oncological patients depends from timely procedures, as WHO outline in: "COVID-19: operational guidance for maintaining essential health

services during an outbreak" (14). These procedures cannot be delayed, but the safe management of oncological patients is still under discussion.

At the moment, guidelines and protocols have been issued to minimize the risk of Covid-19 transmission (7, 9-10). These include radiological investigations and/or nasopharyngeal swabs to identify the infection in symptomatic or asymptomatic patients (9, 11, 13-17). While in emergency conditions the need of a rapid intervention focus the attention on the risk of healthcare personnel, in elective procedures it is the patient who has to be kept under surveillance, to avoid a hidden infection that can lead to potential fatal complications – and this is particularly true for the oncological patient who was treated with neoadjuvant therapy.

Unfortunately, laboratory or instrumental investigations which could predict confidently the absence of infection are not available at present, especially in asymptomatic patients (18).

Up to know quarantine remains the most effective measure to prevent the spread of infection. The quarantine was first introduced in 1468 by the Senate of the Serenissima Venetian Republic as an official action of Public Health (19). The absence of Covid-19 infection is assessed after a 15-days period of household isolation, calculated on the maximum length of the period of incubation (16, 22).

On the basis of previous findings, we designed a protocol of a 14-days long self-isolation for candidates to

surgical interventions, and this period would start right after the completion of pre-operative investigations. During the isolation, patients should be monitored actively by a trained team, as it happens for people in household quarantine, and they should comply with the pre-operative prescriptions displayed by ERAS (Enhanced Recovery After Surgery) guidelines.

According to our protocol, a swab test for CoVID-19 (conducting Reverse Real-Time PCR) should be performed 72-36 hours before the procedure and the patient should be admitted in a new area called COVID FREE. The Covid-free area is an innovative concept. Currently, hospital is divided into “Covid” and “no-Covid” areas. But the so called “no-Covid” areas are uncertain: the presence or absence of infected patient and healthcare personnel is not clearly determined, so it is not possible to consider them as “Covid Free”. Our aim is to create totally clean areas, named “COVID FREE” accessible only to authorized healthcare personnel (through a filter zone) and only to patients after quarantine. Accordingly, Covid Free operating theatres should be prepared. All these areas should have dedicated and safe elevators and paths. Trained operators will guarantee patients isolation during all the steps.

During hospitalization, isolated patients will stay in touch with their family and loved ones using media devices.

The persistence of CoVID-19 negativity should be verified during the postoperative period and monitored until a month after the intervention.

The trial includes a control group composed of patients who could not comply the household isolation for technical reasons, so they should have only the swab done. These patients, without any symptom suggesting a CoVID-19 infection, should be admitted in ordinary wards (not in the Covid Free). Some other hospitals are willing to take part in this study as a control group.

Also, patients undergoing emergency procedures will form a third group that could help us to evaluate the virus spread in this specific population.

Patients should perform also an anti-CoVID-19 antibody test. Serum samples should be preserved for further analysis, while the clinical meaning of this test is not yet validated (circolare del Ministro della Sanità 1 1715, April 3rd 2020). In the meantime, positive patients with negative swab test should observe the quarantine. Data would be recorded for study purposes, because – as soon as the significance of the test would be defined – the serological test could be a source of significant bias in evaluating the differences between the groups in exam (20, 21).

## METHODS

*Trial Name:* Covid Free Oncology – Venice Protocol

*Model of the study:* Not randomized, prospective, multicenter clinical trial

*Aim:* to control the COVID-19 pandemic: Quarantine + Covid RT-PCR for SARS-CoV2 Swab vs Covid RT-PCR for SARS-CoV2 Swab, in elective oncologic surgical procedures.

The study compares two groups of patients undergoing surgical oncological intervention of any surgical specialty.

The aim of the study is to evaluate which way is the most effective to find and control the COVID-19 pandemic in patients undergoing elective surgical interventions that could not be postponed.

Emergency interventions would be included in a third group, in order to evaluate virus dissemination in patients who did not have any screening test done. These patients should perform a nasopharyngeal swab (analysed through RT-PCR for SARS-CoV2) and an abdominal-chest CT scan, when appropriate .

Eligibility criteria: patients undergoing elective or urgent surgical interventions, who have never resulted positive to RT-PCR test for SARS-CoV-2 or radiological investigations or respiratory symptoms consistent with Covid-19.

Members of the treatment group should have an adequate compliance with the 14-days household self-isolation.

### The study involves three different groups:

**Treatment group:** Quarantine (14 days) and swab 72-36 hours before hospitalization. Serology sample collection.

**Control group:** Patients who could not comply with the quarantine. Swab 72-36 hours before hospitalization. Serology sample collection.

**Emergency Surgery:** RT-PCR for SARS-CoV2 swab at the moment of the hospitalization. Serology sample collection. Abdominal-chest CT if recommended (clinical situation and/or fever or other symptoms suggesting COVID-19).

#### Pre-hospitalization management (only treatment group):

- *Quarantine (14 days isolation, on trust):* patients should stay separated from other family members, with the prohibition of leaving the house, the utilization of dedicated bathrooms and other domestic areas arranged in order to avoid contacts, following DISP (Dipartimento di Prevenzione di Sanita Pubblica) issues.

- *Pre-operative work-out:* patients should receive recommendations for daily training (especially respiratory), based on ERAS guidelines.

#### Follow up:

patients should be monitored through telemedicine, measuring body temperature, body weight and other parameters, according to their pathology.

### Intra hospital management:

The 2 groups should be divided into a “Covid Free” ward and a “not Covid Free” ward.

Treatment group members should be recovered in “Covid Free” ward. Both wards should be provided with PPE (Personal Protective Equipment), with the same rules in effect for Haematology ward. Data should be collected systematically, focusing on surgical outcome and complications onset, especially if respiratory. Patients, even if asymptomatic, should perform: chest X-ray in the 2nd postoperative day, RT-PCR for SARS-CoV2 swab in the 6th postoperative day, eventually repeated at the moment of discharge if hospitalization continues beyond the 8th postoperative day.

Patients at risk of postoperative readmission should continue the household isolation, until they would be assessed as clinically recovered from the intervention.

Primary Outcome Measure: incidence of Covid-19 infection in the three groups (patients who develop the disease during the quarantine – drop off, patients who become positive during the preoperative period, patients who become positive in the postoperative period).

Secondary Outcome Measures: percentage of postoperative complications in both groups, especially respiratory, rate of postoperative survival in both groups.

## CONCLUSIONS

To continue surgical activities is essential even during the current pandemic. Teams and facilities need to be flex-

ible in order to adapt to the rapidly evolving situation, in both clinical and organizational ways. To establish a clear surgical strategy during the Covid-19 pandemic would help to increase the resilience of the Sanitary System and to guarantee the best therapy throughout the continuum of care. At the moment, the quarantine and the separation into NOT COVID FREE and COVID FREE areas represent the most innovative and safe strategies to prevent Covid-19 infection, according to the current rules of social distancing outside the hospital. This protocol ensures the patient the best therapeutical standard for his specific pathology, be it laparoscopy, thoracoscopy or robotic approach.

## REFERENCES:

1. JJ. Cavallo, DA Donoho, HP Forman. Hospital Capacity and Operations in the Coronavirus Disease 2019 (COVID-19) Pandemic—Planning for the Nth Patient JAMA health forum March 17, 2020
2. Halpern NA, Pastores SM. Critical care medicine beds, use, occupancy, and costs in the United States: a methodological review. *Crit Care Med.* 2015;43(11):2452-2459. doi:10.1097/CCM.0000000000001227
3. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA.* 2020. doi:10.1001/jama.2020.2648
4. Wang J, Zhou M, Liu F. Exploring the reasons for healthcare workers infected with novel coronavirus disease 2019 (COVID-19) in China. *J Hosp Infect.* 2020. doi:10.1016/j.jhin.2020.03.002
5. Iacobucci G. Covid-19: all non-urgent elective surgery is suspended for at least three months in England. *BMJ.* 2020;368:m1106. Published 2020 Mar 18. doi:10.1136/bmj.m1106
6. Iacobucci G. Covid-19: GP surgeries close for two weeks after staff test positive. *BMJ.* 2020;368:m936. Published 2020 Mar 6. doi:10.1136/bmj.m936
7. Ti LK, Ang LS, Foong TW, Ng BSW. What we do when a COVID-19 patient needs an operation: operating room preparation and guidance. *Can J Anaesth.* 2020
8. Minimally invasive surgery and the novel coronavirus outbreak: lessons learned in China and Italy. M.H. Zheng, L. Boni, A. Fingerhut. *Annals of Surgery* 03/2020
9. Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an emergency response. *JAMA.* 2020. doi:10.1001/jama.2020.4031
10. COVID-19 Outbreak and Surgical Practice: Unexpected Fatality in Perioperative Period. A. Aliminian, S. Safari, A. Razeghian-Jahromi et al. . *Annals of Surgery* 03/2020
11. Badia JM, Rubio-Perez I, Arias Diaz J, Guirao Garriga X, Serrablo A, Jover Navalón JM. Surgical protocol for confirmed or suspected cases of Ebola and other highly transmissible diseases. *Cir Esp.* 2016 Jan;94(1):11-5.
12. Managing COVID-19 in Surgical Systems. M. Brindle, A. Gawande. *Annals of Surgery* 03/2020
13. Surgical Care and Coronavirus Disease 2019 (COVID-19). American College of Surgeons <https://www.facs.org/about-acs/covid-19/information-for-surgeons>
14. <https://www.who.int/publications-detail/covid-19-operational-guidance-for-maintaining-essential-health-services-during-an-outbreak>
15. Guan WJ, Ni ZY, Hu Y, et al; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2020. doi:10.1056/NEJMoa2002032
16. Toner E, Waldhorn R. What US Hospitals should do now to prepare for a COVID-19 pandemic. Published February 27, 2020. Accessed March 13, 2020. <http://www.centerforhealthsecurity.org/cbn/2020/cbnreport-02272020>.
17. Wang CJ, Ng CY, Brook RH. Response to COVID-19 in Taiwan: big data analytics, new technology, and proactive testing. *JAMA.* 2020. doi:10.1001/jama.2020.3151.
18. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations>
19. McNeil WH, La peste nella storia. Epidemie, morbi e contagio dall'antichità all'età contemporanea.
20. Shanmugaraj B, Siri wattananon K, Wangkanont K, Phoolcharoen W. Perspectives on monoclonal antibody therapy as potential therapeutic intervention for Coronavirus disease-19 (COVID-19). *Asian Pac J Allergy Immunol.* 2020;38(1):10–18. doi:10.12932/AP-200220-0773
21. Li Z, Yi Y, Luo X, et al. Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis [published online ahead of print, 2020 Feb 27]. *J Med Virol.* 2020;10.1002/jmv.25727. doi:10.1002/jmv.25727
22. Laurer SA, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application, *Ann Intern Med.* doi:10.7326/M20-0504

## ელექტიური ქირურგიული პროცედურები ონკოლოგიურ პაციენტებში COVID-19-ის ავითქმების პერიოდში. COVID-თავისუფალი კვლევა

ალფონსო რეკორდარე<sup>1</sup>, ჯოვანი პიროცოლო<sup>1</sup>, რუბინა პალუმბო<sup>1</sup>, ლუკრეცია დალიმონტი<sup>1</sup>, ალისა ალბანეზე<sup>1</sup>, ანდრეა ბარელი<sup>2</sup>, სანდრო პანეზე<sup>2</sup>, მაურიციო რიცო<sup>1</sup>

<sup>1</sup>ქირურგიის დეპარტამენტი, <sup>2</sup>ინფექციურ დაავადებათა დეპარტამენტი - დელ'ანჯელოს ჰოსპიტალი, ვენეცია-მესტრე, იტალია

პასუხისმგებელი პირი: ალფონსო რეკორდარე, arecordare@ulss.tv.it

**რეზიუმე** | COVID-19-ის სწრაფმა გავრცელებამ ევროპასა და დანარჩენ მსოფლიოში მკვეთრად გაზარდა სამედიცინო დაწესებულებების დატვირთვა. ეპიდემიის დაწყებიდან საავადმყოფოები იქცა როგორც მკურნალობის, ასევე ვირუსის გავრცელების ეპიცენტრად (1-3). სამედიცინო პერსონალს და პაციენტებს ინფექცია განუვითარდათ კლინიკებში და ამ კონკრეტულმა გარემომებამ განაახლა დებატები: როგორ შეგვიძლია ვიმოქმედოთ სამედიცინო ცენტრების პარადოქსული შიდა საფრთხის გასაკონტროლებლად როგორც პაციენტების, ისე ჯანდაცვის მუშაკებისთვის (4)? COVID-თავისუფალი სივრცე ინოვაციური კონცეფციაა. ამჟამად საავადმყოფო დაყოფილია „კოვიდის“ და „არა-კოვიდ“ სივრცეებად. ე.წ. „არა-კოვიდ“ არეებთან მიმართებაში არსებობს გაურკვევლობა: იქ დაუდგენელია პაციენტების და სამედიცინო პერსონალის ინფიცირების საკითხი, ამიტომაც შეუძლებელია მათი, როგორც „Covid Free“ (covid-თავისუფალი) განხილვა. ჩვენი მიზანია, შევქმნათ სრულიად სუფთა სივრცეები, სახელწოდებით "COVID-თავისუფალი", სადაც დაიშვება მხოლოდ ავტორიზებული პერსონალი (ფილტრის ზონის გავლით) და მხოლოდ პაციენტებისთვის, კარანტინის შემდგომ პერიოდში. შესაბამისად, უნდა მომზადდეს Covid Free საოპერაციო დარბაზები. ყველა ამ სივრცეს უნდა ჰქონდეს საკუთარი და უსაფრთხო ლიფტები და დერეფნები. ტრენირებული ოპერატორები გარანტირებულნი უნდა იყვნენ არიან პაციენტთა იზოლაციით ყველა ეტაპზე. ქირურგიული მოქმედებების გაგრძელება აუცილებელია მიმდინარე პანდემიის დროსაც კი. Covid-19-ის პანდემიის დროს, მკაფიო ქირურგიული სტრატეგიის დამკვიდრება ხელს შეუწყობს სანიტარული სისტემის მდგრადობის ზრდას და იქნება მაღალი ხარისხის მკურნალობის გარანტია სამედიცინო მომსახურების პერიოდში.

საკვანძო სიტყვები: COVID-19, კოვიდ და არა-კოვიდ სივრცეები, COVID-თავისუფალი, Covid-free კვლევა