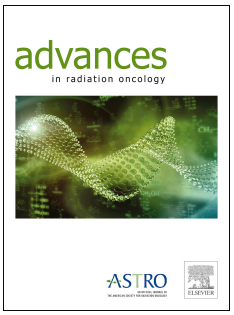
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.



Southern Italy: How the supply of radiation therapy, patient outcomes, and risk to health care providers have changed during the COVID-19 Pandemic

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On March 11th, 2020, after the global spread of the COVID-19 epidemic, the World Health Organization (WHO) declared a spreading pandemic (1). As of 31st of March 2020, 809,608 people globally are registered as confirmed cases and 39,033 died. Italy has been particularly affected, becoming the second most-hit country after US per confirmed cases and the most hit per total deaths (2). In these days health capacity to assure equal assistance is scarce (3). Some radiation oncologists of the North of Italy described their experience in an area with a high incidence of the viral disease (4, 5).

The first COVID-19 patient in Apulia Region (Italy), one of the largest region of the South, was diagnosed on February 24th, 2020 while the first Italian patient in a hospital ward in Italy was diagnosed in Codogno on the 20th of February, a town in the South of Lombardy, the first Italian region for population and gross internal product per capita. The first case diagnosed in Apulia had been some days before in Codogno.

Since many people who live or work in Lombardy are originally from the South, their visit to parents and relatives represented one of the major way the infection spread from affected areas in the North to the South of Italy. Another way of infectious spread could have been by the transfer of patients, mostly cancer patients, who despite living in the South of Italy are treated in health institutions in Lombardy: this phenomenon is called "health migration" and depends on shortage of health care facilities in the South for causes beyond the scope of this letter. According to the Italian Ministry of Health, almost 40,000 hospital admissions per year take place out of the Apulia Region and more than 10,000 take place in Lombardy (6).

On March 28th, 2020, total diagnosed cases in Lombardy amounted to 39,415 and to 1,458 in Apulia. It should be noted that in the night of March 8th 2020, after miscommunications which followed first government restrictions to mobility from Lombardy and some other northern areas, about 25 thousands of students and workers came back to the South. A regional act prescribed them to communicate their arrival to regional authorities and to self-quarantine: in Apulia region about 2000 did so.
This letter describes how COVID-19 pandemic changed the supply of radiation therapy, patient outcomes, and risk to health care providers.

FIRST COVID-19 PATIENTS IN RADIATION ONCOLOGY DEPARTMENT

On March 2nd 2020 in our radiation oncology department (ROd), a male patient with mediastinal syndrome was referred from the Medical Oncology department. He underwent CT simulation and started the treatment of five daily fractions. On March 5th 2020 a woman with brain metastasis

underwent CT simulation for whole brain and another patient with bone metastasis started treatment. During the second session of radiotherapy the patient with brain metastases had vomiting in the treatment room and treatment was stopped. Three technologists and one physician did not used personal protective equipment (PPE) at that time when they went into contact with her. On March 13th 2020 the head of ROd was informed that the aforementioned patients resulted COVID-19 positive. Two of them died some days after. The four professionals were put in quarantine and COVID-19 test was required. On March 16th, 2020, PPE were provided and constituted by surgical mask, FFP2 (Filtering Face Piece) mask to be used during contact with patients, disposable gowns and gloves. FFP1 masks filter nontoxic powder with an admitted leakage of 15%, FFP2 ones filter powder fumes and aerosols damaging the human health with maximum leakage of 11%, and FFP3 as the FFP2 but they also filter viruses and bacteria with a maximum leakage of 5%.
On March 19th, 2020, the Health Direction of the Hospital decided to do COVID-19 tests to all personnel: 1 out of 27 resulted positive. Note that these results were communicated one week after the tests were performed. None of the professionals got ill during this period.
After initial, inhomogeneous reactions across different regions, the testing for all the healthcare workers (HCW) was strongly required by the professional organizations. Following these protests, quarantine was reserved only to HCW coming into a "strict contact" (less than 1 meter) with COVID-19 positive patients without PPE (at least surgical mask) and tests were performed at the 7th day following the contact. In case of other type of contacts with positive patients, the HCW is required to keep working and to self-monitor her health status (temperature monitoring). It is likely that this policy was determined by regional shortage of tests and personnel. In this department the positive nurse was put in quarantine and the remaining HWC were treated as cases with non-strict contact because of the use of surgical masks.

THE SEQUENCE OF LEGISLATIVE PROVISIONS AND THE NEW INTERNAL PROCEDURES

On March 8th, 2020, the Prime Minister (7) decreed a lockdown of the areas where the epidemic originated and of those in which spread faster; in the following days, other decrees extended the lockdown to the entire nation (8, 9). In this latter decree, it was disposed health professionals to adopt all the measures for an effective prevention of the diffusion of the respiratory infection, provided by World Health Organization (10). On March 9th, 2020, a new Decree-Law was published by the National Government for the empowerment of Health Service disposing health professionals to start, differently from general population, quarantine only at the onset of symptoms or after a positive test (11). These provisions obviously applied to the entire personnel of this department, also in the week following the COVID-19 tests, while waiting for the results which found one person positive. As a consequence, the tests are being performed again.

Because health service depends on regional governments, Apulia Government published a general act on 8th march, 2020, obliging people coming from the regions of onset of the epidemic to declare their name and address. Furthermore, an administrative act declared medical activities should still be performed, including radiation oncology (12).
On March 13th, 2020, another administrative act defined a procedure in case of contact between a health professional and COVID-19-positive patients (13). In case of contact without PPE with confirmed COVID-19 patient, the professional must be put in quarantine and tested after 7 days from the contact.
On March 16th, 2020, the local authority mandated the use of FFP2 mask in front of suspected cases and FFP3 in case of confirmed COVID-19 in aerosol generating procedures. Since then radiotherapy personnel in this hospital have used surgical masks and FFP2 in case of suspected cases. The local authority mandated also to perform a daily triage of radiotherapy patients: those

with cough or fever are thus to be excluded from the radiotherapy treatment and sent to a medical practitioner to start the diagnostic procedures for COVID-19

On March 17th, 2020, a hospital directive required physicians to "evaluate, for each patient, the opportunity to perform or delay" radiotherapy, to impose that patients enter individually into the ROd in order to avoid simultaneous waiting of too many patients and to give each of them a protective mask. In particular, treatment of breast and prostate postoperative patients and intact prostate cancers in hormone-deprivation patients was postponed. The scheduled delay was of two weeks.

Conversely, the Italian Health Ministry had published a note on March 10th, 2020, stating that the delivery of radiotherapy treatment in COVID-19 patients should be assured (14). This document declared also that the completion of oncologic treatment to patients who had contacts with COVID-19 infected persons should be assured. In our opinion, since the oncologic treatment could worsen immunosuppression and foster virus infection, this measure could lead to additional problems to patients and medical personnel.

On March 19th, 2020, the Italian Association of Radiation Oncology (AIRO) sent to its associates some guidelines coherent with the procedure provided by the regional and local health authorities in Apulia (15).

ACTIONS

In this department, control visits were delayed unless patients, after telephone call, declared active oncologic problems or persistent acute side effects; for a first consultation the patients were offered the possibility to send the documentation by email and to do a video consultation by means a dedicated internet link not requiring any app installation (16). Up to now, we have treated three patients from the hospital wards who were subsequently diagnosed as COVID-19 positive and, in two cases, the start of outpatient radiotherapy treatment was interrupted as they informed they were under testing following contact with infected relatives.

In order to avoid having different patients at the same time in the waiting room we have distributed them in three sessions per hour and asked accompanying persons not to enter with the patient in the department. This decision has reduced the number of treatments per day. The total number of daily treated patients was reduced from 65 to 45 (two LINACs); as mentioned, one nurse resulted positive to COVID-19 test. According to the above-mentioned rules, there is no forecast of new tests in HCWs without symptoms. Consequently, in our scheduling, postoperative treatments – mostly favorable postoperative breast cancers, prostate cancer under hormone deprivation or with postoperative indication – have been postponed by two weeks. We will keep monitoring the impact of COVID-19 on our service supply.(Fig 1)

We have registered a good compliance with the new rules. Some elderly patients have asked to delay the treatment, most likely because mortality for COVID-19 in Italy is higher for people aged 80 and above. We have observed difficulties for many patients to complete tumor staging on an outpatient basis because of the restriction of ordinary health procedures. At this time, many wards are being closed and changed into COVID-19 wards so many surgical operations were delayed despite the law requiring that they take place.

CONCLUSIVE REMARKS

Although radiotherapy is an activity formally guaranteed by authorities during the pandemic, it is likely that many patients will suffer a real shortage of access to diagnostic and therapeutic procedures, interrupting and postponing their treatment. We expect poorer outcomes for these patients in the near future. We also observed that a delay in providing PPE for medical personnel reduced the available staff, further affecting the treatment schedules.

In the controversial debate on whether people are dying *with* COVID-19 or *due to* COVID-19, there is probably a forgotten category: patients *without* COVID-19 who will still die *due to* COVID-19 and, specifically, for the shortage of resources or delays in treatments it is causing.

REFERENCES

1) Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

2) https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020

3) Rosenbaum L. Facing Covid-19 in Italy — Ethics, Logistics, and Therapeutics on the Epidemic's Front Line N.Engl.J.Med March 18, 2020 DOI: 10.1056/NEJMp2005492

4) Filippi AR, Russi E., Magrini SM, Corvò R. Covid-19 outbreak in northern Italy; first practical indications for radiotherapy departments.Int J Radiat Oncol Biol Phys In press Avalailable on line March 19th, 2002

5) Krengli, M, Ferrara E., Mastroleo F, Brambilla M, Ricardi U. Running a Radiation Oncology Department at the time of coronavirus: an Italian experience. Andvances in Radiation Oncology In press. https://www.astro.org/ASTRO/media/ASTRO/Daily%20Practice/PDFs/COVID-Krengli-et-al-(ADRO).pdf

6) Ministero della Salute. Rapporto annual sull'attività di ricovero. Dati SDO 2017. Direzione Generale Programmazione Sanitaria.Gennaio 2019. http://www.salute.gov.it/imgs/C_17_pubblicazioni_2831_allegato.pdf

7) DECRETO DEL PRESIDENTE DEL CONSIGLIO DEI MINISTRI 8 marzo 2020. Ulteriori disposizioni attuative del decreto-legge 23 febbraio 2020, n. 6, recante misure urgenti in materia di contenimento e gestione dell'emergenza epidemiologica da COVID-19. Gazzetta Ufficiale della Repubblica Italiana. N.59 8 marzo 2020

8) DECRETO DEL PRESIDENTE DEL CONSIGLIO DEI MINISTRI 9 marzo 2020 Ulteriori disposizioni attuative del decreto-legge 23 febbraio 2020, n. 6, recante misure urgenti in materia di contenimento e gestione dell'emergenza epidemiologica da COVID-19, applicabili sull'intero territorio nazionale. Gazzetta Ufficiale n. 62 del 9 marzo 2020

9) DECRETO DEL PRESIDENTE DEL CONSIGLIO DEI MINISTRI 11 marzo 2020. Ulteriori disposizioni attuative del decreto-legge 23 febbraio 2020, n. 6, recante misure urgenti in materia di con- tenimento e gestione dell'emergenza epidemiologica da COVID-19, applicabili sull'intero territorio nazionale. Gazzetta Ufficiale della Repubblica Italiana. N.64 11 marzo 2020

10) World Health Organization Advice on the use of masks in the community, during home care and in healthcare settings in the context of the novel coronavirus (2019-nCoV) outbreak: interim guidance, 29 January 2020

11) DECRETO-LEGGE 9 marzo 2020, n. 14 Disposizioni urgenti per il potenziamento del Servizio sanitario nazionale in relazione all'emergenza COVID-19. Gazzetta Ufficiale della Repubblica Italiana. N.62 9 marzo 2020

12) Regione Puglia Misure per la prevenzione e gestione dell'emergenza epidemiologica da COVID-19 –DISPOSIZIONI. 8 marzo 2020

13) Regione Puglia Emergenza sanitaria COVID-19 – Protocolli operativi e flow chart DISPOSIZIONI 13 marzo 2020

14) Ministero della Salute. Raccomandazioni per la gestione dei pazienti oncologici e oncoematologici in corso di emergenza da COVID-19. 0007023-10/03/2020-DGPROGS-MDS-P (http://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2020&codLeg=73635&parte=1%20&serie=null)

15) Associazione Italiana di Radioterapia Oncologica. Documento di indirizzo per la valutazione e la gestione del rischio dei pazienti e degli operatori nei reparti di radioterapia oncologica in corso di diffusione del COVID-19. 19 marzo 2020.

16) https://about.plusimple.com/

Figure 1. Flow-chart of clinical events and actions (Rod = Radiation Oncology Department; HCW = Health Care Worker)

Clinical Events	Actions
February 20 1st Covid patient in Codogno	
February 28 1st Covid patient in Apulia	
March 2 Treatment of 1st Covid-19 patient in ROd (diagnosed on March 13)	
March 5 Treatment of two Covid-19 patients in ROd (diagnosed on March 13)	
March 8 Lockdown of Lombardy and North-to-South migration of 25k people	
March 10 Health Ministry mandates radiotherapy to be assured for Covid-19 patients	
March 13 Diagnosis of the 3 treated patients	**March 9** PPE provided to HCW **March 13** Postponing and rescheduling of ROd activities **March 13** Quarantine and testing of 4 HWC **March 16** Introduction in ROd of triage for patients **March 19** Tests for all HCW in Rod
March 23 **1 positive result out of 27**	**March 23** Positive HWC is quarantined