Aging Clinical and Experimental Research (2021) 33:443–450
https://doi.org/10.1007/s40520-020-01784-w

ORIGINAL ARTICLE

Response to a massive SARS-CoV-2 infection in a nursing home transformed into a caring center

Paolo Agostinis[1] · Valentina Vianello[2] · Elena Dereani[3] · Giuseppe Caruso[4] · Beatrice Montessoro[4] · Marco Taurian[4] · Antonio Di Chiara[1] · Vincenzo Patruno[5] · Francesco Cavallin[6] · Gian Paolo Fadini[7] · Anna Aldovini[8] · Anna Baritussio[9] · Francesco Curcio[10] · Carlo Tascini[11] · Aldo Baritussio[12]

Received: 4 November 2020 / Accepted: 30 December 2020 / Published online: 28 January 2021

Abstract

Background The best policy to follow when nursing homes are massively hit by SARS-CoV2 is unclear.

Aim To describe COVID-19 containment in a nursing home transformed into a caring center.

Methods Physicians and nurses were recruited. The facility was reorganized and connected with the laboratory of the reference hospital. Ultrasound was used to diagnose pneumonia. Patients needing intensive care were transferred to the reference hospital. Hydroxychloroquine/azithromycin/enoxaparin were used initially, while amiodarone/enoxaparin were used at a later phase. Under both regimens, methylprednisolone was added for severe cases. Prophylaxis was done with hydroxychloroquine initially and then with amiodarone. Period covered: March 22–July 31, 2020.

Results The facility was reorganized in two days. Ninety-two guests of the 121 (76%) and 25 personnel of 118 (21.1%) became swab test positive. Seven swab test negative patients who developed symptoms were considered to have COVID-19. Twenty-seven patients died, 23 swab test positive, 5 of whom after full recovery. Four patients needing intensive care were transferred (3 died). Mortality, peaking in April 2020, was correlated with symptoms, comorbidities, dyspnea, fatigue, stupor/coma, high neutrophil to lymphocyte ratio, C-reactive protein, interleukin-6, pro-calcitonin, and high oxygen need ($p \leq 0.001$ for all). Among swab-positive staff, 3 had pneumonia and recovered. Although no comparison could be made between different treatment and prophylaxis strategies, potentially useful suggestions emerged. Mortality compared well with that of nursing homes of the same area not transformed into care centers.

Conclusion Nursing homes massively hit by SARS-CoV-2 can become caring centers for patients not needing intensive care.

Keywords SARS-CoV-2 infection · Nursing home · Elderly patients · Amiodarone

Introduction

The spreading of SARS-CoV-2 infection (COVID-19) in long-term care facilities is receiving exceptional attention since old persons represent the greatest fraction of those succumbing to the disease [1, 2]. Partnering with local hospitals and public health to manage COVID-19 outbreaks in nursing homes has been advised [3], but it is unclear how to behave in case of large outbreaks.

In this observational study, we describe the spreading of SARS-CoV-2 infection and the way it was contained in a nursing home located in the Italian Alps. The infection started in a catastrophic way and, due to the high number of patients simultaneously affected, the decision was made to transform the nursing home in a caring structure, transferring to the COVID Referral Center only patients needing intensive care. The time covered is from March 22nd to July 31st, 2020, the critical period being April 2020.

At the time of this study, hydroxychloroquine and azithromycin were mainstay of treatment [4]. Initially, our patients were treated with hydroxychloroquine, azithromycin, and enoxaparin, methylprednisolone being added to patients with severe forms of the disease. Later on, due to the emerging evidence that this line of treatment was ineffective, patients were treated with a combination

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40520-020-01784-w.

✉ Aldo Baritussio
aldo.baritussio@unipd.it

Extended author information available on the last page of the article

of amiodarone and enoxaparin, methylprednisolone or tocilizumab being added to severe cases. Prophylaxis of swab-test-negative patients was also done, initially with hydroxychloroquine and later with amiodarone.

Methylprednisolone and tocilizumab were introduced due to the mounting evidence that unchecked inflammation is a hallmark of the disease [5]. Anticoagulation was started since small vessel thrombosis was emerging as a crucial component of lung damage [6].

Amiodarone, an amphiphilic cationic drug used for the control of ventricular and supraventricular arrhythmias, was introduced since it interferes with the processing of Ebola Virus spike protein, inhibits in vitro SARS-CoV-1 infection after viral entry, has antithrombotic properties and had been used safely in patients with COVID-19 [7–10].

We describe here the transformation of the nursing home into a caring structure, patient characteristics and the outcome of the measures taken.

Materials and methods

Study design

In this study, we describe the spreading of SARS-CoV-2 infection and the way it was contained in a long-term care facility located in the Italian Alps. All procedures reported comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained for the compassionate use of drugs and for the use of personal data. The study was notified to the local Ethical Committee.

Setting

The Nursing Home "Matteo Brunetti" is located in Paluzza, in the Carnian Alps (Italy), 65 km away from Udine University Hospital, assigned to the care of patients with COVID-19.

Patients and personnel

As of March 22, 2020, the nursing home hosted 121 guests (27 males and 94 females; median age 85 years, range 53–100 years). All of them were included in the study. The nursing home had a staff of 118 persons for patient care, supportive duties and administration. Two physicians were present on call.

Spread of infection

Owing to the spread of the pandemics, on March 5, 2020, the nursing home was locked.

On March 22, 2020, a female guest with fever had a positive swab test. During the next days, swab tests were done on all patients and personnel. The results were received with delay, due to exhaustion of reagents at the referral center. By April 4, the picture emerged that 59.8% of guests and 13.6% of personnel had SARS-CoV-2 infection (Fig. 1). Considering that the deployment of symptomatic patients to the COVID-19-dedicated structure would have caused an unbearable strain, it was decided that patients were to be cared for at the nursing home and that only those needing intensive care were to be transferred to the COVID center of Udine. During this initial time interval, four patients needing intensive care were transferred to the reference center, where three died soon after arrival.

Nursing home re-organization

Under supervision of the Regional Department of Prevention and the Director of Clinical Infectious Diseases of Udine University Hospital, two physicians with 3 weeks experience at the Udine COVID-19 center were recruited, together with 10 nurses and 10 supporting personnel from the nearby hospital of Tolmezzo. Three general practitioners guaranteed care for swab-negative patients.

Patients were allocated to three areas, "1" for patients with severe COVID, "2" for COVID-positive patients with few or no symptoms, "3" for swab-negative patients. Areas 1 and 2, with 2–4 patients per room, and area "3", with 2 patients per room, were in separate buildings and were

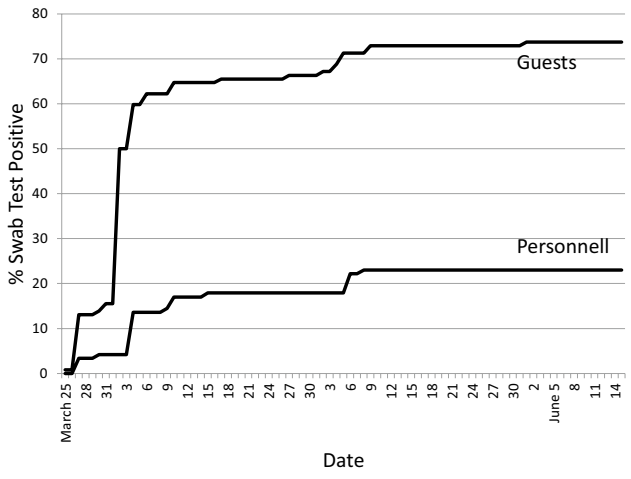

Fig. 1 Time course of SARS-CoV-2 RNA presence in nasal swabs, tracheal aspirates, or gastric aspirates

served by separate caring teams. Clean and at risk areas were identified and the flow of personnel and materials through the facility was defined. Areas for briefing and practice sessions were identified. Donning and doffing were done at opposite locations.

Owing to the rapid spread of infection personnel used in all areas complete personal protection equipment (PPE) according to the official regional rules (total body isolation gown, double gloves, disposable footwear, face shield, FFP2 mask). PPEs were changed at entry into defined areas; gloves were changed after individual patient visits. Personnel were trained during practice sessions or through video recordings available from the Regional Department of Protection.

The air recirculation system was disabled and air was exchanged by opening the windows. Sanitation was performed according to regional rules. Communication between patients and families was assured by phone or tablet.

Two ultrasound systems (MyLab Esaote Sigma), a blood gas analyzer and apparatuses for oxygen delivery (both low and high flow) were obtained. Rapid transport of blood samples was organized to the laboratory of Udine University Hospital, so that bacterial cultures could be performed, blood and urine variables could be measured and quantitative PCR with reverse transcription (RT-PCR) could be done. Aspiration of bronchial secretions under bronchoscopic guidance was assured. The search of viral RNA by RT-PCR was done as needed or at least weekly in swab-negative patients. Positive patients were re-tested until they became negative on two successive measurements. Physical examination was done at least one time a day, two times or more in patients with severe COVID-19. Vital parameters were collected twice a day. Chest echography was performed during the first visit and then as needed. The reorganization of the nursing home took two days.

The diagnosis of COVID-19 was based on RT-PCR performed on throat swabs, tracheal aspirates, or gastric aspirates [11]. Patients with negative swab test, but with symptoms were considered for the diagnosis of COVID-19 on the basis of exposure history, clinical status (including oxygen need: no oxygen, < 6 L/min, ≥ 6 L/min [high flow oxygen]), chest echography (normal pattern, B lines or B lines plus consolidations) or suggestive laboratory data, like lymphopenia, high D-dimer or high levels of Interleukin-6 (IL-6). Disease was defined severe if ultrasound showed increasing B lines or lung densities or if high flow oxygen was needed. Comorbidities were categorized using the Charlson Comorbidity Index [12].

Personnel with infection were quarantined or referred to the COVID center in Udine. The parish of a nearby town and a local hotel offered help for personnel quarantine.

On May 15, 2020, due to lack of personnel, 11 swab-positive patients and 16 swab negative, but with ultrasound signs of possible COVID pneumonia were moved to a nursing home located in Palmanova, 90 km away. At that facility, in addition to the testing offered at Paluzza, high resolution computed tomography (HRCT) was available. To assure the continuity of care, one of the caring physicians moved to Palmanova as well. From there, after recovery, patients came back to the Paluzza Nursing Home and reentry was complete by June 6.

Therapy

Starting April 4, 2020, patients with COVID-19 or strongly suspected of having COVID received a combination of hydroxychloroquine, azithromycin, and enoxaparin. Patients with severe disease also received methylprednisolone (Therapeutic Strategy A, Table 1). Patients not improving under this regimen and from May 6 all patients with COVID-19 or strongly suspected of having COVID-19 received a combination of amiodarone and enoxaparin, methylprednisolone being added for those with severe disease (Therapeutic strategy B, Table 1). In one patient with diabetes difficult to control, methylprednisolone was substituted with tocilizumab (324 mg SC once). Oxygen was administered to obtain at least 90% spO_2. Appropriate antibiotics were administered in case of bacterial infections. Gastric protection was assured. In patients treated with amiodarone the QT interval was measured and plasma levels of amiodarone were measured 3 days after load. Drugs interfering with hydroxychloroquine or amiodarone were discontinued.

Prophylaxis

During April 2020, prophylaxis was done with hydroxychloroquine (200 mg 2 times a day for 5 days). From May 6th prophylaxis was done with amiodarone (200 mg twice a day for 10 days).

Statistical analysis

The data were expressed as median and interquartile range (IQR) (continuous data) or number and percentage (categorical data). Continuous data were compared between two groups with Mann–Whitney test, and categorical data using Chi-square test or Fisher's exact test. All tests were two-sided and a p value less than 0.05 was considered significant. Statistical analysis was performed using R 4.0 (R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

Table 1 Therapeutic strategies

Therapeutic strategy	Drug	Daily dosing	Duration (days)
A	Hydroxychloroquine	400 mg x 2 (load), then 200 mg × 2 PO	5
	Azithromycin	500 mg PO	3
	Enoxaparin	4000 UI SC	5
	Methylprednisolone	1 mg/kg IV	5
B	Amiodarone	15 mg/kg IV (load) then 400 mg × 2 PO	14
	Enoxaparin	100 UI/kg × 2 SC	14
	Methylprednisolone	1 mg/kg IV	14

Results

The spreading of the infection

As shown in Fig. 1, within 12 days of the first case, half of the guests and 13% among personnel became infected. Because of this catastrophic start, the decision was made to transform the nursing home into a caring center, transferring to the COVID Referral Center only patients needing intensive care.

Afterwards the infection continued to spread, although at a lower pace, both among personnel and among guests (Fig. 1). The last positive swab test among personnel was recorded on May 8th and among patients on June 1st, 2020. By July 31st, 2020, on each patient a median of 5 (IQR 4–7) swab tests were performed.

Overall, 92 guests (76%) and 25 staff members (21%) tested positive at the RT-PCR of nasal swabs. In addition, two patients with respiratory symptoms and ultrasound signs of pneumonia, who remained negative after being tested, respectively, 9 and 11 times, were shown to have interstitial pneumonia by computed tomography and developed antibodies to the SARS-CoV-2 spike protein. Thus, the total number of patients with laboratory-proved COVID-19 was 94 (78%). Five further patients had symptoms, blood values or chest HRCT typical of COVID-19, but remained negative after 4–11 swab test. These patients were treated as if they had COVID-19.

Disease manifestations

In patients with COVID-19, prevailing symptoms regarded the respiratory system (Table 2). In some patients, however, a reduced state of alertness was the prevalent manifestation. Others had sepsis-like features with fever as the main symptom. Others still manifested withdrawal as the sole manifestation of disease. Two patients died of sudden death. Forty-nine patients with positive swab test had no or few symptoms. One of five patients suspected to have COVID-19, but with negative swab test, developed ascending paralysis.

Patient characteristics according to swab-test results are shown in Supplementary Table 1. A positive swab test was more frequent in females ($p = 0.04$), patients without gut disease ($p = 0.01$), and those with fever ($p = 0.004$), fatigue ($p = 0.007$), decreased appetite ($p = 0.04$), low blood lymphocytes ($p = 0.03$), high plasma D-dimer ($p = 0.04$) and high serum LDH ($p = 0.002$). Interestingly, cough was not associated with the diagnosis of COVID-19 in our population. Normal chest echography ($p = 0.03$) was higher among swab-positive patients.

Patient characteristics according to the presence of symptoms are shown in Supplementary Table 2. A symptomatic status was more frequent in males ($p = 0.02$), patients with heart disease ($p = 0.04$) and those without dementia ($p = 0.0006$). Symptomatic patients had increased occurrence of fever ($p < 0.0001$), dyspnea ($p < 0.0001$), fatigue ($p < 0.0001$), decreased appetite ($p < 0.001$), and stupor/coma ($p = 0.02$). A symptomatic status was also associated with abnormal chest echography ($p < 0.0001$), lower SpO_2 ($p < 0.0001$) and lower SpO_2/FiO_2 ratio ($p < 0.0001$). Symptomatic patients had lower blood lymphocytes ($p < 0.0001$) and platelets ($p = 0.01$), while higher NLR (neutrophile to lymphocyte ratio) ($p < 0.0001$), C-reactive protein ($p < 0.0001$), IL-6 ($p = 0.01$), myoglobin ($p = 0.007$), AST ($p = 0.001$), ALT ($p = 0.04$), lactate

Table 2 Prevailing clinical aspects in patients with COVID-19

Clinical aspect	*n* (%)
Respiratory insufficiency	31 (32.9)
Withdrawal	5 (5.3)
Decreased alertness	4 (4.2)
Sepsis-like	3 (3.1)
Sudden death	2 (2.1)
Minor or no symptoms**	49 (52.1)

Swab test positive or developed antibodies to SARS-CoV-2 (total 94). Not included are 5 swab-test-negative patients with suspected COVID-19, one of which developed ascending paralysis

**Rash in one patient

dehydrogenase ($p=0.02$), creatinine ($p=0.03$), and procalcitonin ($p=0.002$).

Clinical outcomes

Twenty-seven patients died during the study period (Supplementary Fig. 1). Comparison with historical records showed that excess mortality centered in April 2020 (Fig. 2).

Mortality was 23/94 (24.4%) in patients with at least one positive swab test or antibody-positive; 5 of these died up to two months after full recovery and with at least 3 negative swabs.

Mortality was 4/27 among patients with negative swab (14.8%) (p = 0.42).

Mortality of patients with swab test positive (Supplementary Table 3) was associated with higher Charlson score ($p<0.0001$), heart disease ($p=0.03$), dyspnea ($p<0.0001$), fatigue ($p=0.0001$), decreased appetite ($p=0.002$), stupor/coma ($p=0.0001$), higher heart rate ($p=0.0001$), lower SpO_2 ($p=0.03$) and SpO_2/FIO_2 ratio ($p=0.000$), higher aPTT ($p=0.04$), lower PLTs ($p=0.004$), higher C reactive protein ($p<0.0001$), higher IL-6 ($p=0.001$), higher myoglobin ($p=0.005$), higher CK ($p=0.02$), higher AST ($p=0.03$), lower lymphocyte nadir ($p=0.02$), higher peak NLR ($p=0.02$), lower hemoglobin ($p=0.02$), higher procalcitonin ($p<0.0001$). Therapy with oxygen was more frequent among patients who died ($p<0.0001$).

Considering patients with positive swab test or who developed antibodies to SARS-CoV-2, there was a significant difference in mortality between those who had symptoms and those who had few or none (Supplementary Fig. 1, $p<0.001$ by Chi-square test).

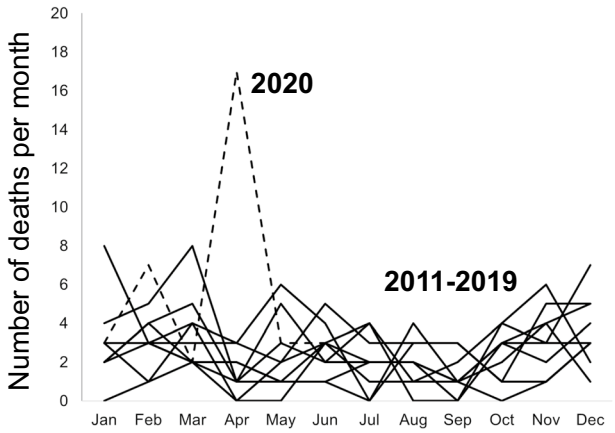

Fig. 2 Monthly mortality in the Paluzza Nursing Home from January 1, 2011 to July 31, 2020

Outcome of different treatment strategies

As shown in Table 3, three seriously ill patients, receiving supportive care before nursing home reorganization, died.

Out of the 49 patients with COVID-19, but few or no symptoms, all treated with regimen A (without steroid) 4 died; one of sudden death around treatment completion, three over one month after symptom resolution respectively of acute abdomen, inhalation pneumonia, and heart failure.

Of the 30 symptomatic patients treated with regimen A, 20 survived and 10 died (one of sudden death 1 month after complete recovery from COVID-19 symptoms). A patient with ascending paralysis recovered completely after treatment with methylprednisolone and immunoglobulins.

Of the five patients switched to regimen B after getting worse with regimen A, 3 survived and 2 died.

Of the 11 patients treated with regimen B, 8 survived and 3 died (one of bacterial infection one month after symptom resolution and normalization of blood values). The other two patients who died had the longest time to death.

Serum levels of amiodarone had a median of 0.60 µmol/L (IQR 0.47). No adverse effects were recorded.

Prophylaxis

Forty-two patients had hydroxychloroquine prophylaxis. Of these 15 became swab test positive and 5 died. Fifteen patients had prophylaxis with amiodarone. None of these became swab positive.

Personnel data

Three persons developed COVID-19 pneumonia, were transferred to the referral center and recovered.

Table 3 Outcome of different treatment strategies

Treatment strategy	Clinical picture	Survived	Died	Total
Supportive	Symptomatic	0	3	3*
A				
	No or few symptoms	45	4	49
	Symptomatic	20	10	30
A then B	Symptomatic	3	2	5
B	Symptomatic	8	3	11
All patients		72	26	98**

A strategy: hydroxychloroquine, azithromycin, enoxaparin ± methylprednisolone. B strategy; amiodarone, enoxaparin ± methylprednisolone

*Patients who died at the study start

**One swab-test positive patient who died of bacterial infection is not included

Discussion

Nursing home re-organization

The Paluzza nursing home was the hardest hit in the Friuli Venezia Giulia region, both for number of cases and speed of infection spread. Since the hospitalization of symptomatic patients would have provoked an intolerable strain to COVID-19 referral center, it was decided to transform the nursing home in a care center for patients not needing intensive care. To that end a staff was created de novo, resources were stepped up and the whole structure was reorganized.

Our experience suggests that this is possible, but planners need to consider realistically the burden of infection. Indeed, at the peak of infection, care providers worked 7 days a week, furthermore at a later point some patients had to be transferred to another structure due to insufficient personnel.

A very positive aspect of the transformation of the nursing home in a care center, was that it allowed patients to remain in a familiar context. They adjusted easily to the new situation and, as the emergency declined, resumed rapidly their usual demeanor [13].

Clinical aspects

Few patients had cough and several had purely neurologic symptoms. Overall, the clinical presentation of our patients was in agreement with the literature, with a strong relationship between the risk of death and symptoms, comorbidities [1, 2, 4], low number of lymphocytes [4], high neutrophil to lymphocyte ratio [14, 15], increased markers of inflammation (CRP, IL-6) [4, 16–19], altered coagulation (low platelets, lengthened aPTT, high levels of D-dimer) [4]. Patients who died had higher levels of serum pro-calcitonin. Wether this was due to SARS-CoV-2 or bacterial super infection, perhaps favored by the emergence of dysfunctional myeloid cells, remains unclear [14, 17].

Differently from other authors [20], we found no relationship between chest echography and COVID-19 status or mortality. This may have resulted from the frequent presence of echographic abnormalities in the elderly [21] and from the fact that echographic scans considered for the analysis were obtained at symptoms start. Furthermore, the categorization used (no anomalies, B lines, lung densities) did not capture the transition from few to many B lines or extension of densities. On the whole, we endorse the use of chest echography, especially when chest X-ray and CT are not available. Indeed in 11 patients with symptoms and negative swab test, a diagnosis of pneumonia by lung ultrasound prompted isolation days in advance of the emergence of swab test positivity.

The absence of gut diseases was associated with a greater incidence of COVID-19. At present, the relationship between intestinal diseases (especially inflammatory) and the risk of SARS-CoV-2 infection remains unclear [22].

Therapy

The entry into target cells of SARS-CoV-2 depends upon the processing of the spike protein, that may happen by two mechanisms. The first mechanism, acidic-pH-dependent, is mediated by the endosomal cysteine protease cathepsin L, is prevalent in cell types like Vero cells and is inhibited by cationic drugs. The second mechanism, pH-independent, is mediated by the plasma-membrane-resident serine protease TMPRSS2, is present on cells of the respiratory epithelium and is insensitive to the action of cationic drugs [20]. The selectivity of SARS-CoV-2 for respiratory epithelia is thought to be the basis for hydroxychloroquine lack of efficacy [23, 24].

Not much was known at the time of this study; however, considering that some of our patients worsened while taking the combination hydroxychloroquine, azithromycin and enoxaparin ± methylprednisolone, we switched to amiodarone and enoxaparin ± methylprednisolone. Amiodarone is a cathionic drug that accumulates in the lumen of organelles with an acidic interior and increases lumenal pH similarly to hydroxychloroquine, a property that explains its interference with the processing of Ebola virus spike protein [7]. Furthermore, amiodarone inhibits SARS-CoV-1 infection acting after the delivery of the viral genome into the cytoplasm of the target cell, a property not known for hydroxychloroquine [8]. Finally, amiodarone inhibits the expression of tissue factor by endothelial cells and has displayed antithrombotic activity in an animal model of arterial damage [8]. Amiodarone dosage was chosen to reach blood concentrations close to those active in vitro (5–10 µmolar). Knowing that amiodarone has a narrow therapeutic window, we checked QT interval and amiodarone serum levels.

Owing to the progressive adjustment of treatment schemes, a comparison between therapeutic regimens A and B cannot be made. Later evidence has shown that hydroxychloroquine and tocilizumab are ineffective. The use of corticosteroids and heparin was in line with the present protocols [25–27]. The effect of amiodarone remains unclear.

It may be worth noting, however, that, as of June 30 2020 the mortality rate among our swab-positive patients compared well with that of other nursing homes hit less strongly by the pandemics and not transformed into care centers: 21/92 (22.8%, Paluzza, Udine) vs 1/4 (25.0% Gemona, Udine), 5/21 (23.8% Lovaria, Udine), 8/27 (29.6% S. Giorgio di Nogaro, Udine), 20/56 (35.7% Mortegliano, Udine) [28].

Prophylaxis

Hydroxychloroquine prophylaxis did not inhibit SARS-CoV-2 infection in some of our patients, confirming that hydroxychloroquine has no efficacy for post-exposure prophylaxis [29]. None of the patients who had amiodarone prophylaxis developed SARS-CoV-2 infection.

Accumulating databases could clarify the question if chronic amiodarone administration has a protective effect towards SARS-CoV-2 infection [2].

Limitations

Main limitations of this work are the lack of a randomized design and lack of information about the viral load. Furthermore, testing for the presence of antibodies against SARS-CoV-2 was available for a small number of patients.

Conclusions

Nursing homes massively hit by SARS-CoV-2 can be transformed into caring centers for patients not needing intensive care. By this approach, patients remain in a familiar context and excessive burden on hospitals can be prevented.

Acknowledgements We would like to thank all patients and their relatives. We'd also thank the personnel of the Nursing Home Matteo Brunetti, Rev. Harry Della Pietra, Regional Health Authorities and Local Authorities.

Author contributions PA patient care, study and therapy planning, data analysis, manuscript preparation. VV patient care. ED nursing home reorganization and patient care. GC patient care. BM patient care. MT patient care. ADC patient care, consultant cardiologist. VP patient care. FC data analysis. GPF prophylaxis planning. AA data analysis, manuscript preparation. AB data collection and analysis, manuscript preparation. CF biochemical and microbiological analyses. CT study and therapy planning. Infectious diseases referent. AB data collection and analysis, manuscript preparation.

Funding Not applicable.

Data availability Available on reasonable request to the corresponding author.

Compliance with ethical standards

Conflict of interest Nothing to declare.

Ethics approval The study was notified to the local Ethical Committee; in consideration of the study design, formal ethical approval was waived.

Statement of human and animal rights All procedures reported comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Informed consent Informed consent was obtained for the compassionate use of drugs and for the use of personal data.

Consent to participate Informed consent was obtained for the compassionate use of drugs.

Consent for publication Informed consent was obtained for the compassionate use of personal data.

Code availability (Software application or custom code): not applicable.

References

1. McMichael TM, Currie DW, Clark S et al (2020) Epidemiology of COVID-19 in a long-term care facility in King County, Washington. N Engl J Med 382:2005–2011
2. Williamson EJ, Walker AJ, Bhaskaran K et al (2020) Factors associated with COVID-19-related death using OpenSAFELY. Nature 584:430–436
3. Montoya A, Jenq G, Mills JP et al (2020) Partnering with local hospitals and public health to manage COVID-19 outbreaks. J Am Geriatr Soc. https://doi.org/10.1111/jgs.16869
4. Gautret P, Lagier JC, Parola P et al (2020) Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: a pilot observational study. Travel Med Infect Dis 34:101663. https://doi.org/10.1016/j.tmaid.2020.101663
5. Huang C, Wang Y, Li X et al (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395:497–506. https://doi.org/10.1016/S0140-6736(20)30183-5
6. Varga Z, Flammer AJ, Steiger PM et al (2020) Endothelial cell infection and endotheliitis in COVID-19. Lancet 395:1417–1418
7. Salata C, Baritussio A, Munegato D et al (2015) Amiodarone and metabolite MDEA inhibit Ebola virus infection by interfering with the viral entry process. Pathog Dis 73:ftv032
8. Stadler K, Ha HR, Ciminale V et al (2008) Amiodarone alters late endosomes and inhibits SARS coronavirus infection at a post-endosomal level. Am J Respir Cell Mol Biol 39:142−149
9. Breitenstein A, Stampfli SF, Camici GG et al (2008) Amiodarone inhibits arterial thrombus formation and tissue factor translation. Arterioscler Thromb Vasc Biol 28:2231–2238
10. Castaldo N, Aimo A, Castiglione V et al (2020) Safety and efficacy of amiodarone in a patient with COVID-19. JACC Case Rep 2:1307–1310
11. Huang Y, Chen S, Yang Z et al (2020) SARS-CoV-2 viral load in clinical samples from critically ill patients. Am J Respir Crit Care Med 201:1435–1438
12. Charlson ME, Pompei P, Ales KL et al (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40:373–383
13. Marshall M (2020) The lasting misery of coronavirus long-haulers. Nature 585:339–341
14. Kuri-Cervantes L, Pampena MB, Meng W et al (2020) Comprehensive mapping of immune perturbations associated with severe COVID-19. Sci Immunol. https://doi.org/10.1126/sciimmunol.abd7114
15. Schulte-Schrepping J, Reusch N, Paclik D et al (2020) Deutsche COVID-19 OMICS initiative (DeCOI). Severe COVID-19

Is marked by a dysregulated myeloid cell compartment. Cell 182:1419–1440. https://doi.org/10.1016/j.cell.2020.08.001
16. Lucas C, Wong P, Klein J et al (2020) Longitudinal analyses reveal immunological misfiring in severe COVID-19. Nature 584:463–469
17. Del Valle DM, Kim-Schulze S, Huang HH et al (2020) An inflammatory cytokine signature predicts COVID-19 severity and survival. Nat Med 26:1636–1643
18. Laing AG, Lorenc A, Del Molino Del Barrio I et al (2020) A dynamic COVID-19 immune signature includes association with poor prognosis. Nat Med 26:1623–1635
19. Zhou F, Yu T, Du R et al (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 395:1054–1062
20. Veronese N, Sbrogiò LG, Valle R et al (2020) Prognostic value of lung ultrasonography in older nursing home residents affected by COVID-19. J Am Med Dir Assoc 21:1384–1386
21. Ciccarese F, Chiesa AM, Feletti F et al (2015) The senile lung as a possible source of pitfalls on chest ultrasonography and computed tomography. Respiration 90:56–62
22. Monteleone G, Ardizzone S (2020) Are patients with inflammatory bowel disease at increased risk for COVID-19 infection? J Crohn Colitis 14: 1334-1336. https://doi.org/10.1093/ecco-jcc/jjaa061
23. Hoffmann M, Mosbauer K, Hofmann-Winkler H et al (2020) Chloroquine does not inhibit infection in lung cells with SARS-CoV-2. Nature 585:588–590
24. Maisonnasse P, Guedj J, Contreras V et al (2020) Hydroxychloroquine use against SARS-CoV-2 infection in non-human primates. Nature 585:584–587
25. Kasour Z, Riaz M, Garbati MA et al (2020) Efficacy of chloroquine and hydroxychloroquine in COVID-19 patients: a systematic review and meta-analysis. J Antimicrob Chemother 76:30–42
26. Salvarani C, Dolci G, Massari M et al (2021) Effect of Tocilizumab vs Standard Care on Clinical Worsening in Patients Hospitalized With COVID-19 Pneumonia: A Randomized Clinical Trial. JAMA Intern Med 181: 24-31. https://doi.org/10.1001/jamainternmed.2020.6615
27. National Institute for Health and Care Excellence (2020). COVID-19 rapid guideline: critical care in adults. NICE, NG159 [published 20 March 2020, last updated 3 September 2020]. Available from: https://www.nice.org.uk/guidance/ng159.
28. Regione Autonoma Friuli Venezia Giulia. Coronavirus - portale informativo regionale. Data published July 30 2020. Available at http://www.regione.fvg.it/rafvg/cms/RAFVG/salute-sociale/COVID19/
29. Boulware DR, Pullen MF, Bangdiwala AS et al (2020) A randomized trial of hydroxychloroquine as postexposure prophylaxis for COVID-19. N Engl J Med 383:517–525

Authors and Affiliations

Paolo Agostinis[1] · Valentina Vianello[2] · Elena Dereani[3] · Giuseppe Caruso[4] · Beatrice Montessoro[4] · Marco Taurian[4] · Antonio Di Chiara[1] · Vincenzo Patruno[5] · Francesco Cavallin[6] · Gian Paolo Fadini[7] · Anna Aldovini[8] · Anna Baritussio[9] · Francesco Curcio[10] · Carlo Tascini[11] · Aldo Baritussio[12]

1 Department of Medicine, Ospedale Sant'Antonio Abate, Azienda Sanitaria Universitaria Friuli Centrale, Tolmezzo, Italy

2 Department of General Surgery, Ospedale Santa Maria della Misericordia, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

3 Nursing Home Matteo Brunetti, Paluzza, Udine, Italy

4 Special Continuity Care Units, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

5 Department of Pulmonology and Respiratory Medicine, Ospedale Santa Maria della Misericordia, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

6 Independent Statistician, Solagna, Italy

7 Department of Medicine, Section of Diabetes and Metabolic Diseases, University of Padua, Padua, Italy

8 Department of Medicine and Harvard Medical School, Department of Pediatrics, Boston Children's Hospital, Boston, MA, USA

9 Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padua, Padua, Italy

10 Department of Medicine and Clinical Pathology Institute, University of Udine and Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

11 Clinical Infectious Diseases, Ospedale Santa Maria Della Misericordia, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

12 Senior Researcher, University of Padua, Padua, Italy