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CLINICAL GUIDELINES AND PRACTICE RECOMMENDATIONS

Recommendations for Cardiovascular Prevention During the Sars-Cov-2 Pandemic: An Executive Document by the Board of the Italian Society of Cardiovascular Prevention

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Abstract
In 2020, the Sars-Cov-2 pandemic is causing a huge and dramatic impact on healthcare systems worldwide. During this emergency, fragile patients suffering from other comorbidities, especially patients susceptible to or affected by cardiovascular disease, are the ones most exposed to the poorer outcomes. Therefore, it is still mandatory to continue to strictly adhere to the rules of cardiovascular prevention. This document aims to provide all doctors with simple and clear recommendations in order to spread useful messages to the widest number of subjects in order to continue the battle against cardiovascular diseases even in times of pandemic.

Keyword Covid-19 · Sars-Cov-2 · Cardiovascular risk · Cardiovascular prevention

For the first time since the Second World War, the entire planet is facing an event, the Sars-Cov-2 pandemic, which is undermining our lifestyle and perception of health, as we are used to perceive them. The latest data show that over fifteen million people worldwide are affected by Covid-19 and about 600,000 have died from it [1]. In addition, the burden of morbidity and mortality indirectly dependent on this pandemic is still not estimable, just as the consequent socio-economic damage. Those who have undergone quarantine measures, have already experienced significant changes in daily life and in the management of their health issues, even in the fortunate case of not having contracted the Sars-Cov-2. On the one hand, the fear of contracting the infection as consequence of a simple access or admission to hospitals has led to a reduction in the request for medical treatment by patients, with heavy and in some cases fatal consequences. For instance, efforts to reduce social contact and community concerns regarding potential transmission have led to reduction in emergency department presentations for acute coronary syndromes including ST elevation myocardial infarction by more than 50% [2, 3]. On the other hand, due to the emergency, all health resources from the general practitioners' offices to hospitals, to intensive care units, have been almost completely involved and devolved in

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the management of Covid-19 patients. Hospitals have been hurriedly transformed creating specific wards and units and outpatients' clinics have been shut down for months. Beside this, there are other more impalpable consequences of the Covid-19 pandemic that might changing our lifestyle in a potentially fearsome way, especially for the most fragile population groups. In fact, it should be remembered that elderly people and patients with existing comorbidities, and especially those of the cardiovascular (CV) system such as hypertension or diabetes, got sick more often for Covid-19 and presented a very high risk of intubation and death [4–7]. These patients have been primary asked to stay at home and avoiding human contacts including those with relatives and doctors. These measures have obviously restricted health controls especially for those with chronic diseases and with physical restrictions.

Therefore, primary and secondary CV prevention efforts should not be forgotten at this time, since having direct implications for reducing the burden of current and eventual future viral outbreaks and not only to improve CV health [8–10]. For patients with established atherosclerotic CV disease (CVD), limitations in the access to the healthcare system resources has potential implications to receive secondary prevention strategies. This is important given that patients with coronary heart disease have between 20–35% absolute risk over 5 years of experiencing a new heart attack, stroke or cardiovascular death with the greatest risk occurring during the first year following hospitalization for acute coronary syndrome [11]. Therefore, it is essential not to neglect the management of chronic diseases during the pandemic. To do this it is not possible to simply recall the routine recommendations adopted before the pandemic (i.e. recommending to a hypertensive patient to go to the pharmacy for measuring blood pressure), but it is necessary to integrate the limitations imposed de facto by the spread of the coronavirus in the management of patients with chronic diseases with alternative measures, for instance an implemented use of telemedicine which can represent a valid alternative approach for several conditions [12].

In this regard, there are global recommendations of general behavior rules aimed at limiting the spread of the virus, that we wish to reinforce and summarize here again in view of their importance and of potential new waves of the disease [13]:

- *Recommendation 1* To stay at home as much as possible. In terms of primary prevention, one approach may be to recommend additional isolation measures and social distancing for those with pre-existing CVD, similar to 'high-risk' cohort such as immunosuppressed patients [7].
- *Recommendation 2* If one experiences flu-like symptoms (fever, cough) or difficulty in breathing, family doctor needs to be contacted immediately or in more serious cases refer to the emergency numbers is a life-saving practice [13].
- *Recommendation 3* To keep the safety distance with others, which must be at least one meter. Avoid shaking hands or embrace people who are not cohabitants and wash hands often and carefully [13].
- *Recommendation 4* If one is forced to leave home, wearing disposable gloves, which, on returning home, must be placed in a closed envelope and thrown away is a protection practice. If one has a mask, the recommendation is to wear it well covering nose and mouth. The wearable surgical mask prevents the spreading of droplets on the air [13].
- *Recommendation 5* If one coughs or sneezes, a tissue should always put in front of mouth and nose and then must be thrown it in the toilet or in a sealed envelope [13].

Beside these general recommendation, and although the attention is focused on addressing the acute situation created by the Covid-19 illness, it is imperative to continue our efforts to prevent CV morbidity and mortality, particularly during a period of prolonged social isolation which may limit physical activity and adversely affect mental health and psychological attitude. Indeed, the quarantine period allowed us to identify future battle fields for the management of people affected by chronic diseases, that we could list in:

- underestimation of CV symptoms by the patients,
- limitation of the chance to access to the visit in presence with the doctor and to drug refill,
- limitation of the chance to practice physical activity,
- limitation of access to healthy dietary advice and food.

As for the first point,

- *Recommendation 6* Patients with established CVD are at the greatest risk of future CV events. In case of chest pain, dyspnea, syncope or tachycardia seeking emergency medical attention remains of vital importance.
- *Recommendation 7* Measure CV risk factors at home and stick to current treatment regimens. Promptly contacting your doctor, even remotely, for any modification of therapy.

As for the second point, many considerations are necessary. One indirect consequence of the continuing diversion of clinical resources required by the acute management of Covid-19, as mentioned above, is represented by a considerable reduction of routine CVD risk screening and delays in

follow-up appointments [14]. On the one hand, the loss of free access to doctors is worrying, but on the other the current technological evolution allows us to be able to integrate clinical practice with telemedicine and with home control of risk factors [10]. Through the implementation of these two approaches, in fact, a constant medical relationship with patients can and should be preserved, in order to detect CV risk factors early, manage them carefully, avoiding medical inertia by doctor as well as poor adherence by patients [15, 16]. In fact, the control of chronic comorbidities is fundamental both to reduce the direct consequences of the virus as well as to avoid its indirect consequences given by the onset of CV pathologies, up to the most extreme consequences. The practical consequences of treatment inertia have been studied in registry studies. Data from The Health Improvement Network (a UK primary-care database) followed 88,756 adults with hypertension over a median follow-up of 37 months after initial assessment [17]. During the follow-up period, 9985 (11%) participants had an acute CVD event or died. Retrospective analysis showed that for systolic blood pressure intervention thresholds, delays more than 1.4 months until medication intensification were associated with adverse outcomes (HR: 1.12, 95% CI 1.05–1.20; $P < 0.009$). Similarly, delays more than 2.7 months in subsequent follow-up appointments were also associated with adverse outcomes (HR 1.18, 95% CI 1.11–1.25; $P < 0.001$). In the recent NICE hypertension guideline, immediate initiation of antihypertensive medication was cost-effective compared with a one-year delay for reducing CVD events in most individuals with stage 1 hypertension [18]. For this reason, we recommend the purchase of validated devices for home pressure monitoring, as well as the dissemination by doctors, through the most adequate communication channels, of the indications on how to measure blood pressure and what targets are to be reached, but also how to recognize concerning symptoms and monitor vital sings at home. Moreover, with a view to a general decrease in access to treatment, it has also been proposed to undertake anti-hypertensive therapy with drugs that require fewer laboratory checks and potential side effects such as calcium channel blockers and angiotensin receptors blocker/angiotensin converting enzyme inhibitors. Patients should also be instructed how to maintain adequate supplies of their chronic medication during this pandemic i.e. through email or home-delivery [19, 20]

At this time, telehealth can be particularly useful in CV medicine which heavily relies on clinical history and can make care more accessible and affordable potentially reducing disparities in access to care for rural, regional and remote areas [10], and for vulnerable populations (people with disabilities).

- *Recommendation 8* Refer to reliable scientific sources to evaluate the impact of chronic therapies during the pandemic.

  It is very important not only to adhere to chronic therapies which are of key importance in the prevention of CV disease such as anti-hypertensive therapies, lipid lowering and antidiabetic drugs, but also to avoid quitting a therapy on the basis of unproven information or even on scientific reports of questionable value. Probably, never in the history of Medicine so many uncontrolled information claiming that a certain drug was harmful or protective towards the virus or the course of the disease were delivered to the physician community or even directly to the public. This is for instance the case of the renin-angiotensin blockers e.g. angiotensin receptors blocker/angiotensin converting enzyme inhibitors, which were initially thought to expose more to the contagion or to worsen the course of the disease, then were thought to be protective, and finally, as shown in many articles, considered substantially neutral in Covid-19. As in all fields of science, these conclusions must always be supported by scientific proofs and patients should be encouraged to continue therapy which provide certain benefits vs uncertain and debatable harm [21–23].
- *Recommendation 9* Do about 150 min of moderate physical activity per week or 75 min of intense physical activity per week since physical activity strengthens the immune system and performs an anti-inflammatory and anti-stress action [8].

  The measures undertaken to limit the spread of coronavirus have also substantially changed habits regarding physical activity. In fact, for a long period the sport centers have been locked-down and even the reopening presents significant limitations that do not allow a turnaround comparable to the past. Moreover, sport centers remain a place perceived as potentially dangerous. Furthermore, the decrease in working trips and commuting, in favor of the smart working regimes, has favored sedentary lifestyle. A study in the USA has shown that physical activity, measured objectively by Fitbit trackers, has fallen by 39% in the month of March since social distancing measures were implemented [24]. This is of great concern, as physical activity has well-established benefits for primary and secondary prevention of CVD [25, 26]. Indeed, a sedentary life leads to an increase in oxidative stress with apoptotic cell death of endothelial cells, reduction of nitric oxide levels, increase in vascular inflammation, promotion of vasoconstriction and LDL cholesterol oxidation [27]. Oxidative stress is mutually linked to inflammation, often associated with an increased risk of endothelial dysfunction [28]. For this reason, the maintenance of a healthy lifestyle must be encouraged, favoring activities that can be practiced

outdoors or at home, like treadmill or stationary cycling also through distance coaching, which has now become a viable alternative for many sports centers. Moreover, the use of wearable devices, such as activity trackers and smart watches, should be encouraged since it has demonstrated potential advantages for patients to monitor behaviors such as physical activity and heart rate [10].

- *Recommendation 10* Stick to a healthy diet by checking its calories. The Mediterranean Diet proves to be fundamental, since different foods (vegetables, fruit, extra-virgin olive oil) are rich in vitamins and polyphenols, antioxidant substances that determine a lower inflammatory state and a strengthening of our immune system and CV health [29].

  During the lockdown period the opportunities for the supply of necessities were reduced to a minimum. This indication has favored the consumption of preserved material, often rich in salt, added sugars and saturated fat, or pre-cooked meal instead of a diet rich in fresh food, promoting the development of CV and metabolic diseases. Therefore, it is recommended to stick as much as possible to a Mediterranean style diet, replacing the fresh components with the frozen ones if necessary and preferring the vegetable protein such as legumes over the preserved animal ones. indeed, a habitual legume intake confers a decreased risk of hypertension, type 2 diabetes, and hypercholesterolemia. Diets rich in fruits and vegetables have several positive effects: known health benefit of high flavonol intake, potential increase in nitric oxide species, concomitant weight loss, reduction of blood pressure, and reduction of inflammatory markers [30].
- *Recommendation 11* Quit smoking, which is a risk factor for CVD and worse outcome related to Covid-19. Never restart smoking because of lockdown frustration.

One more crucial issue in disease prevention in Covid-19-time, is smoking. Smoking presents a significant risk for patient during the Covid-19 pandemic. Indeed, smoking not only promotes a greater risk of future CV events, but also increases the risk of infection via hand-to-mouth contact, provides a potential adhesion site for the Sars-Cov-2 virus through upregulation of angiotensin-converting enzyme-2 receptors and associates with more severe pulmonary complications [10].

In summary, even though we are currently still facing a viral pandemic, the burden of chronic disease non-communicable diseases still put human civilization in great danger as CVD are the leading cause of morbidity and mortality worldwide [31]. Moreover, since it is now clearly documented that mortality from Covid-19 is higher in patients with established CVD or CV risk factors, primary and secondary CV prevention is a crucial tool to reduce the burden of Covid-19 related consequences on health. Even though it is uncertain whether the greater impact of chronic disease states on outcome with Covid-19 is unique to this pathogen or a more generalized susceptibility to illness, a healthier population may be more resilient to future unplanned global threats.

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