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## Commentary

**The importance of rehabilitation in the secondary prevention of cardiovascular disease**

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*If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health.*

*Hippocrates*

### *Introduction*

In the secondary prevention of cardiovascular disease (CVD) a wide spectrum of interventions are recommended or should at least be made available to the patient, including coronary revascularisation, prescription of cardioprotective medication, dietary/healthy food intervention, exercise training or rehabilitation, psychosocial support and counselling, and smoking cessation.<sup>1</sup> In the endeavour to prevent the worsening in CVD profile and incidence of new CVD events, structured cardiovascular rehabilitation represents a highly effective measure complementing acute therapy that deserves extra attention. However based on the EUROASPIRE IV database, it is reported that only 51% of the patients are advised to participate in a cardiac rehabilitation programme.<sup>2</sup>

### *Secondary prevention of CVD without rehabilitation: is this effective?*

Cardiovascular rehabilitation should be, next to coronary revascularisation and medication prescription, offered in a multidisciplinary setting, including dietary intervention/healthy food, exercise training, psychosocial support and counselling, and smoking cessation. However, for many parts in Europe (especially in the south and east) it remains difficult to provide such comprehensive treatment, often due to logistic, financial and/or institutional/federal reasons. This situation is unfavourable to patients with CVD as landmark studies have proven that such comprehensive treatment and follow-up, long-term outcome is significantly improved, hereby leading to lower medical consumption, disease burden and health care costs. The latter is of particular importance to governments seeking for cost efficacy in their healthcare systems.

For example, in Germany, 101 patients with stable angina pectoris were randomly assigned to coronary revascularisation with standard medical follow-up (including medication prescription) vs. structured exercise intervention/rehabilitation without coronary revascularisation.<sup>3</sup> Within one year of follow-up patient prognosis (in terms of event-free survival) was significantly better in those patients who participated in the physical activity intervention (88%) vs. those patients who underwent coronary revascularisation without such lifestyle intervention (70%, OR 0.33, 95% CI 0.12 to 0.90,  $p < 0.05$ ), despite the full restoration of coronary blood flow. As a result, to gain one Canadian Cardiovascular Society class, 6,956 dollars was spent in the PCI group versus 3,429 dollars in the exercise training group ( $p < 0.001$ ), thus halving the cost related to CVD prevention by offering an exercise intervention.<sup>3</sup>

The importance of cardiovascular rehabilitation in heart failure (HF) has been notified by another landmark study from Belardinelli and colleagues from Italy.<sup>4</sup> In this study, 123 stable HF patients (with reduced left-ventricular ejection fraction) were randomly assigned to usual care vs. exercise intervention/rehabilitation twice weekly for a total duration of ten years. The results from this study were, next to its impact on physical fitness and quality of life, impressive: patients who followed the exercise intervention had a significant lower rate of hospital readmission (HR: 0.64,  $p<0.001$ ) and cardiac mortality (HR: 0.68,  $p<0.001$ ) vs. usual care, and also prevented the worsening in left-ventricular ejection fraction within this timeframe (a 28% difference between groups was noted,  $p<0.01$ ).<sup>4</sup>

In line with these results, a recent meta-analysis (CROS study)<sup>5</sup> in which data from randomised controlled trials (RCT's) (usual care vs. supervised cardiovascular rehabilitation) since 1995 (start of statin prescription in patients with CVD) were analysed (25 studies,  $n= 219,702$  patients) it became apparent that cardiovascular rehabilitation led to significant reductions in fatal events and hospitalisations in diverse populations of patients with coronary artery disease ( $p<0.05$ ). In addition to these findings, other meta-analyses established that in patients with HF, cardiovascular rehabilitation leads to significant reductions in hospitalisations due to cardiac reasons (46 RCT's, compromising  $>28,000$  patients, relative risk ratio 0.65,  $p=0.001$ ) and a trend towards reductions in mortality (relative risk ratio 0.88,  $p=0.08$ ).<sup>6</sup> This shows that CV rehabilitation is a cost-effective intervention both in patients with coronary artery disease as well as in HF and should be considered within every healthcare system.

An important notice must however be made here. Cardiovascular rehabilitation (including lifestyle modification and exercise activities) is offered for a limited period of time after the index event and often fades out after three or six months. Morbidity and mortality are assessed in clinical trials years later. In contrast, medical therapy is administered and adhered to ideally for years without interruption. Comparing the efficacy between temporary rehabilitation and continued medical therapy is clearly biased by this inequality in duration of treatment application. The reality is that cardiovascular rehabilitation may very often be equally effective to reduce CV events or mortality as compared to medical cardiovascular therapy if adhered to in a continued way.<sup>7</sup> Indeed, when cardiovascular rehabilitation is offered and pursued for years without interruption (which is currently quite rare in clinical practice) its impact is much more impressive as opposed to the effects of cardiovascular drugs.<sup>4</sup> It can be concluded with great confidence that the follow-up of patients with coronary artery disease or HF without the implementation of cardiovascular rehabilitation is missing out essential options to improve health status and to prevent the recurrence of cardiovascular events and/or premature death, even when all recommended cardiovascular drugs would be prescribed and taken. In extent, such

incomplete follow-up in medical care will be associated with a higher economic cost to society and may no longer be considered ethically justified.

*But how much, what type and dose of cardiovascular rehabilitation is appropriate? The importance of proper individualised exercise prescription.*

When prescribing cardiovascular drugs, detailed recommendations based on the individual patient's conditions are followed in terms of dosage, timing and drug-drug/drug-food interactions. And rightfully, suboptimal effects or even side-effects can appear from this therapy when being non-adhered to these recommendations. For exercise prescription, exactly the same individualised approach should be applied: Exercise is medicine. The full impact of cardiovascular rehabilitation depends on the proper selection of training modalities based on clinical conditions, capability and needs of the individual patient (see Figure 1).

In exercise prescription for patients with CVD and HF, the healthcare professional has to decide what type of exercise, intensity, session- and program duration, and frequency should be applied. In recent meta-analyses, changing exercise prescriptions can lead to significant differences in clinical outcomes.<sup>8,9</sup>

So, exercise prescription clearly does matter to the patient's recovery and outcome, and secondary prevention. Are we then currently offering the right exercise intervention, especially in patients with different CVD settings and different risk profiles? This has been examined in a recent European survey in which clinicians were requested to formulate the type, intensity, duration and total volume of exercise for the same five patient cases.<sup>10</sup> This survey revealed a significant and worrisome variance across clinical centres in exercise prescription for patients with different CVDs. There is an obvious need for improved standardization of integrated exercise prescription in CV rehabilitation. For example, the total exercise volume for these five cases ranged from 300 up to 10,000 peak-effort training hours.<sup>10</sup> It is obvious that the clinical impact may be substantially different within this wide range of exercise activity. The European cardiovascular rehabilitation community (as represented by the European Association of Preventive Cardiology: Section for Secondary Prevention and Rehabilitation), on behalf of clinicians involved in cardiovascular rehabilitation, has decided to remediate these difficulties in proper exercise prescription and to improve individualised and standardised application of exercise rehabilitation programs. Together with Hasselt University, a digital training and decision support system named the Exercise Prescription in Everyday Practice and Rehabilitative Training (EXPERT) tool was created.<sup>11</sup> This tool assists the clinician how to prescribe exercise, based on the patient's characteristics, medication intake, CVD's and risk factors and observations during exercise testing (see Figure 1). It is a vivid example how the cardiovascular rehabilitation community turns an observed weakness into a new opportunity and hereby contributes

to better CVD prevention across Europe. A patient who demonstrates to follow proper exercise training programme, can easily adhere to healthy lifestyle and prescribed medication.<sup>1</sup>

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**Figure 1** How to tailor exercise prescription in multidisciplinary cardiovascular rehabilitation

