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Prehabilitation and heart failure: main outcomes in the COVID-19 era

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Abstract. – OBJECTIVE: The advent of the SARS-CoV-2 pandemic has resulted in an increase in sedentary behavior, with consequences on cardiopulmonary capacity, especially in the elderly population. Prehabilitation is a strategy usually used before a surgical procedure to improve functional capacity; however, it can be used for non-surgical patients and not in the acute phase of disease. The purpose of this study is to evaluate the effectiveness of a prehabilitation program, using telerehabilitation, in frail elderly patients with chronic heart failure.

PATIENTS AND METHODS: This is a randomized, controlled, single-blind study. Fifteen patients with chronic heart failure were randomized into three groups: two active groups (telerehabilitation and in-person) and the control group. Patients in the active groups underwent a rehabilitation program divided into two 4-week periods, for 45-60 minutes per day, 2 days per week.

RESULTS: In the Study Group, the quality of life significantly improved (EQoL-5D), and between the two groups a statistically significant difference in the motor dimension of SF-36 was identified.

CONCLUSIONS: The telerehabilitation prehabilitation program for patients with chronic heart failure was confirmed to be effective and not inferior to a prehabilitation program performed in-person, avoiding the worsening of some domains of quality of life and motor performance, and leading to the improvement of others.

Key Words:
Prehabilitation, Heart failure, Personalized medicine, Aging, Quality of life.

Introduction

Heart failure (HF) is a syndrome of cardiac dysfunction, characterized by the inability of the heart to meet its normal demands at normal filling pressures[1]. Indeed, the heart muscle may weaken and generate less contractile force, leading to a reduction in ventricular ejection volume and cardiac output and an increase in intracardiac pressure, which can occur both at rest and during exercise.

Chronic HF is characterized by a gradual development of long-term symptoms. These include dyspnea when supine or during exercise, fatigue and weakness, lower extremity edema, rapid or irregular heartbeat, persistent cough and shortness of breath, elevated jugular venous pressure, and pulmonary crackles, among others. HF is commonly encountered in elderly patients, with an incidence of 1% above age 65 and 4% after 85 years old. The prevalence of HF is 10-20% in the population aged 70-80 years. In persons over 65 years old heart failure is the leading cause of hospitalization, as well as incidence of polypharmacy associated to those patients[2]. Physical activity is directly associated with a lower risk of adverse cardiovascular outcomes as HF. It is highly recommended in patients with stable HF, and recent literature demonstrated that appropriate exercise programs are able to positively affect cardiovascular outcome[3,4].

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The terms "prehabilitation", or "pre-rehabilitation", refer to an education strategy to increase functional abilities before a surgical procedure[5,6], in order to improve postoperative outcomes. Prehabilitation is a multidisciplinary approach that aims to improve the psychophysical abilities of individuals and enhance functional recovery. It is compliant with the concept of reserve, cognitive or motor, and it has an impact on the rehabilitation outcome as reported in recent investigations[7-12]. The term "reserve" indicates that the number of experiences and/or of physical activities done by an individual in his/her pre-morbid life plays a key role in a sudden change of individual lifestyle. On this basis, we can hypothesize that an increase in functional ability before a surgical intervention could ameliorate post-surgery condition and outcomes.

Some authors[13] suggest the possibility of applying a multimodal pre-rehabilitation model even to patients who are not planning surgery and who are not in the acute phase of the disease. Our previous work[14] has shown how a prehabilitation program, in patients with HF, significantly improved both functional and quality of life indexes.

With the advent of the SARS-CoV-2 pandemic, there has been an increase in sedentary behavior resulting from the attitude of "social distancing", which has translated into decreased cardiopulmonary physical activities. This is likely to result in increased morbidity and mortality, especially in older adults or in patients with chronic conditions[15,16].

To counteract this, home-based prehabilitation programs have been developed[16,17]. It is possible to guide the patient's rehabilitation pathway at home by using different types of communication technologies (video, simulcasting chat, etc.). Telerehabilitation can be performed in synchronous, asynchronous and mixed modes. Several studies[18-21] have shown that telerehabilitation is effective in improving clinical outcomes in conditions of disability, musculoskeletal disorders, cardiovascular diseases, stroke and depression.

Therefore, the purpose of the study is to evaluate the effectiveness of a prehabilitation program, using telerehabilitation, in frail elderly patients with chronic heart failure.

Patients and Methods

This is a randomized, controlled, single-blind study involving patients diagnosed with chronic HF from the Geriatric Day Hospital of the Fondazione Policlinico Universitario A. Gemelli IRCCS. Patients considered frail according to Fried criteria and showing at least 3 out of the 5 criteria, were included: unintentional weight loss (10 lbs in past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity[22,23].

Inclusion criteria: patients of 65 years of age or older, a diagnosis of clinically stable HF, able to ambulate safely and to sign informed consent. Exclusion criteria: patients with cognitive impairment, spatial or temporal disorientation, a diagnosis of dementia or Alzheimer's disease, Parkinson's disease and/or parkinsonism not pharmacologically compensated, acute osteoarticular disease, unable to walk or with adverse conditions during the study and not able to sign informed consent.

Fifteen patients were included in the study and were casually randomized, in Ratio 1:1, in three different groups: the TeleRehabilitation Group (TR-G), the Presence Group (PR-G) that carried out rehabilitation "in presence" and the Control Group (C-G), which did not carry out any kind of rehabilitation program. The exercise-based rehabilitation was organized in patients' groups to allow a better allocation of economic resources and it resulted to be as effective as individual physiotherapy after orthopedic surgery, as recently documented[24].

PR-G and TR-G patients underwent a prehabilitation program divided into two a 4-weeks period, interspersed with a further 4 weeks of pause. In each treatment period, patients performed rehabilitation for 45-60 minutes per day, 2 days a week (Figure 1).

All patients underwent the following evaluations: Six Minutes Walking Test (6MWT)[25], Chair Sit to Stand Test[26], and Handgrip Strength test[27], to assess gait speed, fall risk, and muscle strength. To investigate patients' perceptions of their disease, how they live with it, and whether

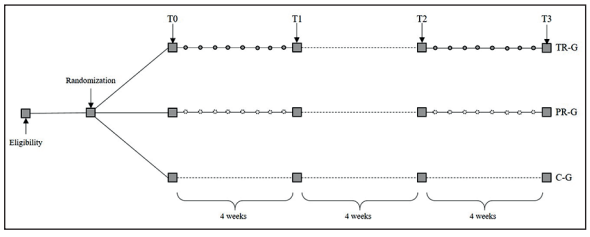

Figure 1. Study design.

it affects nutrition, all patients were assessed with New York Heart Association Index (NYHA)[28], Short Form-12 (SF12)[29], Mini Nutritional Assessment (MNA)[30], Activities of Daily Living Scale (ADL)[31], Instrumental Activities of Daily Living Scale (IADL)[32], and European Quality of Life (EQ-5D)[33,34]. The presence of psychological disorders, such as anxiety and/or depression was also investigated. Finally, the patients underwent echocardiogram[26].

At the end of the evaluation, a brochure containing nutritional advice was given to the TR-G patients.

Procedures

Synchronous and asynchronous remote mode was used for TR-G. The synchronous mode was performed using an internet-based video conferencing platform. A trained physical therapists guided the patients to correctly perform the exercises, through a two-way audiovisual communication, which allowed interaction between the physical therapist and the participants. Physical therapists were able to correct patients and provide feedbacks in real time.

The asynchronous mode, on the other hand, consisted in sending audio-video material containing the explained exercises to be performed at home by patients every two weeks. In this case, caregivers were asked to observe and to monitor the progress of the activities of the participants.

For both groups, TR-G and PR-G, the same exercises were administered. Taking into account the characteristics of the patients, the level of the exercises was gradually increased, without requiring excessive effort, in order to maintain an optimal level of participation and to make the proposed activities stimulating.

Moreover, both groups underwent breathing exercises, exercises with aids (e.g., elastics, sticks, tennis balls, hoops), free body exercises and walking exercises. The planned exercises aimed to teach the correct breathing pattern during stress situations and daily life activities, to improve aerobic and functional capacity, to increase resistance to fatigue, to strengthen the abdominal muscles and limbs, to improve motor coordination and to stimulate and maintain high sustained attention during the performance of exercises.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA)

Due to the small sample size, the statistical analyses were carried out using nonparametric tests. The evolution of the condition of individuals has been analyzed through dependent sample tests (Wilcoxon test), separately for the two groups.

In order to study the differences between the two treatments, the relative variation for each measure of outcome, between the two evaluation times, has been calculated using the following formula:

$$\frac{\{X(T_1) + X(T_0)\}}{\{X(T_0)\}}$$

where "X" is the considered measure of outcome.

So, the difference between the two groups was assessed by testing for independent samples (Mann-Whitney test). The statistical significance was set as $p < 0.05$. The results were given as median values.

15 patients, 7 males and 8 females, with a mean age of 82 years (range 68-98 years) were included in the study. In TR-G, there was one dropout at T1 because of the death of the patient.

Baseline characteristics were similar in the three groups (Table I).

Results

15 patients, 7 males and 8 females, with a mean age of 82 years (range 68-98 years) were included in the study. In TR-G, there was one dropout at T1 because of the death of the patient. Baseline characteristics were similar in the three groups and are reported in Table I.

The mean ejection fraction (EF) for the entire sample was 52%: more specifically, RT-G and PR-G had a mean EF of 54%, while C-G had a mean EF of 49%. With regard to NYHA class attribution, the mean for the entire sample was 2.1: specifically, RT-G and PR-G had a mean EF of 2.1, while C-G had a mean EF of 2.4. Statistical analysis showed that C-G had a statistically significant worsening at the SF-12 Mental Component Summary (MCS) between T0 and T3 ($p = 0.04$) (Figure 2).

Similarly, C-G showed a statistically significant worsening on the Hand Grip Test compared to T0 and T3 ($p = 0.04$) (Figure 3). Regarding the 6MWT, both TR-G and PR-G showed a statistically significant improvement at T3, compared to

Table I. Clinical characteristics at baseline (T0).

	Population	TR-G	PR-G	C-G
Gender (M:F)	7:8	3:2	2:3	2:3
Age (years)	81.27 ± 6.61	80.80 ± 3.70	77 ± 8.94	86 ± 2.83
NYHA	2.1	2.1	2.1	2.4
Ejection Fraction	52.4%	54.0%	54.2%	49%
BMI	29.04 ± 8.49	28.94 ± 9.56	30.75 ± 7.09	27.42 ± 10.18
MNA T0	21.81 ± 3.38	20.62 ± 4.02	25.37 ± 1.37	19.9 ± 1.43
C-STS T0	7	8	9	9
PCS T0	38.57 ± 9.45	46.47 ± 10.32	42.38 ± 5.03	30.77 ± 5.99
MCS T0	48.98 ± 11.16	45.22 ± 12.12	55.06 ± 10.22	46.35 ± 11.59
6MWT T0	418 ± 180.69	447.33 ± 199.62	583 ± 121.17	281.60 ± 91.24
Hand GripT0	26.99 ± 14.98	41.32 ± 21.05	28.02 ± 9.05	17.55 ± 8.19
IADL T0	4/8	5/8	5 / 8	3/8
ADL T0	5/6	6/6	6 / 6	3/6
EQ-5D T0	0.33 ± 0.73	0.79 ± 0.24	0.65 ± 0.23	-0.22 ± 0.66
EQ-5D VAS T0	66.25 ± 15.09	81.67 ± 10.40	61.25 ± 14.36	61 ± 13.41

C-G (p = 0.03) (Figure 4). Noteworthy, the data collected on pain perception, through the VAS section of the EQ-5D, show a statistically significant difference between PR-G and TR-G (p = 0.02) (Figure 5).

Discussion

For patients with heart diseases and the prevalence of chronic HF, exercise-based rehabilitation is highly recommended to improve quality of life, increase physical activity and reduce disease-related hospitalizations[35].

Despite these positive effects and the recommendations of international guidelines, participation in this type of rehabilitation treatment remains low. This could be attributable, in addition to advanced age and the presence of comorbidities, to the presence of logistical problems[36]. To attempt this difficulty, the scientific community lately is focusing on the development of home rehabilitation programs, which have been shown to be comparable to programs carried out in-presence, in terms of improving quality of life and involvement in home physical activity[37,38].

Moreover, in addition to the low compliance of patients with chronic HF[39], the advent of pandemic SARS-CoV-2 added new barriers to the participation in rehabilitation programs at dedicated centers, fueled the fear of leaving home[40,41] and made difficult for patients to participate in targeted physical activity programs.

A possible solution to this problem is the use of telerehabilitation protocols: through a personal computer, a tv and using an internet-based video conferencing platform, it is in fact possible to reach the patients at home and follow them in their

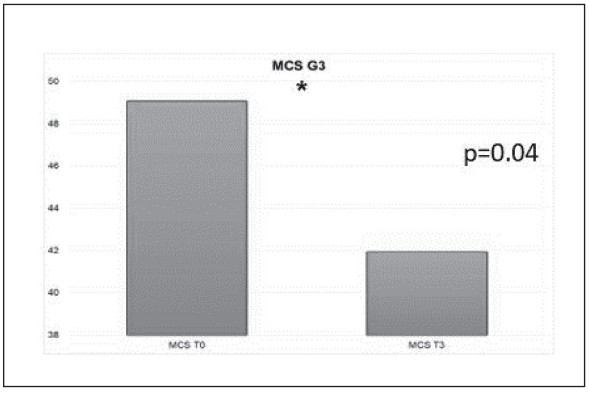

Figure 2. Mental Component Summary (MCS) between T0 and T3 in the Control Group.

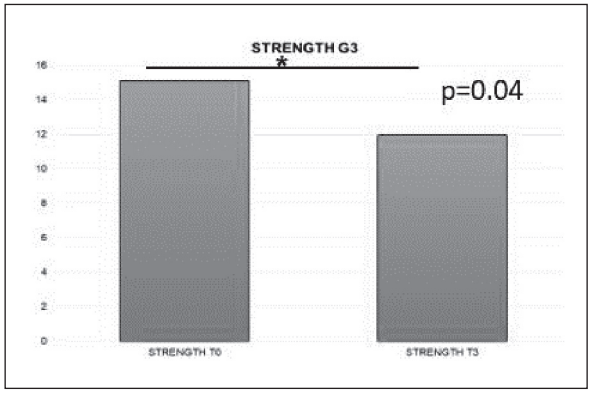

Figure 3. Handgrip strength test between T0 and T3 in the Control Group.

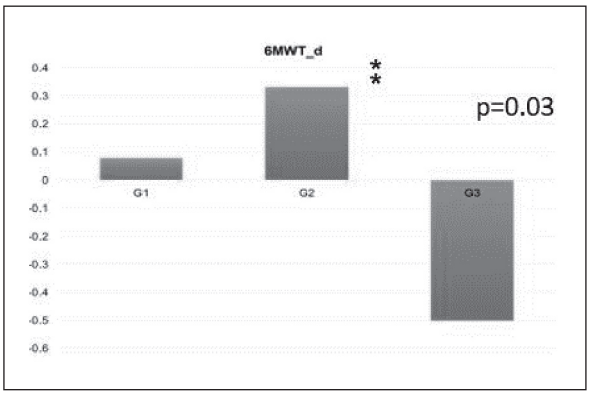

Figure 4. 6MWT at T3 between three groups.

treatment, avoiding the manifestation of a feeling of exclusion and abandonment[42]. Telerehabilitation is as effective as face-to-face rehabilitation approach in ameliorate physical function and balance, autonomy in daily living activities and perceived quality of life in patients with musculoskeletal, neurological, and cardiorespiratory conditions[43-45].

Despite the small sample size, the results that emerge would seem to demonstrate the effectiveness of the application of a multidimensional model of prehabilitation in frail older adults with multimorbidity. Our previous study[14] showed that in a population of patients with HF, a prehabilitation program could bring significant improvements in the quality of life and in balance performances, as measured by the C-STS. The results emerging from this study show that the C-G presented a significant worsening in the MCS of the SF12 and in the Handgrip test. This can be considered a very interesting result: it is then possible to infer that a period of inactivity

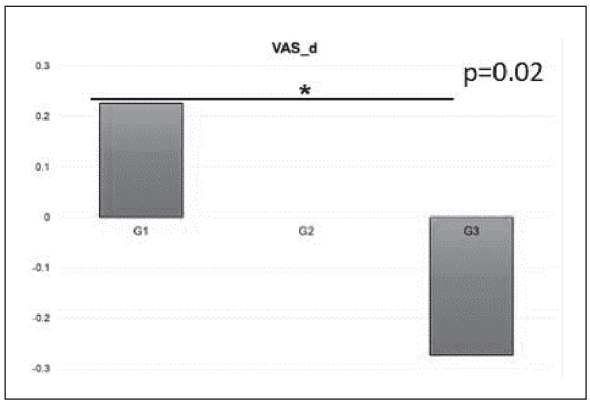

Figure 5. EQ-5D VAS at T3 between three groups.

determines an impoverishment in the mental component of perceived quality of life and a reduction of handgrip strength. Evidence showed that inactivity in the elderly, in addition to being a risk factor for chronic diseases[46], can significantly contribute to the decline in physical and cognitive functions[47,48].

The analysis also showed that patients who underwent rehabilitation treatments in both groups, had an improvement in walking, compared to the group of patients who did not undergo any rehabilitation treatment. In particular, it was found that the patients in the TR-G group improved more than the PR-G. This could be related to the fact that the TR-G patients performed the exercises more frequently, with physiotherapists and alone. There are two randomized studies[49,50] evaluating telerehabilitation in HF patients. The first one showed that an 8-week home-based telerehabilitation program provided improvements in physical capacity and quality of life similar to that of a standard outpatient rehabilitation program[49]. The second one demonstrated that an 8-week home-based telemonitored training program was well accepted, safe, effective and had high adherence among HF patients[50].

The improvement of pain perception in PR-G patients may derive from the presence of physical contact: in fact, touching the patient, the physiotherapist is able to correct his/her posture. Therefore, the patient has the possibility to learn immediately and more easily the corrections and perform exercises without errors.

The non-significance of some assessments, such as the C-STS, the PCS, EQ-5D and the MNA, has not to be considered a negative result. Although there was no improvement in these scales, in fact, there was not even a worsening. In a pandemic situation, which has altered the perception of certain areas and motor performances, even avoiding a picture of worsening can be considered an acceptable result. Above all, in patients with chronic HF, the priority is to keep the parameters as stable as possible over time and to be followed up, avoiding worsening and potential hospitalizations. The same principle can be applied to ADL and IADL outcomes: the proposed prehabilitation program was effective in preventing the decline in daily life activities. In fact, in both TR-G and PR-G patients no worsening at the end of the treatment program was detected.

In a health emergency situation, in which the possibility of leaving home was limited, telerehabilitation proved to be an effective approach in

different conditions[51-54]. This study shows that even in the case of elderly and frail patients telerehabilitation proved to be a very effective tool. In fact, through this modality it was possible to provide guidelines that the patient was able to follow independently and more frequently, even compared to the in-person group. A crucial issue regarding home-based telerehabilitation was to ensure the safety of HF patients who participate. To our knowledge, there were no published data reporting major adverse events or severe complications during telerehabilitation[55], being the benefits of regular physical training superior to the relative risks.

Our study wanted to emphasize the importance of preventive aspects of rehabilitation in frail elderly patients: through a counselling strategy, we wanted to make the patient understand the importance of the prehabilitation treatment, associated with a proper diet, considering the important impact of nutrients in elderly[56,57].

To conclude the analysis of the study, it is necessary to formulate a critical thought about the future of the prehabilitation approach in patients with heart failure. These results should be confirmed by studies performed in a larger sample size, which may demonstrate the validity and effectiveness of the prehabilitation intervention. The results obtained in the tele-rehabilitation group showed that remote prehabilitation is not inferior to an outpatient prehabilitation program.

Therefore, telerehabilitation could be used as a tool to overcome some difficulties, such as low compliance and patients' logistical problems. Telerehabilitation would also allow patients to perform more frequently the exercises. Therefore, it would be desirable to perform the sessions more often than twice a week. The nutrition assessment through the MNA was not statistically significant despite the nutritional counselling and the delivery of a booklet with some advice. Probably, in the future, a specialized nutritional intervention tailored to each patient should be considered, and patients' compliance with the program should be periodically checked.

In addition, with the creation of a multidisciplinary team between physicians and physical therapists, it might be possible to take care of patients through tailored, structured, progressive, multi-domain rehabilitation. In this way, patients might feel more reassured and motivated and, consequently, increase their adherence to the rehabilitation program.

Conclusions

In conclusion, a prehabilitation program through tele-rehabilitation for patients with chronic heart failure was confirmed to be effective and not inferior to a prehabilitation program carried out in person[14], avoiding the worsening of some domains of life quality and motor performances, and leading to the improvement of others.

Furthermore, telerehabilitation has proven to be as useful as face-to-face rehabilitation in keeping the patient active and to be even superior in some domains, such as in improving walking activity, probably for the characteristic of being repeatable by the patient alone. Telerehabilitation could be a form of rehabilitation approach to help patients maintaining an active lifestyle and slow the decline in motor and cognitive function. Telerehabilitation also allows prehabilitation to be transformed into an innovative approach by promoting physical activity in the home environment.

More studies with higher sample size will be needed to better explore the wide possibilities of prehabilitation.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval

This study was conducted in accordance with the International Guidelines for Good Clinical Practice and the Declaration of Helsinki. The institutional ethics committee approved the study protocol on April 21, 2020 (Prot. 0017298/20).

Informed Consent

All subjects gave written informed consent prior to participation.

Availability of Data and Material

Data supporting the results are not available.

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Authors' Contribution

All authors contributed, read, and approved the final version of the manuscript.

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References

1) Albert NM, Boehmer JP, Collins SP, Ezekowitz JA, Givertz MM, Katz SD, Klapholz M, Moser DK, Rogers JG, Starling RC, Stevenson WG, Tang WH, Teerlink JR, Walsh MN. HFSA 2010 Comprehensive Heart Failure Practice Guideline. J Card Fail 2010; 16: e1-194.
2) Onder G, Giovannini S, Sganga F, Manes-Gravina E, Topinkova E, Finne-Soveri H, Garms-Homolová V, Declercq A, van der Roest HG, Jónsson PV, van Hout H, Bernabei R. Interactions between drugs and geriatric syndromes in nursing home and home care: results from Shelter and IBenC projects. Aging Clin Exp Res. 2018; 30: 1015-1021.
3) Leggio M, Fusco A, Loreti C, Limongelli G, Bendini MG, Mazza A, Loreti C, Serafini E, Biscotti L, Bernabei R, Padua L, Giovannini S. Effects of exercise training in heart failure with preserved ejection fraction: an updated systematic literature review. Heart Fail Rev 2019; 25: 703-711.
4) Leggio M, Fusco A, Loreti C, Limongelli G, Bendini MG, Mazza A, Coraci D, Padua L. Effects of exercise training in heart failure with preserved ejection fraction: an updated systematic literature review. Heart Fail Rev 2020; 25: 703-711.
5) Liu Z, Qiu T, Pei L, Zhang Y, Xu L, Cui Y, Liang N, Li S, Chen W, Huang Y. Two-week multimodal prehabilitation program improves perioperative functional capability in patients undergoing thoracoscopic lobectomy for lung cancer: A randomized controlled trial. Anesth Analg 2020; 131: 840-849.
6) Treanor C, Kyaw T, Donnelly M. An international review and meta-analysis of prehabilitation compared to usual care for cancer patients. J Cancer Surviv 2018; 12: 64-73.
7) Castelli L, De Giglio L, Haggiag S, Traini A, De Luca F, Ruggieri S, Prosperini L. Premorbid functional reserve modulates the effect of rehabilitation in multiple sclerosis. Neurol Sci 2020; 5: 1251-1257.
8) Ursin MH, Ihle-Hansen H, Fure B, Tveit A, Bergland A. Effects of premorbid physical activity on stroke severity and post-stroke functioning. J Rehabil Med 2015; 18; 47: 612-617.
9) Padua L, Imbimbo I, Aprile I, Loreti C, Germanotta M, Coraci D, Piccinini G, Pazzaglia C, Santilli C, Cruciani A, Carrozza MC; FDG Robotic Rehabilitation Group. Cognitive reserve as a useful variable to address robotic or conventional upper limb rehabilitation treatment after stroke: a multicentre study of the Fondazione Don Carlo Gnocchi. European J of Neurol 2020; 27: 392-398.
10) Padua L, Imbimbo I, Aprile I, Loreti C, Germanotta M, Coraci D, Piccinini G, Pazzaglia C, Santilli C, Cruciani A, Carrozza MC. The role of cognitive reserve in the choice of upper limb rehabilitation treatment after stroke. Robotic or conventional? A multicenter study of the Don Carlo Gnocchi Foundation. In: Biosystems and Biorobotics 2019; 21: 513-517.
11) Piccinini G, Imbimbo I, Ricciardi D, Coraci D, Santilli C, Lo Monaco MR, Loreti C, Vulpiani MC, Silveri MC, Padua L. The impact of cognitive reserve on the effectiveness of balance rehabilitation in Parkinson's disease. European J Phys Rehab Med 2018; 54: 554-559.
12) Imbimbo I, Coraci D, Santilli C, Loreti C, Piccinini G, Ricciardi D, Castelli L, Fusco A, Bentivoglio AR, Padua L. Parkinson's disease and virtual reality rehabilitation: cognitive reserve influences the walking and balance outcome. Neurol Sci 202; 42: 4615-4621.
13) Bloom E. Prehabilitation evidence and insight review. Macmillan Cancer Support. 2017.
14) Giovannini S, Coraci D, Di Caro F, Castelli L, Loreti C, Chicco A, Fiori M, Bellieni A, Gerardino L, Nigito C, Laudisio A, Brau F, D'Angelo E, Caliandro P, Biscotti L, Padua L, Zuccalà G, Bernabei R. Prehabilitation and heart failure: perspective in primary outcomes, a randomized controlled trial. Eur Rev Med Pharmacol Sci. 2021; 25: 6684-6690.
15) Lorenzi M, Bonassi S, Lorenzi T, Giovannini S, Bernabei R, Onder G. A review of telomere length in sarcopenia and frailty. Biogerontology 2018; 19: 209-221.
16) Sell NM, Julie Silver ÃK, Rando S, Draviam AC, Santa Mina D, Qadan M. Prehabilitation Telemedicine in Neoadjuvant Surgical Oncology Patients During the Novel COVID-19 Coronavirus Pandemic. Ann Surg 2020; 272: e81-e83.
17) Silver JK. Prehabilitation may help mitigate an increase in COVID-19 peripandemic surgical morbidity and mortality. Am J Phys Med Rehabil 2020; 99: 459-463.
18) Mani S, Sharma S, Omar B, Paungmali A, Joseph L. Validity and reliability of Internet-based physiotherapy assessment for musculoskeletal disorders: a systematic review. J Telemed Telecare 2017; 23: 379-391.
19) Piotrowicz E, Baranowski R, Bilinska M, Stepnowska M, Piotrowska M, Wójcik A, Korewicki J, Chojnowska L, Malek LA, Klopotowski M, Piotrowski W, Piotrowicz R. A new model of home-based telemonitored cardiac rehabilitation in pa-

tients with heart failure: effectiveness, quality of life, and adherence. Eur J Heart Fail. 2010; 12: 164-171.

20) Jagos H, David V, Haller M, Kotzian S, Hofmann M, Schlossarek S, Eichholzer K, Winkler M, Frohner M, Reichel M, Mayr W, Rafolt D. A Framework for (Tele-) Monitoring of the Rehabilitation Progress in Stroke Patients: eHealth 2015 Special Issue. Appl Clin Inform 2015; 6: 757-768.

21) Holst A, Nejati S, Björkelund C, Eriksson MC, Hange D, Kivi M, Wikberg C, Petersson EL. Patients' experiences of a computerised self-help program for treating depression - a qualitative study of Internet mediated cognitive behavioural therapy in primary care. Scand J Prim Health Care 2017; 35: 46-53.

22) Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56: M146-156.

23) Op het Veld LP, van Rossum E, Kempen GI, de Vet HC, Hajema K, Beurskens AJ. Fried phenotype of frailty: cross-sectional comparison of three frailty stages on various health domains. BMC Geriatr 2015; 15: 77-88.

24) Aprile I, Rizzo RS, Romanini E, De Santis F, Marsan S, Rinaldi G, Padua L. Group rehabilitation versus individual rehabilitation following knee and hip replacement: a pilot study with randomized, single-blind, cross-over design. Eur J Phys Rehabil Med 2011; 47: 551-559.

25) Enright PL. The six-minute walk test. Respir Care 2003; 48: 783-785.

26) Millor N, Lecumberri P, Gómez M, Martínez-Ramírez A, Izquierdo M. An evaluation of the 30-s chair stand test in older adults: Frailty detection based on kinematic parameters from a single inertial unit. J Neuroeng Rehabil 2013; 10: 86-95.

27) Jakobsen LH, Rask IK, Kondrup J. Validation of handgrip strength and endurance as a measure of physical function and quality of life in healthy subjects and patients. Nutrition 201; 26: 542-550.

28) Spacie R, Duffell JM, Jones M. Heart failure. InnovAiT 2019; 12: 243-251.

29) Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996; 34: 220-233.

30) Guigoz Y, Vellas B, Garry PJ. Assessing the nutritional status of the elderly: The Mini Nutritional Assessment as part of the geriatric evaluation. Nutr Rev 1996; 54: S59-S65.

31) Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. the index of adl: a standardized measure of biological and psychosocial function. JAMA 1963; 185: 914-919.

32) Lawton MP, Brody EM. Assessment of Older People: Self-Maintaining and Instrumental Activities of Daily Living. Gerontologist 1969; 9: 179-186.

33) Balestroni G, Bertolotti G. EuroQol-5D (EQ-5D): An instrument for measuring quality of life. Monaldi Arch Chest Dis 2012; 78: 155-159.

34) Devlin NJ, Brooks R. EQ-5D and the EuroQol Group: Past, Present and Future. Appl Health Econ Health Policy 2017; 15: 127-137.

35) Ambrosetti M, Abreu A, Corrà U, Davos CH, Hansen D, Frederix I, Iliou MC, Pedretti RF, Schmid JP, Vigorito C, Voller H, Wilhelm M, Piepoli MF, Bjarnason-Wehrens B, Berger T, Cohen-Solal A, Cornelissen V, Dendale P, Doehner W, Gaita D, Gevaert AB, Kemps H, Kraenkel N, Laukkanen J, Mendes M, Niebauer J, Simonenko M, Zwisler AO. Secondary prevention through comprehensive cardiovascular rehabilitation: From knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. Eur J Prev Cardiol 2021; 28: 460-495.

36) Ruano-Ravina A, Pena-Gil C, Abu-Assi E, Raposeiras S, van 't Hof A, Meindersma E, Bossano Prescott EI, González-Juanatey JR. Participation and adherence to cardiac rehabilitation programs. A systematic review. Int J Cardiol 2016; 223: 436-443.

37) Anderson L, Sharp GA, Norton RJ, Dalal H, Dean SG, Jolly K, Cowie A, Zawada A, Taylor RS. Home-based versus centre-based cardiac rehabilitation. Cochrane Database Syst Rev 2017; 6: CD007130.

38) Reeves GR, Whellan DJ, O'Connor CM, Duncan P, Eggebeen JD, Morgan TM, Hewston LA, Pastva A, Patel MJ, Kitzman DW. A Novel Rehabilitation Intervention for Older Patients With Acute Decompensated Heart Failure: The REHAB-HF Pilot Study. JACC Heart Fail 2017; 5: 359-366.

39) Piepoli MF, Conraads V, Corrà U, Dickstein K, Francis DP, Jaarsma T, McMurray J, Pieske B, Piotrowicz E, Schmid JP, Anker SD, Solal AC, Filippatos GS, Hoes AW, Gielen S, Giannuzzi P, Ponikowski PP. Exercise training in heart failure: From theory to practice. A consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation. Eur J Heart Fail 2011; 13: 347-357.

40) Kowalski E, Schneider A, Zipfel S, Stengel A, Graf J. SARS-CoV-2 Positive and Isolated at Home: Stress and Coping Depending on Psychological Burden. Front Psychiatry 2021; 12: 748244.

41) Gómez-Corona C, Ramaroson Rakotosamimanana V, Sáenz-Navajas MP, Rodrigues H, Franco-Luesma E, Saldaña E, Valentin D. To fear the unknown: Covid-19 confinement, fear, and food choice. Food Qual Prefer 2021; 92: 104251.

42) Seery T, Wu F, Hendricks E, McDonald J, Laza-Cagigas R, Elliott S, Rampal T. Patients' ex-

periences of virtual prehabilitation during the COVID-19 pandemic. Patient Educ Couns 2022; 105: 488-489.

43) Chan C, Yamabayashi C, Syed N, Kirkham A, Camp PG. Exercise Telemonitoring and Telerehabilitation Compared with Traditional Cardiac and Pulmonary Rehabilitation: A Systematic Review and Meta-Analysis. Physiother Can 2016; 68: 242-251.

44) Laver KE, Adey-Wakeling Z, Crotty M, Lannin NA, George S, Sherrington C. Telerehabilitation services for stroke. Cochrane Database Syst Rev. 2020; 1: CD010255.

45) Wang X, Hunter DJ, Vesentini G, Pozzobon D, Ferreira ML. Technology-assisted rehabilitation following total knee or hip replacement for people with osteoarthritis: a systematic review and meta-analysis. BMC Musculoskelet Disord 2019; 20: 506.

46) Cecchini M, Sassi F, Lauer JA, Lee YY, Guajardo-Barron V, Chisholm D. Tackling of unhealthy diets, physical inactivity, and obesity: health effects and cost-effectiveness. Lancet 2010; 376: 1775-1784.

47) Marshall SC, Berg K. Cessation of exercise in the institutionalized elderly: effects on physical function. Physiother Can 2010; 62: 254-260.

48) Volkers KM, Scherder EJA. Impoverished environment, cognition, aging and dementia. Rev Neurosci 2011; 22: 259-266.

49) Piotrowicz E, Baranowski R, Bilinska M, Stepnowska M, Piotrowska M, Wójcik A, Korewicki J, Chojnowska L, Malek LA, Klopotowski M, Piotrowski W, Piotrowicz R. A new model of home-based telemonitored cardiac rehabilitation in patients with heart failure: effectiveness, quality of life, and adherence. Eur J Heart Fail 2010; 12: 164-171.

50) Piotrowicz E, Zieliński T, Bodalski R, Rywik T, Dobraszkiewicz-Wasilewska B, Sobieszczańska-Małek M, Stepnowska M, Przybylski A, Browarek A, Szumowski Ł, Piotrowski W, Piotrowicz R. Home-based telemonitored Nordic walking training is well accepted, safe, effective and has high adherence among heart failure patients, including those with cardiovascular implantable electronic devices: a randomised controlled study. Eur J Prev Cardiol 2015; 22: 1368-1377.

51) Menici V, Barzacchi V, Filogna S, Beani E, Tinelli F, Cioni G, Sgandurra G. Tele-Rehabilitation for Postural Control by Means of Virtual Reality Rehabilitation System in an Adolescent With Motor Disorder: A Case Study. Front Psychol 2021; 12: 720677.

52) Cacciante L, Cieślik B, Rutkowski S, Rutkowska A, Kacperak K, Kuligowski T, Kiper P. Feasibility, Acceptability and Limitations of Speech and Language Telerehabilitation during COVID-19 Lockdown: A Qualitative Research Study on Clinicians' Perspectives. Healthcare (Basel) 2021; 9: 1503.

53) Dennett A, Harding KE, Reimert J, Morris R, Parente P, Taylor NF. Telerehabilitation's Safety, Feasibility, and Exercise Uptake in Cancer Survivors: Process Evaluation. JMIR Cancer 2021; 7: e33130.

54) Mihai EE, Popescu MN, Beiu C, Gheorghe L, Berteanu M. Tele-Rehabilitation Strategies for a Patient With Post-stroke Spasticity: A Powerful Tool Amid the COVID-19 Pandemic. Cureus 2021; 13: e19201.

55) Piotrowicz E, Stepnowska M, Leszczyńska-Iwanicka K, Piotrowska D, Kowalska M, Tylka J, Piotrowski W, Piotrowicz R. Quality of life in heart failure patients undergoing home-based telerehabilitation versus outpatient rehabilitation--a randomized controlled study. Eur J Cardiovasc Nurs 2015; 14: 256-263.

56) Giovannini S, Onder G, Leeuwenburgh C, Carter C, Marzetti E, Russo A, Capoluongo E, Pahor M, Bernabei R, Landi F. Myeloperoxidase levels and mortality in frail community-living elderly individuals. J Gerontol A Biol Sci Med Sci 2010; 65: 369-76.

57) Giovannini S, Onder G, Lattanzio F, Bustacchini S, Di Stefano G, Moresi R, Russo A, Bernabei R, Landi F. Selenium Concentrations and Mortality Among Community-Dwelling Older Adults: Results from ilSIRENTE Study. J Nutr Heal Aging 2018; 22: 608-612.