

Cardiac rehabilitation activities during the COVID-19 pandemic in Italy. Position Paper of the AICPR (Italian Association of Clinical Cardiology, Prevention and Rehabilitation)

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Key words: Cardiac rehabilitation; COVID-19; healthcare organization; AICPR; Position Paper.

Received for publication: 8 June 2020.
Accepted for publication: 10 June 2020.

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Licensee PAGEPress, Italy
Monaldi Archives for Chest Disease 2020; 90:1439
doi: 10.4081/monaldi.2020.1439

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Introduction

The COVID-19 outbreak is having a significant impact on both cardiac rehabilitation (CR) inpatient and outpatient healthcare organization. The variety of clinical and care scenarios we are observing in Italy depends on the region, the organization of local services and the hospital involved. Some hospital wards have been closed to make room to dedicated beds or to quarantine the exposed health personnel. In other cases, CR units have been converted or transformed into COVID-19 units [1]. While the epidemic curve has shown exponential growth that is flattening only now, the incidence of hospitalizations of cardiac patients in the acute phase has undergone an inverse trend. A widespread reduction in the access of cardiac patients with heart attack or acute heart failure in the emergency room has been observed throughout Italy, causing the partial or total "paradox" of empty CCUs and cardiology units. Many patients with acute myocardial infarction had possibly underestimated their symptoms and did not go to hospital for fear of contagion and had a late access to treatment and interventions. This still

happens to CR facilities, which have undergone an abrupt interruption or reduction of their activities, thus exposing many patients to the risk of new clinical instabilities. As various clinical scenarios of acute heart disease have emerged during the COVID-19 outbreak [2], up to this time the potential chronic cardiovascular complications of viral disease are unknown, and the management of the chronic phase could be even more critical than the acute one. First of all, the lack of access to rehabilitation programs or its reduction could generate an increase in re-hospitalizations for MACE in the near future [3-5]. Furthermore, it is not known exactly how the SARS-CoV-2 will affect the cardiopulmonary function of patients who have survived severe forms, or what might be the role of cardiopulmonary rehabilitation in the follow-up of these patients. After the emergency outbreak, CR Units as well as cardiovascular secondary prevention Outpatient Clinics should be prepared to implement necessary protections for all CR health-care professionals as well as for all patients [1]. These interventions will not be satisfactory without a huge investment in telemonitoring and teleconsultation technologies that should be organized in a “health plan”, on a national basis, avoiding arbitrary and disordered actions. The problem of epidemiological surveillance now joins that of the treatment of chronic diseases, never really tackled and never solved. The Italian Association of Clinical Cardiology, Prevention and Rehabilitation (AICPR) has launched an online survey whose results could be the basis to understand the best way to propose how reorganize the activities after the outbreak [1], combining safety, appropriateness and technology.

The present document aims at defining the state of the art of CR during COVID-19 pandemic, through the description of the clinical and management scenarios frequently observed during this period and the exploration of the future frontiers in the management of cardiac rehabilitation programs after the COVID-19 outbreak.

Clinical scenarios frequently observed in CR during the COVID-19 pandemic

Post-surgery and post-acute coronary syndromes patients

The exponential increase in COVID-19 positive patients and the dramatically increasing need for intensive care units (ICUs) for the management of critically ill patients has led the emergency task-force of the Italian regions to reallocate ICU resources. In addition, elective surgery has been cancelled and beds dedicated to cardiac, neurosurgery and partially coronary care units reassigned to COVID-19-patients. Patients who need cardiac surgery are likely to be more susceptible to severe complications of COVID-19 because they often have pre-existing comorbidities. Moreover, after coronary artery bypass graft the need for invasive mechanical ventilation could represent a predisposing factor to lung disease. During this transitional phase, patients recovering from an operation in hospital should be safely managed and those with a regular postoperative course should be managed and discharged as quickly as possible if physical conditions allow it. The creation of a network for home CR including telecardiology systems is recommended [6]. Once the clinical conditions have improved, these patients could be transferred to Intensive Cardiovascular Rehabilitation in order to continue their cardio-respiratory functional recovery. Despite an established system of care for ST-segment-elevation myocardial infarction (STEMI), due to the control measures established in the COVID-19 era a sharp increase in time from the onset of symptoms

to the first doctor contact in a representative quote of STEMI patients has been observed; furthermore, the door-to-device times may be compromised. Delays in seeking care or not seeking care at all could have a detrimental impact on outcomes [7].

Two areas of major concern are identifiable for patients requiring acute cardiac care: i) delays in presentation, and ii) delays in treatment. Cardiac centers should consider the necessity to defer elective procedures and to carefully monitor employee health and availability for duty. Regional STEMI systems should develop reliable alternatives to default receiving centers, Cardiologists, ED staff, and intensive care nurses accustomed to the 24/7 availability of primary percutaneous coronary intervention for STEMI should probably re-familiarize themselves with the use of thrombolytic therapy. Strategies to maximize acute care resources, to maintain access to services, and to limit nosocomial spread will rely on careful planning, teamwork, and investment in education and training [8]. A pivotal role in the management of acute STEMI patient treated with thrombolytic therapy is played by CR: in fact, in the post-acute phase Cardiovascular Rehabilitation should optimize medical therapy, stratify patient’s ischemic residual risk and help for the psychological aspects developed in this time of pandemic. Our ability to adapt to the demands of a global pandemic will be determined by our willingness to develop resilient care systems in order to protect vulnerable patients. The consequences may continue long after the pandemic resolution, and new management modalities for cardiology may originate from the COVID-19 disaster. Learning from experience may help to cope with future major social changes [9].

Chronic heart failure patients

One direct and one indirect effect of the COVID-19 pandemic deserve consideration with respect to heart failure (HF): the possible damage of COVID-19 to the heart and the secondary impact of the outbreak on HF patients. Since the beginning of the present COVID-19 pandemic, evidence has been accumulating that cardiac involvement is a prominent feature of the illness. In addition to increased propensity and worse outcomes for COVID-19 in patients with pre-existing cardiovascular diseases, including chronic HF, patients with COVID-19 infections can also develop HF along with the illness. In one of the first reports from Wuhan including 416 patients, chronic HF was present in 4.1% of patients but an acute cardiac injury, defined as significant elevation of cardiac troponins, was found in 70% of them and was associated with increased mortality [10]. Troponin level increased up to 20 times, associated with increased CRP and lymphopenia, in patients with severe HF [11].

Brain natriuretic peptide (BNP) levels were also elevated in a series of patients admitted to ICU, among whom congestive HF was present in 42%, and cardiomyopathy developed in 33% [12]. It is unclear whether this acute cardiac injury is attributable to the viral infection itself or it is a consequence of the systemic inflammatory response associated with the more severe forms of the illness. Case reports of myocarditis in COVID-19 provide evidence for cardiac inflammation but there are insufficient data to determine whether HF might be secondary to post-COVID-19 infection myocarditis. At the time we are writing, it is impossible to provide any data on the burden that COVID-19 will pose on the epidemiology of heart failure and its phenotypes. A systematic echocardiographic evaluation of cardiac function among recovered patients will allow understand the prevalence.

The secondary or indirect impact of COVID-19 on HF patients may be more sizable but similarly dramatic. The COVID-19 pandemic has strained health care resources around the world causing

many institutions to stop some routine clinical services, including center-based and outpatient CR, or to reschedule routine follow-up visits [13]. This issue is expected to have a significant negative impact in the short-term, as the inability to care for patients with HF in a timely fashion place these patients at increased risk for adverse cardiovascular complications including death. In addition, the impact of the quarantine-induced stress with the restriction in physical activity may result in reduced adherence to prescribed therapy, depression, social isolation, behavioral addiction disorders, thus triggering hemodynamic instability and adverse events. Until vaccination is available, testing for COVID-19 status may represent a further limitation for the supply of in-hospital and outpatient group activities, either physical or educational. Sectors of care are recognizing the need to redesign strategies to deliver non COVID-19 related medical care, including rehabilitation, in order to optimize treatment of heart failure patients. Expanding the use of tele-health services to deliver care including CR, is essential to guarantee continuity of care to handle the current pandemic. A recent statement from the Heart Failure Society of America provides guide about provision of “virtual visits” to care for HF patients even in the context of inpatient setting [14]. However, due to the lack of high-quality randomized data, it will be mandatory to verify the best practices and the outcomes, as the optimal transition between inpatient to outpatient phase, and hospital readmissions.

Venous and arterial thromboembolism

Pulmonary embolism (PE), deep vein thrombosis (DVT), disseminate intravascular coagulation (DIC), acute coronary syndrome (ACS), ischemic stroke, systemic arterial embolism and peripheral vascular occlusion (capillary embolism), have been observed in approximately 20% of infected patients [15]. The underlying pathophysiological mechanism seems to be related to an abnormally increased inflammatory response to viral particles, mainly mediated by IL-6 and other cytokines [16]. Platelets activation due to pronounced inflammatory response, with cytokine storm and endothelial dysfunction, partly explains the dramatic thromboembolic events that occur in some patients [17,18]. The most used treatment in this setting seems to be pharmacological or mechanical thrombolysis [18], and unfractionated or low molecular weight heparin at therapeutic doses. In Sars-CoV2 patients, ACS is secondary to plaque rupture, resulting in intracoronary thromboembolism. Dual antiplatelet therapy and full dose anticoagulation have to be administered, unless contraindications are present. Interventional treatment, when possible, is indicated as well [18].

When DIC is diagnosed, COVID-19 has a particularly poor outcome. Treatment is not clearly defined: prophylactic transfusion of platelets, fresh frozen plasma, fibrinogen, and prothrombin complex concentrate may be considered; low molecular weight heparin (LMWH) prophylaxis should be added to decrease thrombin generation during the course of DIC [19]. Systemic arterial thromboembolism secondary to Covid-19 infection, even in absence of pre-existing symptoms of peripheral vascular disease, has been described as well. However, the most relevant and prevalent thromboembolic complication of Sars-CoV2 infection is PE, usually presenting with sudden chest pain, haemoptysis and worsening of dyspnoea and hypoxemia. Furthermore, a sudden increase of D-dimer levels, despite the lack of worsening of pulmonary infiltrates, should be evaluated carefully.

Once Sars-CoV2 infection is diagnosed, prophylaxis with Heparin should be introduced as soon as possible. Evidences suggest that LMWH, like enoxaparin, should be preferred to UFH or other anticoagulant drugs, due to better safety profile, way of administration and minor drug interactions with anti-viral drugs

[2]. A daily dose of 4000 UI of enoxaparin is recommended, according to standard international guidelines. If anticoagulant prophylaxis could not be administered for elevated bleeding risk, mechanical pneumatic compression can be an alternative to take in consideration. Finally, direct oral anticoagulants should be considered with caution, especially if patients are in treatment with HIV protease inhibitors antiviral drugs [15].

Utilization of cardioprotective drugs

COVID-19 treatment: cardiovascular side-effects

Drug therapy against COVID-19 can be divided into antiviral, support for concomitant infections (bacterial or viral) and anti-inflammatory (*i.e.*, steroids or tocilizumab).

Hydroxychloroquine (HCQ) could block the entry of the virus into the host cell by reducing the binding with the receptor ACE-2 and the viral replication for the elevation of the pH of the lysosomes. An immunomodulatory action is hypothesized with reduction of pro-inflammatory cytokines, and activation of CD8+ T cells [20]. Some side effects such as retinopathy, peripheral neuropathy, myopathy, depression, adverse skin and gastrointestinal effects or an HCQ-induced restrictive cardiomyopathy are mainly related to chronic therapy and to high dosages (>5 mg/kg/day). HCQ in short-term use, as in COVID-19 patients, can prolong the QT interval, inducing potentially lethal arrhythmias as torsade de pointes [21,22]. The risk is increased by underlying heart disease in elderly patients, especially if treated with drugs that prolong the QT. HCQ dose is relevant: in a RCT evaluating high dose vs the standard dose (600 mg twice daily vs 450 mg daily, total dose 12 vs 2.7 g) the first was associated with higher rates of ventricular tachycardia and increased mortality [23]. Whether either hydroxychloroquine or chloroquine are associated with improved survival in COVID-19 patients is still debated [23]. The combination of ritonavir/lopinavir, in addition to lengthening the PR up to 2nd and 3rd degree atrio-ventricular block, may increase QT, also for inhibition of the metabolism of other QT-prolonging drugs [24-26]. Remdesivir does not prolong QT like ribavirin and darunavir [24-26]. The risk of QT prolongation is considered low for atazanavir and favipiravir and is enhanced by pre-existing risk factors (electrolyte imbalances, drugs that prolong QT, underlying heart disease) [24-26]. Finally, no effect on QT has been demonstrated for interferon beta [24-26].

Azithromycin, widely used in these patients, can increase arrhythmic risk; furthermore, there are no data on the concomitant use with HCQ, with the exclusion of the RCT above mentioned. Beyond the effect on QT (due to I_{Kr} block), the drug may potentiate cardiac Na current that increase intracellular Na^+ , activating the Na^+/Ca^{++} exchange, leading to a dysregulation of intracellular Ca^{++} and creating a substrate similar to that of the polymorphic catecholaminergic ventricular tachycardia [22]. Actually, this is a QT-independent pro-arrhythmic mechanism. Other drug interactions, able to prolong the QT are ceftriaxone and lansoprazole (but not cephalosporins), loperamide and antidepressants. Oseltamivir (for concomitant influenza), can lengthen the QTc.

Tocilizumab lead to a QTc reduction in proportion to the cut of inflammatory mediators, and is currently under investigation in an RCT [27].

To minimize the arrhythmic risk in COVID 19 patients it is advisable [28] to: 1) stop the drugs that prolong QT, if feasible, and correct electrolyte imbalances; 2) arrange a consultation with a cardiologist in patients with a cardiac disease especially if at arrhythmic risk; 3) if baseline QTc is >500 ms do not use HCQ and azithromycin; 4) do a baseline ECG and perform another one, after

48 h of initiation of therapy, and if QTc Increases by ≥ 60 ms or is ≥ 500 ms, antimicrobial drugs should be discontinued; 5) minimize the infectious risk for care-givers: in low-arrhythmic-risk patients, start therapy without the baseline ECG.

ACE-inhibitors and ARB

The pathophysiology of COVID-19 involves the binding of SARS-CoV-2 to the angiotensin-converting enzyme-2 (ACE2)-receptor to mediate entry into lung epithelial cells. ACE-2, which is expressed in the lungs, heart and vessels, is a key factor of the renin angiotensin system (RAS), which in turn plays a central role in the pathophysiology of cardiovascular diseases [2]. Basically, ACE2 cleaves Angiotensin II and angiotensin I into angiotensin 1-7 (Ang1-7) that, in turn, through a specific receptor, counteracts Angiotensin II activity promoting vasodilation and both anti-inflammatory and antiproliferative effects thus exerting definitely a cardioprotective effect. In several conditions such as in ischemic heart disease, heart failure, arterial hypertension and diabetes, as well as in all conditions associated with Angiotensin II-mediated damage, ACE2 is hyper-expressed [29]. Given that the binding of the SARS-CoV 2 to ACE2 is the mechanism by which the virus enters lung alveolar epithelial cells, the hypothesis that the overexpression of ACE2 in hypertensive and/or diabetic patients affected by COVID-19 could increase the risk of mortality has been advanced [30-32]. However, it has been demonstrated that SARS-CoV2 can down-regulate the ACE2 receptor not affecting ACE, which in turn causes an ACE/ACE2 imbalance with a consequent excessive angiotensin production. According to this hypothesis, the up-regulation of ACE2, caused by the chronic intake of ARBs and ACE Inhibitors, could be protective: both by blocking the AT1 receptor and by increasing the levels of ACE2 that reduce the production of angiotensin by ACE and increase the production of angiotensin 1-7 by ACE2. Experimental studies indicate that the up-regulation of ACE2 could be a powerful protective mechanism against organ damage mediated by Angiotensin II [33].

Organization and delivery of CR programs during the COVID-19 pandemic

General recommendations

General recommendations to CR facilities during the emergency and post-emergency phase of COVID-19 pandemic are as follows: 1) to ensure as far as possible adequate delivery of CR programs, in order to facilitate the continuity of care and to mitigate unmet needs of cardiac patients after an acute event and/or with chronic disabilities; 2) to contribute to limit the spread of infection, by protecting at the same time patients and health care operators; 3) to accumulate expertise on the new phenotype of the “cardiac-COVID” patient, *i.e.* a cardiac patient who develops COVID-19 as a comorbidity, or a COVID-19 patient displaying *de novo* cardiovascular conditions as a consequence of the viral disease and its treatment; 4) to manage processes such as de-powering/closure of CR services, transformation into COVID units, re-employment of CR staff, and restoration of the activities.

For these purposes, the CR community could refer to the Decalogue that has been recently released by the European Association of Preventive Cardiology (EAPC) [34], here summarized:

- 1) Evaluate regularly the COVID-19 pandemic situation
- 2) Be prepared to handle COVID-19 patients

- 3) Consider systematically consequences of COVID-19 pandemic on cardiac patients
- 4) Deliver as much CR as possible under the given circumstances
- 5) Be prepared to address patients' requests
- 6) Educate patients to not postpone medical care
- 7) Detect and fight fake-news
- 8) Develop and organize tele-rehabilitation programs
- 9) Provide psychosocial support to patients
- 10) Prepare resumption of activities from the center point

With special reference to the Italian CR situation [35] and the heterogeneous diffusion of COVID-19 infection, recommendation #1 and #3 are particularly devoted to residential and outpatient CR facilities working in the worst hit areas, where the maintenance of routine CR could be extremely difficult. At the same time, these areas – often highly urbanized and with many acute cardiac wards – could present large populations of cardiac patients without adequate care.

Concerning recommendation #2, the provision by CR facilities of structured care pathways, in case of COVID-19 diagnosis during CR programs, has a remarkable relevance by reducing the risk to “lose” the patient and taking responsibility for resumption of the rehabilitative phase. The “Individual Rehabilitation Plan” (*i.e.* the formal document identifying in the Italian health system purposes, modalities, and outcomes of the CR program) - rather than invalidated in case of COVID infection - should be conversely kept opened and ready to take charge of the sequelae of the viral infection.

General organization of CR activities

Covid-19 is an infectious disease characterized by a rapid human-to-human transmission capacity and has opened up new scenarios, particularly for environments such as hospitals and gyms where human contact is often the norm. We propose that CRP gyms should be modified in “COVID-19 version”, seeking a balance between minimal care and enhanced health security. We suggest to significantly reduce the number of patients accessing the gym by creating dedicated paths and a distance of three meters with a maximum of two simultaneous accesses. During the supervised exercise training, all patients and physiotherapists must wear a surgical mask, and all materials must be disinfected before and after each activity, avoiding sputum-inducing exercises. In the majority of patients, exercise training should be carried out inside the inpatient rooms (exercise bikes, pedal exerciser, *etc.*) and it should be supported by video footage transmitted *via* USB stick and TV supplied in each room. Patient education is a main process, and patients should be instructed on how to protect themselves from contact with the virus (hand washing, masks, gloves, constant sanitization) and information is also provided in illustrative format. In addition, post-acute cardiac/COVID-19 patients should be admitted only after two negative nasopharyngeal tests. Several studies have shown that asthenia and generalized weakness are some of the symptoms most reported by these patients, in addition to loss of muscle mass. All these are preconditions for targeted physical reconditioning. During the evaluation phase and always before performing a reconditioning program, the acquisition of vital parameters (blood pressure, peripheral oxygen saturation, heart rate, respiratory rate, telemetric monitoring) is an essential rule.

Evaluation phase

- a) Oxygen saturation monitoring during walking and where indicated telemetric monitoring
- b) Evaluation of daily life activities (Barthel Index)
- c) Evaluation of functional frailty degree of using Short Physical Performance Battery (SPPB); (classification moderate frail with a level of SPPB scale 7-9)

- d) If SPPB = 0 strength assessment by MRC Scale for Muscle Examination
- e) Functional capability assessment by 6-minute walking test according to guidelines, with the addition of ΔSpO_2 beginning to end and recovery HR 1 min after the end of the test
- f) Evaluation of resting and exertion-induced dyspnea by modified Borg Scale for dyspnea evaluation
- g) Quality of Life Assessment (EuroQol VAS 0-100)

Recommendations on exercise training

To date, there are no known rehabilitation programs to counteract the effects of the virus on the systems involved and on functional recovery. The intensity and modalities of the reconditioning training should be individualized according to the stratification of the degree of functional frailty through the SPPB scale [36], classifying 4 different degrees of functional frailty (Table 1). For the progression of the individualized physical training program, it would seem logical to stick to guidelines [5] of the major scientific societies in the cardio-respiratory field. Our proposal for physiotherapy programs [37] for these patients is described in Table 2, with the recommendation to modulate it according to needs, symptoms and possible changes in health status.

Recommendation on nutrition

The overall nutritional management principles for patients in CR during COVID-19 pandemic (patients at risk for COVID-19 or those post COVID-19 infection) are the same as for period without this pandemic. Lifestyle recommendations and interventions are described in the Minimal Care paths for dieticians [38]. However, as for increased danger of developing COVID-19 in persons with

cardiovascular diseases, a few main points should be taken into account. Preserving nutritional status and preventing or treating malnutrition are essential to reduce complications and negative outcomes in patients with nutritional risk who might incur in COVID-19 in the future. In particular, nausea, vomiting and diarrhea impairing food intake and absorption can accompany COVID-19, thus a good nutritional status is an advantage for people at risk for severe COVID-19 [39]. Prolonged hospitalization, with enhanced catabolism and immobilization, induces a decrease in weight and muscle mass, which can result in sarcopenia, a condition that impairs respiratory and cardiac function, prolonging patient's hospitalization and worsening the prognosis [40].

In case of patients with malnutrition or at risk detected with validated screening, if the oral diet does not meet the nutritional needs and the patient finds it difficult to eat, it would be necessary to provide fortified or high energy density meals [41]. For patients who have difficulty in swallowing (dysphagia), chewing or mucositis, specialist phoniatric-speech therapy indications should be followed to carry out a careful multispecialty assessment [41]. If, however, the meals do not cover the requirements rate (27–30 kcal/kg/die; >1 g protein per kg body weight and day), an oral supplement should be carried out [39].

In malnourished elderly subjects, the indication is to consume oral supplements for at least 400 kcal/day that bring 30 g or more of protein per day [41]. If offered to an elderly person who is malnourished or at risk of malnutrition, these supplements must be consumed for at least one month and the expected effectiveness and benefit should be re-evaluated once a month [41]. Usually, it is recommended to consume liquid oral supplements slowly, in small sips, over 60-120 min, in order to avoid the sense of gastric and abdominal swelling [41].

Table 1. AICPR proposal for classification of functional frailty through SPPB assessment.

SPPB score	SPPB classification	Functional fragility
0-3	Severe limitations	Very severely frail
4-6	Moderate limitations	Severely frail
7-9	Mild limitations	Moderately frail
10-12	Minimal limitations	No frail

SPPB, short physical performance battery.

Table 2. Physiotherapy program.

Physiotherapy program	Very severely frail	Severely frail	Moderately frail	No frail
Change of posture / therapeutic posture	X			
Passive mobilization and active assisted	X			
Active mobilization	X	X		
Neuromuscular electrostimulation	X			
Standing station recovery	X	X		
Supervised walking		X		
Walk test training			X	
Effort reconditioning (pedal exerciser)		X	X	
Aerobic training (exercise bike, treadmill)			X	X
Muscle strengthening (weights, elastics)		X	X	X
Balance exercises	X	X	X	X
Training on stairs				X
Educational	X	X	X	X

There are no limitations for enteral or parenteral nutrition use, according to patient age or diagnosis [39].

Protein supplementation is more effective in combination with progressive resistance training: consider 20 g of protein supplement after exercise. Data suggest that milk and other dairy products containing different bioactive compounds (*i.e.* protein, leucine) can enhance muscle protein synthesis, particularly when combined with resistance exercise [42].

In the pandemic period, social distancing and an individual approach using masks besides distancing are recommended. Since the patient has to stay in his room as long as possible, education oriented on healthy food choices can be found in brochures, video, interactive quizzes involving family by remote. Education should be oriented to suggest alimentary safety and how to organize shopping for food over a long period. It is also important to exclude raw foods and cold cuts from the hospital menus and use disposable tableware to ensure more protection against foodborne infections (as the normal procedure adopted for patient underwent heart transplantation).

Recommendations on psychological activities

Studies have confirmed that individuals who have experienced public health emergencies still have varying degrees of stress disorders, even after the event is over, or after they have been cured and discharged from hospital. Psychological intervention should be based on a comprehensive assessment of psychosocial risk factors, including poor mental health before the crisis, bereavement, injury to self or family members, life threatening circumstances, separation from family and low household income. The list below outlines key psychological activities that should be implemented as part of the response to COVID-19, in Italian CR Unit.

- *Assessment*

- 1) Queries about COVID-19-related stressors: exposures to infected sources, infected family members, loss of loved ones.
- 2) Post-traumatic Stress Disorder (PTSD) associated with ICU hospitalization.
- 3) Cognitive impairment following acute respiratory distress syndrome (ARDS).
- 4) Psychosocial effects of quarantine/social isolation.
- 5) Secondary adversities (economic loss, for example).

- *PTSD*

Literature highlights the insight that ICU-related PTSD appears to have a unique clinical profile, which includes avoidance and future-oriented worries about medical condition recurrence resulting in problematic engagement in recommended health care and medical treatment. Most importantly, PTSD sub-symptoms, including re-experiencing, negative alterations in cognition or mood and hyper-arousal, are more common in females than males.

- *Psychosocial effects of quarantine/social isolation*

Patients who are quarantined are very likely to develop a wide range of symptoms of psychological stress and disorder: depression, anxiety, anger, irritability, emotional exhaustion, psychosomatic pre-occupations, insomnia, changes in eating patterns, increased substance use (alcohol, tobacco, other drugs). Patients with preexisting mental health conditions (obsessive-compulsive thoughts and behaviors, a predominance of somatic symptoms, or those previously exposed to severe trauma) may be particularly vulnerable [43].

- *Cognitive impairment*

Cognitive impairment following ARDS has been noted to affect the majority of survivors at hospital discharge and in around 10% impairments are persistent at long-term follow-up.

Neuropsychological impairments are multidimensional and include memory, attention and higher order executive functions.

- *Secondary adversities*

In light of the widening economic crisis and numerous uncertainties surrounding this pandemic, suicidal ideation may emerge.

Intervention

- Psychological and/or psychotherapeutic interventions on depression, anxiety, PTSD, anger, sleep disturbance, substance abuse, in relation to the severity of the problem emerging
- Educational programs about the common adverse psychological consequences following COVID-19 crisis and health-promoting behaviors.

Mobile health platforms provide a fertile ground for disseminating important and accurate health information to ensure that patients keep themselves healthy during pandemic and do not trivialize their risks of CV disease.

Psychosocial impact of COVID-19 on the elderly

The psychological impact for these populations can include anxiety and feeling stressed or angry and can be particularly difficult for those who may be experiencing cognitive decline.

The rapid transmission of COVID-19 infection as well as the higher case-fatality rate might exacerbate existing psychiatric disorders, and enhance the risk of new episodes: namely, severe delirium, psychomotor agitation, anxiety and depressive symptoms [44-46]. Elderly patients usually suffer from lower social support and may be less familiar with services and technology that can make social distancing easier, thus enhancing loneliness, despair and hopelessness [43-46].

Safety of health procedures

Health care professionals (HCP) are considered at high risk for contracting the virus SARS-CoV-2 because of their potential risk of direct or indirect biological exposure to contact with infected patients or objects like corporeal fluids, medical devices, environmental surfaces or contaminated area [47].

All HCP must follow international statement for IPC (Infection prevention and control) [48]:

- Body temperature control at the beginning of each shift;
- Hands cleaning;
- Use of work uniform with daily change;
- Use of correct personal protective equipment (PPE);
- Environment disinfection with sodium hypochlorite (0,1-0,5%), ethanol (62-71%) or hydrogen peroxide (0.5%);
- Proper management of medical devices.

ESC guidance recommends 3 levels of protection against COVID-19 according to patient risk status, setting and type of procedures [49] (Table 3).

CR settings

Ambulatory setting

- A nurse/administrative triage (*e.g.* by phone or mail) should be performed the day before the exam/CR activity;
- Each outpatient must be equipped with a surgical mask;
- Patient's care giver should wait outside the facility;
- HCP PPE is described in Table 3.

Ward setting

- Every inpatient and caregiver must wear a surgical mask;
- Newly admitted patients in a cardiology ward should be regarded as possibly infected until a swab test is performed and managed, hopefully in a dedicated area with level II/III PPE;

- Confirmed cases should be managed with level II or III PPE and with the use of dedicated medical equipment (*e.g.* blood pressure cuffs, stethoscopes and thermometers, vital signs telemonitoring); if not possible, equipment must undergo disinfection;
- Negative cases, but with a suspicion of COVID-19, must perform a second swab test, and/or a lung CT scan, depending on local capabilities and symptoms. These patients should be maintained in a dedicated area of the ward;
- Confirmed negative cases should be managed with level I PPE, in a “clean” area of the ward.

Physiotherapy activities

- The aim is to reduce the time of exposure with suspected/probable or confirmed patients;
- Physiotherapy activities should follow the 1 to 1 ratio;
- Group activities must be avoided at current time;
- Respiratory physiotherapy could be performed in patient with SARS-CoV-2 infection in acute setting following the current guidelines [50]; it's reasonable to continue these activities also in the post-acute phase;
- Negative patients affected by ischemic heart disease, HF or post cardiac surgery patients should be treated as usual;
- HCP must use the right PPE (Table 1).

Cardiac imaging

Cardiac imaging should be performed if appropriate and only in case of predictable outcome improvement [51]. Trans thoracic echocardiogram (TTE): a focused study is recommended to reduce exposure; measurements should be performed offline. Transesophageal echocardiography (TOE) is considered a high-risk procedure and must be reserved only if it's necessary for diagnosis or to guide treatment. HCP must use the appropriate PPE. Correct disinfection of surfaces and medical devices after each exam is mandatory. Dedicated disposals of PPE are required.

Structured secondary prevention after the COVID-19 emergency phase

Out-patients and community activities in the long term

The ongoing COVID-19 pandemic and its consequential extraordinary measures to prevent the spread of this disease urgently imposed a new organization of cardiovascular rehabilitation (CR)

services. Therefore, even though inspired to the same principles [5], outpatients and community activities have been accordingly re-modulated [1]. Overall, restarting interrupted or postponed CR programs, both in COVID-19 and no-COVID-19 patients is strategic for ensuring secondary prevention advantages [5,13].

Admission to CR programs

Patients during outpatient phase-2 CR should be carefully screened out for inclusion into CR programs. No admission to CR programs is granted if fever, symptoms and other signs of COVID-19 are present. Patients directly tracked by acute wards should have double negative pharyngeal tests or lab tests suggestive for COVID-19. After COVID-19 resolution, patients should be referred to CR. Eligible patients must use surgical masks during the whole stay in outpatient services. All patients that have been into contact with a confirmed COVID-19 case must be isolated.

Recommendations for on-site exercise training programs

All patients and staff (*i.e.* physicians, nurses, physiotherapists, *etc.*) have to wear surgical mask. Provide a minimal distance of 2 meters between patients during use of gym-machines (cycloergometers, treadmill, *etc.*). Individual sessions represent the optimal strategy; however, if not feasible, reduce at minimum the number of patients per session. Avoid sputum-inducing exercises and appropriate disinfection of material should be warranted before and after each session. Since CR programs might be shortened to ease patients' turnover, efforts should be made for every main core component (*i.e.* lifestyle risk management, psychosocial support, medical advice, education). All these procedures should be inspired by an individualized approach based in turn on psychological symptoms, residual cardiac risk and lifestyle assessment. All community activities interfering with social distancing, self-quarantine, and isolation rules must be interrupted.

Home-based CR programs and telecardiology

In-hospital sessions should be replaced by remote assessment and monitored home-based CR programs. Telemedicine represents a suitable modality of delivery of CR programs in COVID-19 times, to be particularly tailored on individual needs and social distancing. An example of how a telemedicine program could be adapted on CR activities during the COVID-19 pandem-

Table 3. SARS-CoV-2 related personal protection management. Edited by ESC Guidance for the Diagnosis and Management of CV Disease during the COVID-19 Pandemic [3]

Protection level	PPE Personal protective equipment	APPLICATION Setting/procedure
LEVEL I ment	<ul style="list-style-type: none"> • Disposable surgical cap • Disposable surgical mask • Work uniform • Latex gloves 	<ul style="list-style-type: none"> • No suspected/not probable patients medical and physiotherapy manage-
LEVEL II	<ul style="list-style-type: none"> • Disposable surgical cap • Medical protection mask (FPP2-FPP3) • Work uniform • Disposable surgical gloves • Gown • Goggles 	<ul style="list-style-type: none"> • Suspected/probable or confirmed COVID-19 patients medical and physiotherapy management (ambulatory/ward settings) • TEE in suspected/probable or confirmed COVID-19 patients
LEVEL III	<ul style="list-style-type: none"> • Disposable surgical cap • Full face respiratory protective device 	<ul style="list-style-type: none"> • Aerosol generation procedures (AGP); nasopharyngeal swab; TOE in suspected/probable or confirmed COVID-19 patients

ic is shown in Box 1 [1-10,52-65]. According to local equipment and expertise, telephone interviews, text messaging, emails, video consultations, web-based platforms and applications can help patients. Precise prescription is needed to guarantee an appropriate exercise program aimed to maintain or improve the principal health related physical fitness components. Implementing these strategies in COVID-19 scenario might be

strategic for future inclusion into CR programs of patients that for logistic issues or other barriers cannot attend traditional CR sessions and programs [62]. Not knowing how long the state of emergency will last, we recommend structuring a telephone follow-up and developing a standardized questionnaire administered to patients and/or to their caregiver to evaluate clinical stability and adherence after discharge.

Box 1. How to adapt telemedicine during COVID-19 outbreak: a case history.

Background

Telemedicine during COVID-19 outbreak was of particular value in Lombardy, the hardest-hit region in Italy due to the rapid increase in cases and limited medical resources during the early phase of the pandemic. In this area, previous experience was built with the support of authorities in the use and management of technological innovations in remote surveillance programs for chronic patients suffering from chronic heart failure and COPD. During the COVID-19 outbreak, several hospitals made themselves available to the Regional Health Service and, in a few days, completely converted from a Rehabilitation center to a hospital for COVID-19 patient's management, as the case of Lumezzane (BS), where the local telemedicine program was also adapted to COVID-19 requirements.

Target patients

The program was targeted on patients after hospital discharge for interstitial pneumonia from COVID-19 with an acute respiratory insufficiency and with a high incidence of comorbidity, following an in-hospital rehabilitation program of two-three weeks. When discharged at home, these patients require special attention due to the still frail health conditions, complex therapies, often still breathing difficulties and gas exchange impairment during effort, symptoms of lodging and other disabilities related to the acute event. For this reason, it is important to discharge patients safely and to follow them in an appropriate manner by trained nurses and therapist during the transitional phase after hospital discharge, attending quickly if symptoms restart (telesurveillance) and continuing the physical activity done during hospitalization (telerehabilitation). Whichever the chosen program, this should have the aim of facilitating the resolution of the clinical problems and allowing the patient to achieve the best possible level of autonomy on the physical, functional, social, intellectual, and relational level.

Telesurveillance intervention

Operatively, the purpose of the "telesurveillance intervention" is to keep under control the evolution of the state of health, to give counselling support to help recovery and to have early identification of signs and symptoms related to a possible resumption of COVID-19 disease and / or comorbidities. The key element of the program (for which only patients who refuse or without a smartphone are excluded) is a structured nurse-managed telephone support and, when necessary, video consultations, to follow patients, for one month. During the first two weeks daily contacts are usually performed according to the clinical needs of the patients, while an additional contact could be made approximately two months after. At the beginning and after three months, patients could also be tested quality of life questionnaire. During the program, the service records clinical parameters, adherence and changes to therapy, any signs and symptoms aimed at capturing indicators of instability, requests for specialist advice, emergency room access or re-hospitalizations. The clinical parameters should be collected through a standardized interview (body temperature, muscle soreness, coughing, dyspnea, blood oxygen saturation, *etc.*) following indication of World Health Organization. Patients are usually provided with a pulse oximeter to measure O₂ saturation, and when necessary, a portable one lead electrocardiograph to determine the electrocardiographic changes (*e.g.* QT prolongation) caused by the use of drugs for the treatment of COVID-19 and the presence of arrhythmias. In the presence of symptoms or problems, the patient should preferably call within pre-established time slots.

Telerehabilitation intervention

In the "telerehabilitation intervention", in addition to the above described provided to all patients, enrolled subjects are also evaluated and stratified to provide a suitable rehabilitation program at home. For this purpose, patients could be divided into 1) patients to whom only autonomous home rehabilitation is recommended, and 2) patients to whom home telerehabilitation is provided with videoconference support. Patients are also stratified based on the level of effectiveness of the gas exchange during effort, the presence of effort intolerance and the residual disability during the activities of daily life. All patients are usually evaluated for the following measures: gas exchange at rest by SpO₂/FiO₂, physical disability by Short Physical Performance Battery (SPPB), perceived dyspnea /fatigue at rest by Borg Scale, dyspnea during ADL by Barthel dyspnea, effort tolerance by Six-minute walking test (6MWT) if SPPB ≥10 or by 1-minute Sit to Stand (1MSTS) if SPPB <10, exercise desaturation during effort tolerance tests evaluating the change of SpO₂ (baseline SpO₂ -mean SpO₂ during test) peripheral muscle strength by Dynamometer of quadriceps / biceps. In the group 1, patients could be provided with a brochure dedicated to the physiotherapy home intervention and are educated to the autonomous execution of the exercises. In the group 2, home rehabilitation is provided with videoconference support. Patients perform daily physiotherapy as prescribed (the program is structured into different levels of intensity in relation to the initial assessment) and are contacted with individual / group video calls no less than 2 times a week. Exercises of chest physiotherapy (lung expansion and / or respiratory muscles training) may be prescribed, when necessary.

Outcome measures for telerehabilitation

The main outcome measures of telerehabilitation could be as follows:

- For symptoms: Barthel dyspnea (expected delta improvement of 10 points)
- For exercise tolerance: 1 min-STs (expected delta improvement of 5 rises during the test)
- For organizational: adherence to the pathway (expected to be attended at least 80% of scheduled sessions; expected at least 6 video-calls in 30 days).

Low socio-economic status and risk for secondary prevention

Patients with a lack of social support, low education, low income, undetected depression or anxiety, are at greater risk of continuing to smoke, making unhealthy food choices, achieving inadequate physical activity and having poor adherence to medication. These factors are exacerbated as a consequence of COVID-19 pandemic, for clinical or socioeconomic reasons. It is important to provide regular contacts also after CR program: communication and education after CR can have a positive effect on the patients' outcomes and self-management skills.

Communication dynamics

Patients' experiences of communication and health education interactions are influenced by the relationship with the health professional as well as the language and terminology used. An "open-dialogue" which is perceived as honest and nonjudgmental is important. Expressing uncertainty about a health outcome is not seen as negative, but as part and parcel of honest clinical communication. By contrast, there are several instances in which participants received conflicting and confusing information. Finally, patient demographics, health literacy levels and the perceived attitudes and gender of health professionals are powerful factors influencing the level of patient engagement in health care [66,67]. We recommend that health professionals be given the opportunity to reflect on how they communicate with patients and their families, to provide support for recovery after a cardiac event in the context of COVID-19. Health professionals will benefit from skills training. Focus needs to be given to supporting health professionals to individualize health communication, using plain language for the topics that matter to patients. Some techniques used to broach difficult conversations about risk would be a valuable addition to communication of skills education along with the use of "Teach-back" to support patient comprehension [68]. More attention is required to ensure that educational content focuses on topics that are currently "missing" from heart health curricula. At the moment, with the uncertain trajectory of the COVID-19 outbreak, when adopting these approaches, patients may have a more realistic understanding of their cardiac risk combined with relevant information to enable them to make lifestyle changes and manage their medications. During the COVID-19 outbreak communication has been used as a public health strategy to reduce adverse psychological responses and increase behavioral adherence. There is evidence that communication of threat is effective when it expresses empathy, when it promotes action and improves engagement [69].

The messages below are focused on promoting cardiovascular health and wellbeing during COVID-19 pandemic (Table 4).

Observational research

So far, much attention has been reasonably devoted to acutely ill patients in acute care settings. However, as COVID-19 pandemic emergency reduces its spreading and vulnerability, post-acute healthcare system capacity to manage numerous cardiac patients after COVID-19 should be implemented. In this context, research agenda should focus on new emerging scenarios [70-72]. COVID-19 patients undergoing urgent procedures (*i.e.* coronary artery bypass grafting, aortic valve replacement, repair of an aortic dissection) may more likely develop myocardial dysfunction after surgery. Studies aiming at investigating the effect of COVID-19 on myocardial protection during cardiac surgery should be implemented [73]. Similarly, patients undergoing percutaneous coronary intervention or coronary stenting may have poor outcome due to the additive effect of myocardial ischemia and poor underlying myocardial function due to COVID-19 infection [71].

At medium term, toward the end of acute COVID-19 storm, whether cardiovascular reliquates are present after COVID-19 recovery should be investigated. Since it is too early for answering these questions, studies from cardiac outcomes of SARS-CoV2, which is structurally similar to SARS-CoV-2, provide evidence that cardiovascular outcomes should be carefully monitored. A longitudinal study following patients that recovered from SARS-CoV2 reported that 68% had dyslipidemia, 4% had cardiovascular system abnormalities, and 60% had impaired glucose metabolism after recovery [74]. Emerging cardiometabolic risk, as coronavirus-associated pathology must be considered and further investigations of cardiac conditions after COVID-19 are warranted.

Referral to CR and secondary prevention programs of pre-existing cardiovascular diseases patients infected by coronavirus should be implemented due to possible negative influence on several cardiovascular functional and pathophysiological parameters through deconditioning, thrombophilia or pulmonary function abnormalities. In consideration of the multifaceted and coordinated intervention of these programs (exercise programs, pulmonary rehabilitation, psychological support, smoking cessation programs, dietary and nutritional counselling, *etc.*), stakeholders should recognize the great value of CR programs in this new cohort of patients. A permanent registry exploring the impact of COVID-19 on secondary prevention and rehabilitation programs and outcome in patients with pre-existing cardiovascular diseases is eagerly encouraged. In addition, registry on non-COVID-19 cardiac

Table 4. Defeat the COVID-19 and save your heart in 10 moves.

1. Stay at home but manage your time and give yourself a new routine
2. Fight the feeling of emptiness and anxiety by doing things you always neglected due to lack of time.
3. Counteract sadness and depression, smile, sing, listen to music, call someone you love.
4. Don't smoke out of boredom; actually, why don't you take advantage of this radical change to quit smoking?
5. Beware that desire to eat that comes when you feel alone, bored, and sad. It is not hunger, therefore resist.
6. Every single step counts, even those taken in the hallway of your house or around the table. You have no excuses, stay active.
7. Manage the stress of isolation or forced cohabitation: we are all in this together and you are doing your part.
8. Stay informed, but do not get overwhelmed by the daily flood of news and numbers.
9. Take it lightly as often as you can and never use alcohol to relax a little.
10. Take your medicines regularly, pay attention to cardiovascular symptoms and, if you need it, ask for help.

Table 5. Integration of AICPR indications and requirements to assist CR activities in COVID-19 patients.

Domain	Integration	Comment
Qualifying diagnosis for referral to CR	COVID-19 pneumonia in pre-existing cardiac disease	A pre-existing cardiac disease might be exacerbated by COVID-19, providing the need for updated risk stratification, drug titration, rehabilitation plans, nutritional and psychosocial management, <i>etc.</i> Acute cardiac events complicated by COVID-19 infections are to be considered cardiac conditions <i>ab initio</i> for referral to CR
	COVID-19 pneumonia complicated by ACS, exacerbation of heart failure, cardiogenic shock, myocarditis, arrhythmias, resuscitated SCD, pericarditis/cardiac tamponade, and/or arterial/venous thromboembolic events	Acute cardiac events occurring after COVID-19 are always to be considered at very high risk Arterial/venous thromboembolism needs high consideration in view of the pathophysiology of COVID-19
	COVID-19 pneumonia requiring percutaneous coronary intervention and/or CIED implantation COVID-19 pneumonia developing PAH	Not only persistent PAH, but transient PAH also should be referred to CR, due to the risk of poor prognosis
	COVID-19 pneumonia with prolonged stay in ICU	Particularly when hemodynamic imbalance has occurred after mechanical ventilation
	COVID-19 pneumonia developing markedly reduced exercise tolerance	Particularly when reduced cardiorespiratory fitness has been supposed as the first cause of exercise intolerance
	COVID-19 pneumonia developing cardiovascular complications from therapeutic agents	<i>i.e.</i> hypertension or glucose intolerance by steroids; prolonged QT interval taking hydroxychloroquine; bleeding after use of anticoagulants
	COVID-19 pneumonia with multiple and serious cardiovascular risk factors and/or persistent coagulation alterations	<i>i.e.</i> high and very high cardiovascular risk by validated charts; elevated D-dimer of fibrinogen levels
Core components of CR intervention	- Patient evaluation also oriented to respiratory impairment and other COVID-19 features - Active research of frailty at the beginning of the CR program as part of routine patient evaluation	- <i>i.e.</i> adoption of other than NYHA scales such as the MRC dyspnea scale; serology testing and NP specimens for COVID-19; radiologic testing for COVID-19 pneumonia monitoring; serial testing for hemoglobin saturation, blood gases analysis, oxygen consumption, diffusing capacity of the lung for CO for evaluation and follow-up of respiratory impairment - Adequate skills on oxygen therapy and noninvasive mechanical ventilation by the multidisciplinary staff - Frail patients represent the most vulnerable subjects to COVID-19 and those with the worse sequelae
	- IMT and other respiratory techniques to be included among exercise training when appropriate - Specific focus on strength training in frail COVID-19 patients	The consideration of IMT as a complementary intervention is derived by current evidence in the field of heart failure
	Assessment nutritional risk and intervention particularly devoted to malnutrition as a consequence of prolonged immobilization and ventilatory support	1. validated nutritional risk screening 2. fortified or high energy density meal and/or oral supplement 3. enteral nutrition and/or parenteral nutrition.
	Lifestyle and psychosocial management particularly focused on smoking cessation, fear of infection, fighting of fake news, caregiver-limiting restrictive measures, and working resume	
Structure-based metrics	<ul style="list-style-type: none"> • The CR unit has equipment for health operators' safety • The CR unit has different logistics for COVID and non-COVID patients • The CR unit has availability of pulmonology consultation on demand 	

To be continued on next page

Table 5. Continued from previous page.

Domain	Integration	Comment
Process-based metrics	The CR unit has structured quick reaction in case of suspected or confirmed new emerging COVID-19 cases	<i>i.e.</i> patient isolation, case confirmation, treatment of respiratory distress, screening of contacts, communication with relatives and caregivers
Quality indicators	The following quality indicators should be added: <ul style="list-style-type: none"> • % eligible patients to CR, enrolled after discharge from COVID units (>50%) • Median waiting time from referral to start of CR: 0 days for residential programs (direct track from COVID units); within 14 days for out-patient programs • % of CR uptake: minimal 24 sessions with an aim of 36 sessions 	

ACS, acute coronary syndrome; CIED, cardiac implantable electronic device; CO, carbon monoxide; ICU, intensive care unit; IMT, inspiratory muscle training; MRC, medical research council; NYHA, New York heart association; NP, nasopharyngeal; PAH, peripheral arterial hypertension; SCD, sudden cardiac death.

patients having acute cardiac event coming to CR should encouraged to keep track of the possibly more severe functional and clinical status of these patients. In both cases, CR programs will have to be re-tailored to the new clinical scenarios.

Advocacy for CR after the COVID-19 acute phase

The mission (*i.e.* “sum of activities required to influence favorably the underlying cause of the disease, as well as the best possible physical, mental and social conditions, so that they may by their own efforts, preserve or resume when lost, as normal a place as possible in the society”) [75] **and core components** (*i.e.* baseline patient assessment, nutritional counselling, risk factor modification, psychosocial interventions, physical activity counselling and exercise training) **of CR** are coherent with care needs of several patients surviving from the acute phase of COVID-19 [5]. Moreover, CR (both in the residential and outpatient setting) holds specific background and instruments to meet several COVID-related situations (*e.g.* attitude to perform risk stratification, disability mitigation, and comorbidity management after devastating acute events; multi-comprehensive patients care; optimal bridge from hospital wards to tertiary care; availability of programs remotely delivered and/or provided by digital health tools or telemedicine, to be adapted to restrictive measures and social distancing).

For these reasons, **we strongly recommend health authorities, policy makers, and institutional managements to consider the potential role of CR in the pathway of COVID-19 patients**, by identifying appropriate referral and delivery processes. To assist CR staff in the design, evaluation and development of their care delivery organization, the AICPR proposal is to integrate previous official document on standards and outcome measures [76] with the following items related to COVID-19 (Table 5).

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