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Research Article

Nutraceutical Supplementation Linking Metabolic and Functional Activity as Complementary Treatment During Cardiovascular Rehabilitation: Effects on Functional Capacity and Quality of Life

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Abstract

In post-acute and chronic heart patients, Cardiovascular Rehabilitation is highly recommended, in order to help patients to improve quality of life, and to reduce the chance of future hospitalization.

The constant drive towards identifying the best cardiovascular prevention strategies adapted to modern epidemiology and the needs of referred patients, has led to a growing interest in the use of nutraceuticals in addition to classic cardioprotective therapies.

A clinical, observational, prospective, experience on seven cardiovascular centers belonging to the Italian Alliance for Cardiovascular Rehabilitation and Prevention (ITACARE-P ETS) scientific society was performed.

One-month oral supplementation by a nutraceutical preparation containing Ubiqsome, creatine, ginseng extract, and vitamins (PP, B5, B2, B6, B1 and B12) showed a significant increase in exercise capacity as evaluated by cardiopulmonary test (CPET) walking test, where applicable, or by short physical performance battery (SPPB) in patients with reduced "performance". All functional capacity tests and the quality-of-life assessment scale showed significant improvement at the end of the supplementation cycle.

The encouraging results obtained supported the use of that nutraceutical preparation within CR programs, in addition to traditional multidisciplinary interventions, with the aim of further improving functional capacity and quality of life.

Keywords: cardiovascular diseases, prevention, rehabilitation, nutraceuticals

Introduction

Cardiovascular Rehabilitation (CR) is widely recommended in the post-acute and chronic heart disease care pathway [1]. The main access groups are patients with recent acute coronary syndrome (ACS), percutaneous or surgical myocardial revascularization, heart failure and chronic coronary syndromes [2]. Current guidelines also consider populations with specific issues, for example elderly, frail subjects or those with oncological problems [2]. Overall, CR ensures an improvement in patients' functional capacity, quality of life, lifestyle and above all a reduction in mortality and rehospitalization rates [3,4]. CR programs, managed both in the inpatient or outpatient setting, are based on the essential provision of fundamental core components such as clinical stabilization, structured physical training, nutritional support, and psychosocial intervention by a multidisciplinary team [2].

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The constant drive towards identifying the best cardiovascular prevention strategies and CR programmes, adapted to modern epidemiology and the needs of referred patients, has led to a growing interest in the use of nutraceuticals in addition to classic cardioprotective therapies (i.e. antithrombotic, antiremodelling, antihypertensive, lipid-lowering) [5]. In this context, the CR field is ideally suited to the integrated evaluation of such a combined intervention, especially regarding the overall effect on exercise tolerance (the cornerstone of disability assessment in cardiac patients) and on quality of life. The aim of this experience was to evaluate the efficacy in terms of changes in functional capacity and subjective perception of health status of the additional use of a nutraceutical supplement based on Ubiqsome (highly soluble Q10), creatine, ginseng and vitamins of the PP and B groups in patients undergoing a CR program. This nutraceutical combination was selected due to the positive results already highlighted in previous studies on the condition of asthenia associated with chronic diseases [6-8].

Methods

Clinical Study

The clinical, observational, prospective, multicenter experience was carried out in the period from March, 1, 2025 to May 31, 2025. The network was composed of seven CR centers located throughout the country, all affiliated to the Italian Alliance for Cardiovascular Rehabilitation and Prevention (ITACARE-P ETS) scientific society. The center network was selected on a voluntary basis, provided that they had the usual settings for rehabilitation intervention (inpatient and/or outpatient), accreditation with the national health service, and the structural and performance metrics recommended by the current guidelines [9].

Procedures

Patients eligible for nutraceutical supplementation were selected through individualized clinical judgment, based on the anamnestic and instrumental data available during the rehabilitation process, particularly regarding functional and nutritional capacity.

Changes in global functional capacity and subjective perception of health status were assessed from the beginning to the end of the nutraceutical supplementation period. The choice of the evaluation method for functional capacity was made at the center level, in relation to local practices and the patient's clinical status, considering as possibilities the short physical performance battery (SPPB), the 6-minute walking test (6MWT) and the cardiopulmonary test (CPET), all tests appropriately validated in the context of CR activities [2]. For each of the methods used, the Minimal Clinically Important Differences (MCID) were considered, that is, the minimum variations in the test result judged relevant for the patient in accordance with current literature, i.e. an increase in score of at least 3 for the SPPB [10], an increase of at least 15 metres covered at the 6MWT [11] and an increase in oxygen consumption at peak effort (VO2 at peak) of at least 6% at the CPET [12].

The change in subjective perception of health status was similarly evaluated at the beginning and at the end of the supplementation cycle using the EuroQoL VAS visual analogue scale, considering as MCID an increase in score of at least 10 points [13].

Following the characterization of the selected population for nutraceutical supplementation, a case-control analysis was conducted through retrospective data extraction at one of the seven clinical centers. The control group was limited to consecutive patients who underwent CPET during rehabilitation between 2020 and 2024, matched by age/gender/cardiac condition at referral, and in the absence of nutraceutical supplementation in the clinical records, until the sample size was the same as that of the main prospective observational experience. In these patients, the change in VO2 at peak effort and EuroQoL VAS score between the start and end of the rehabilitation program was assessed.

Supplement

The supplementation strategy was standardized as a one-month (every day for 30 days) oral administration of Eufortyn (Scharper SpA), containing Ubiqsome (coQ10) 80 mg, creatine 148.75 mg, vitamin PP 5 mg, vitamin B5 2 mg, vitamin B2 0.8 mg, vitamin B1 0.6 mg, vitamin B6 0.6 mg, vitamin B12 0.6 µg, ginseng extract 65 mg.

Statistical analysis

Clinical and instrumental variables were analyzed using descriptive statistics. The comparison between means and proportions was performed by means of two-sample t-tests and chi-square tests, respectively, using the open-source software package PSPP 2.0.1 [14].

Results

A total of 102 subjects were considered, 88 of whom were males (86%), with a mean age of 67±9 years and a body mass index (BMI) of 27±4 (presence of obesity characterized by a BMI >30 in 16% of cases). The prevalence of cardiovascular risk factors and comorbidities is summarized in Table 1.

CR intervention in the considered population was activated mainly following coronary events and cardiac surgery (Table 2), with an average distance from the index event of 32 days and a prevalent rehabilitation management in an out-of-hospital setting.

Nutraceutical supplementation was initiated in the majority of cases (n = 76, 75%) after completing the process of cardioprotective therapy optimization. Unsatisfactory adherence to nutraceutical

Table 1: Cardiovascular risk factors and comorbidities in patients undergoing nutraceutical supplementation during cardiac rehabilitation.

		n	%
Risk Factors	Smoking	20	20
	Hypertension	84	82
	Diabetes	38	37
	Dyslipidemia	86	84
	Family history	38	37
Comorbidities	Respiratory	22	22
	Osteoarticular	26	25
	Neurological	12	12
	Hematological	22	22
	LVEF	50±9%	
	LVEF ≤30%	4	4
	GFR <30 ml/min /1.73 sqm	10	10

LVEF: Left Ventricular Ejection Fraction; GFR: Glomerular Filtration Rate.

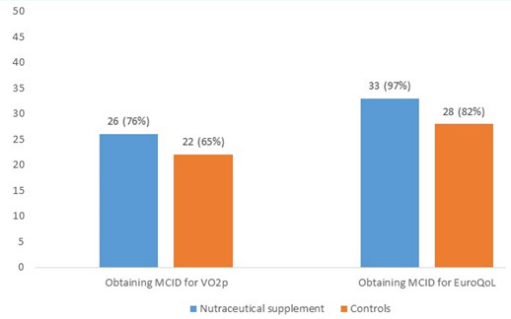

Figure 1: Changes in functional capacity and quality of life parameters between the population subjected to supplementation during cardiac rehabilitation and the Control group.
MCID: Minimal Clinically Important Difference; VO2p: Oxygen Consumption at Peak Effort.

Table 2: Index event for cardiac rehabilitation referral and setting of intervention in the patient population.

Index		n	%
Event type index	Acute coronary syndrome / coronary angioplasty	38	37
	Cardiac surgery on coronary arteries and/or valves/large vessels	40	39
	Chronic coronary syndrome	10	10
	Heart failure	14	14
Distance from index event		32±17 days	
Rehabilitation setting	Residential	24	24
	Day-hospital	36	35
	Outpatient	42	41

Table 3: Changes in functional capacity and subjective perception of health status at the end of the nutraceutical supplementation intervention during cardiac rehabilitation.

Assessment tests (subjects assessed)	Indicator	n (Mean ± S.D.)	%	p
CPET (n= 34, 33%)	VO2p pre (mL/Kg/min)	17.6±2.0		<0.01
	VO2p post (mL/Kg/min)	20.6±3.5		
	Obtaining MCID	26	76	
6MWT (n=102, 100%)	Distance before (m)	376.1±150.6		<0.01
	Distance post (m)	468.7±144.2		
	Obtaining MCID	94	92	
SPPB (n= 66, 65%)	Pre-score	8.5±2.8		<0.01
	Post Score	10.8±1.7		
	Obtaining MCID	36	55	
EuroQoL VAS (n= 102, 100%)	Pre-score	54.3±16.0		<0.01
	Post Score	81.1±10.5		
	Obtaining MCID	96	94	

6MWT: Six Minute Walking Test; CPET: Cardiopulmonary Exercise Testing; MCID: Minimal Clinically Important Difference; SPPB: Short Physical Performance Battery; VO2p: Oxygen Consumption At Peak Effort; EuroQoL VAS: EuroQOL Visual Analogue Scale

supplementation, defined as >3 missed doses per day, was documented in 6 patients (6%). Changes between the start and end of the supplementation intervention, in terms of functional capacity assessed by direct tests and the EuroQoL score, are summarized in Table 3. The walking test was performed in the entire population, while cardiopulmonary testing and SPPB were used in one-third and two-thirds of cases, respectively. All functional capacity tests and the quality of life assessment scale showed significant improvement at the end of the supplementation cycle, with high rates (>90%) of achieving MCIDs, especially for the walking test and the EuroQoL score.The case-control subanalysis based on the monocentric historical group (population characteristics in Table 4) showed a greater increase in functional capacity in the nutraceutical supplementation group (Figure 1), although not statistically significant MCID achieved for VO2 at peak in 76% and 65% of cases respectively, p=0.287) and a significant increase in the perception of health status (MCID achieved for EuroQoL score in 97% and 82% of cases respectively, p<0.05).

No undesirable effects were described during supplementation, so supplementation was well tolerated.

Table 4: Comparison between the supplemented population during cardiac rehabilitation and a retrospective single-center control group matched for age/sex/cardiac condition of referral and in the absence of nutraceutical supplementation (Control) in the clinical documentation.

	Supplementation		Control		
	n	%	n	%	p
Total	34	100	34	100	1
Males	30	88	30	88	1
Females	4	12	4	12	1
Age	65±7		67±6		0.21
Heart failure	20	59	20	59	1
Acute coronary syndrome/coronary angioplasty	6	18	6	18	1
Chronic coronary syndrome	6	18	6	18	1
Cardiac surgery on coronary arteries and/or valves/great vessels	2	6	2	6	1

Discussion

This experience has demonstrated that nutraceutical supplementation with a "pro-energetic" compound may contribute to the short-term improvement of main functional outcomes and subjective perception of health status in cardiac patients enrolled into CR programs.

The specific composition of the product, designed to support and optimize energy metabolism, aims to counteract physical and mental fatigue, particularly evident in patients with heart failure, following cardiac surgery or after acute coronary syndrome [15-17]. In particular, highly soluble coenzyme Q10 has already been shown to improve asthenia and the main functional performance parameters in elderly subjects with asthenia associated with the use of statins [18]; it is also known that creatine is able to contribute to the recovery of muscle strength after physical exercise, both in athletes and in disease states [19,20] and that ginseng extract is able to possess a tonic-adaptogenic action, aimed at improving resistance to physical exercise and stress [21]; finally, the multivitamin complex (PP, B2, B5, B6, B12) allows to guarantee the cofactors necessary for the energy production cycle at mitochondrial level and at the same time to reduce cardiovascular risk [22].

In this experience, the nutraceutical supplementation was primarily considered in "young-old," non-obese subjects, following cardiac surgery or acute coronary syndrome. Nutritional supplementation was initiated approximately one month after the index event, in a predominantly outpatient rehabilitation setting and

with already extensively optimized cardioprotective medical therapy. The majority of enrolled patients did not present with severe left ventricular dysfunction and/or severe renal insufficiency at the start of treatment. These findings therefore appear useful for assessing the average aptitude of rehabilitation cardiologist in directing the supplementation strategy, describing the types of patients for whom it is most considered.

In almost all cases, very high adherence to supplementation was observed (94% of patients showed >90% adherence to the total nutritional intake), demonstrating an almost total absence of disorders or adverse reactions to the supplement.

After one month of treatment, the increase in exercise capacity as evaluated by CPET (where applicable), walking test or, in patients with reduced "performance", by SPPB was significant. These findings can obviously be attributed in the first instance to the neuromuscular and metabolic effects induced by the rehabilitation sessions based on physical exercise [23], however the nutritional supplementation may have positively influenced the results especially in terms of reduction of recovery times and subjective improvement in parameters such as strength and agility. In particular, by analyzing CPET results, we observed an achievement of the MCID in a relatively short time (one month) in a large percentage of patients (about three quarters), a possible expression of improvements in the availability of substrates at cellular and mitochondrial level, optimization of the enzymatic chain for energy production, and reduced membrane and sub-cellular oxidative stress. Many of the fundamental substrates for energy production at the cellular and mitochondrial level can in fact become deficient after a certain age or in certain pathological states of the brain, cardiac muscle or skeletal system [24,25]. Similar functional data have also been recorded by using other assessments tools such as the walking test and the SPPB battery.

Satisfactory results also emerged from the subjective perception of health status assessed using the Euro-QoL 5D, with almost all patients reporting a significant improvement compared to the pre-supplementation period. In this regard, the speculative "case-control" comparison with a historical population of patients with homogeneous baseline characteristics highlighted the advantage of nutritional supplementation over the "standard" management of the rehabilitation program, underscoring (albeit with significant limitations related to the small sample size, the single-center historical control, and the selection bias from CPET) the potential for additional efficacy of nutritional supplementation with regard to quality of life. A favourable trend in achieving the MCID (however lacking statistical significance) was also observed for oxygen consumption at peak exercise measured by CPET, paving the way for future more in-depth evaluations.

In conclusion, nutraceutical supplementation—likely with multicompounds with synergistic action, as in this experience—could be considered within CR programs, in addition to traditional multidisciplinary interventions, with the aim of further improving functional capacity and quality of life. At present, given the heterogeneity of clinical situations affecting CR, this strategy deserves a detailed, personalized evaluation based on a recognition of current needs and reasonably achievable treatment goals.

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References

1. Thomas RJ. Cardiac Rehabilitation - Challenges, Advances, and the Road Ahead. N Engl J Med. 2024; 390(9): 830-41.
2. Ambrosetti M, Abreu A, Corrà U, Davos CH, Hansen D, Frederix I, et al. 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(5): 460-95.
3. Dibben GO, Faulkner J, Oldridge N, Rees K, Thompson DR, Zwisler AD, et al. Exercise-based cardiac rehabilitation for coronary heart disease: a meta-analysis. Eur Heart J. 2023; 44(6): 452-69.
4. Molloy CD, Long L, Mordi IR, Bridges C, Sagar VA, Davies EJ, et al. Exercise-based cardiac rehabilitation for adults with heart failure - 2023 Cochrane systematic review and meta-analysis. Eur J Heart Fail. 2023; 25(12): 2263-73.
5. Fleenor BS, Carlini NA, Martens CR. Nutraceuticals in the Prevention and Therapeutic Treatment of Cardiovascular and Cerebrovascular Disease. J Cardiopulm Rehabil Prev. 2023; 43(3): 162-9.
6. Fumagalli S, Fattirolli F, Guarducci L, Cellai T, Baldasseroni S, Tarantini F, et al. Coenzyme Q10 terclatrate and creatine in chronic heart failure: a randomized, placebo-controlled, double-blind study. Clin Cardiol. 2011; 34(4): 211-7.
7. De Benedetto F, Pastorelli R, Ferrario M, de Blasio F, Marinari S, Brunelli L, et al. Supplementation with Qter. Respir Med. 2018; 142: 86-93.
8. Di Gregorio A, de Blasio F, De Chiara A, Scalfi L, de Blasio F. Utilità della supplementazione con nutraceutici alla riabilitazione respiratoria nei pazienti con Broncopneumopatia Cronica Ostruttiva (italian). Pneumorama. 2019; 97: 57-62.
9. Abreu A, Frederix I, Dendale P, Janssen A, Doherty P, Piepoli MF, et al. Standardization and quality improvement of secondary prevention through cardiovascular rehabilitation programmes in Europe: The avenue towards EAPC accreditation programme: A position statement of the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology (EAPC). Eur J Prev Cardiol. 2021; 28(5): 496-509.
10. Tamura S, Miyata K, Igarashi T, Iizuka T, Otani T, Usuda S. Minimal clinically important difference of the short physical performance battery and comfortable walking speed in old-old adults with acute cardiovascular disease: a multicenter, prospective, observational study. Disabil Rehabil. 2023; 45(6): 1079-86.
11. Khan MS, Anker SD, Friede T, Jankowska EA, Metra M, Piña IL, et al. Minimal Clinically Important Differences in 6-Minute Walk Test in Patients With HFrEF and Iron Deficiency. J Card Fail. 2023; 29(5): 760-70.
12. Swank AM, Horton J, Fleg JL, Fonarow GC, Keteyian S, Goldberg L, et al. Modest increase in peak VO2 is related to better clinical outcomes in chronic heart failure patients: results from heart failure and a controlled trial to investigate outcomes of exercise training. Circ Heart Fail. 2012; 5(5): 579-85.
13. Cheng LJ, Chen LA, Cheng JY, Herdman M, Luo N. Systematic review reveals that EQ-5D minimally important differences vary with treatment type and may decrease with increasing baseline score. J Clin Epidemiol. 2024; 174: 111487.
14. System GO. GNU PSPP program for statistical analysis.
15. Piepoli MF, Guazzi M, Boriani G, Cicoira M, Corrà U, Dalla Libera L, et al. Exercise intolerance in chronic heart failure: mechanisms and therapies. Part I. Eur J Cardiovasc Prev Rehabil. 2010; 17(6): 637-42.
16. Barnason S, Zimmerman L, Nieveen J, Schulz P, Miller C, Hertzog M, et al. Relationships between fatigue and early postoperative recovery outcomes over time in elderly patients undergoing coronary artery bypass graft surgery. Heart Lung. 2008; 37(4): 245-56.

17. Johnston S, Eckhardt AL. Fatigue and acute coronary syndrome: a systematic review of contributing factors. Heart Lung. 2018; 47(3): 192-204.

18. Fogacci F, Giovannini M, Tocci G, Imbalzano E, Borghi C, Cicero AFG. Effect of Coenzyme on Physical Performance in Older Adults with Statin Associated Asthenia: A Double-Blind, Randomized, Placebo-Controlled Clinical TrialQ. J Clin Med. 2024; 13(13).

19. Wax B, Kerksick CM, Jagim AR, Mayo JJ, Lyons BC, Kreider RB. Creatine for Exercise and Sports Performance, with Recovery Considerations for Healthy Populations. Nutrients. 2021; 13(6).

20. Valaei K, Taherkhani S, Arazi H, Suzuki K. Cardiac Oxidative Stress and the Therapeutic Approaches to the Intake of Antioxidant Supplements and Physical Activity. Nutrients. 2021; 13(10).

21. Zhu J, Xu X, Zhang X, Zhuo Y, Chen S, Zhong C, et al. Efficacy of ginseng supplements on disease-related fatigue: A systematic review and meta-analysis. Medicine (Baltimore). 2022; 101(26): e29767.

22. Zhang B, Dong H, Xu Y, Xu D, Sun H, Han L. Associations of dietary folate, vitamin B6 and B12 intake with cardiovascular outcomes in 115664 participants: a large UK population-based cohort. Eur J Clin Nutr. 2023; 77(3): 299-307.

23. Patti A, Merlo L, Ambrosetti M, Sarto P. Exercise-Based Cardiac Rehabilitation Programs in Heart Failure Patients. Heart Fail Clin. 2021; 17(2): 263-71.

24. Kalén A, Appelkvist EL, Dallner G. Age-related changes in the lipid compositions of rat and human tissues. Lipids. 1989; 24(7): 579-84.

25. Marshall RP, Droste JN, Giessing J, Kreider RB. Role of Creatine Supplementation in Conditions Involving Mitochondrial Dysfunction: A Narrative Review. Nutrients. 2022; 14(3).