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Title page

Effect of comprehensive cardiac telerehabilitation on 1-year cardiovascular rehospitalisation rate, medical costs and quality of life: a cost-effectiveness analysis

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Previous presentation of part of the work: preliminary results from the Telerehab III trial were presented at Europrevent 2015 (Lisbon) in the Rapid Fire Abstract Session II - Cardiac Rehabilitation & Exercise Basic & Translational Research. Title: Investigating the effectiveness of an internet-based telerehabilitation program on coronary artery disease and heart failure patients' physical activity level and physical fitness.

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Structured abstract

Background: Notwithstanding the cardiovascular disease (CVD) epidemic, current budgetary constraints do not allow for budget expansion of conventional cardiac rehabilitation (CR) programs. Consequently, there is an increasing need for cost-effectiveness studies of alternative strategies such as telerehabilitation. The present study evaluated the cost-effectiveness of a comprehensive cardiac telerehabilitation program.

Design and methods: This multi-center randomized controlled trial comprised 140 CR patients, randomized (1:1) to a 24-week telerehabilitation program in addition to conventional CR (intervention group) or to conventional CR alone (control group). The incremental cost-effectiveness ratio (ICER) was calculated based on intervention and health care costs (incremental cost), and the differential incremental quality adjusted life years (QALY's) gained.

Results: The total average cost per patient was significantly lower in the intervention group (2156 ± 126 €) than in the control group (2720 ± 276 €) ($p = 0.01$) with an overall incremental cost of -564.40 €. Dividing this incremental cost by the baseline adjusted differential incremental QALY's (0.026 QALY's) yielded an ICER of -21,707 €/QALY. The number of days lost due to cardiovascular rehospitalisations in the intervention group (0.33 ± 0.15) was significantly lower than in the control group (0.79 ± 0.20) ($p = 0.037$).

Conclusions: This paper showed the addition of cardiac telerehabilitation to conventional center-based CR to be more effective and efficient than center-based CR alone. These results are useful for policy

makers charged with deciding how limited health care resources should best be allocated in the era of exploding need.

Abstract word count: 243 words.

Keywords

Telerehabilitation, telemonitoring, telecoaching, cost-effectiveness

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Text

Introduction

According to the European Heart Network's statistics (2012), each year cardiovascular disease (CVD) causes over four million deaths in Europe and over 1.9 million deaths in the European Union, attributing to respectively 47% and 40% of all deaths.¹ Following a cardiac event, secondary prevention by means of cardiac rehabilitation (CR) is a Class IB recommendation by the European Society of Cardiology (ESC).² For heart failure patients, regular aerobic exercise is encouraged to improve functional capacity and symptoms (Class IA recommendation).³ Despite the proven clinical effectiveness of conventional center-based CR programs⁴, long-term benefits are often disappointing, mainly due to low CR uptake and adherence rates.⁵ The escalation of healthcare costs over the past years, however, has restricted the budget for expansion of CR programs and prompted the need for alternative care strategies. Innovations in telecommunication technologies enabled the advent of cardiac telerehabilitation programs, in which patients rehabilitate remotely using telemonitoring, telecoaching and e-learning. Two recent systematic reviews on the feasibility, safety and effectiveness of cardiac telerehabilitation showed non-inferiority and/or superiority of this approach, compared to center-based CR.^{6,7} The majority of reviewed studies however, did not include cost-effectiveness assessment. The Telerehab III trial was a multi-center prospective, randomized, controlled trial investigating the long-term effectiveness of a patient-specific, comprehensive cardiac telerehabilitation program, focusing on telemonitoring and telecoaching. As part of this study, cost-utility analysis based on intervention costs, cardiovascular disease related health care costs and health-related quality of life was performed. We hypothesized the addition of telerehabilitation to standard CR to be cost-effective, when compared to standard CR alone. This paper reports on the results from the cost-utility analysis.

Methods

Study design

The present study was part of Telerehab III; a multi-center, prospective, randomized, controlled clinical trial, investigating the long-term effectiveness of a comprehensive cardiac telerehabilitation program at Jessa Hospital (Hasselt), Ziekenhuis-Oost Limburg (Genk) and St. Franciscus Hospital (Heusden-Zolder) in Belgium. The study was conducted in accordance with the principles stated in the Declaration of Helsinki (reviewed version of 2008), local and national regulations. All patients provided written informed consent prior to study enrollment. The study protocol was approved by Jessa Ethics Committee (reference number: B243201216043). The protocol has been described in detail elsewhere.⁸

Study population and randomization

The sample size calculation; based on a 20 % effect size for the primary outcome measure with a power (1- β) of 95% , an α -error probability of <0.05 and an expected dropout rate of 30%, resulted in 140 patients to be included. Patients were eligible for participation in the study when they entered CR for (i) coronary artery disease (CAD) and treated conservatively, with a percutaneous coronary intervention or with coronary artery bypass grafting; (ii) chronic heart failure (CHF) with reduced EF (NYHA I, II and III) or (iii) CHF with preserved EF (NYHA I, II and III) (as defined in the ESC guidelines). Patients were required to have a computer at home with internet access. The main exclusion criteria were (i) CHF NYHA class IV, (ii) symptomatic and/or exercise induced cardiac arrhythmia within the previous six months, (iii) physical disability related to musculoskeletal or neurological problems and (iv) severe cognitive impairment. Eligible patients were randomly assigned (1:1) to internet-based telerehabilitation in addition to center-based rehabilitation (intervention group) or center-based rehabilitation alone

(control group). A central computerized randomization system, using block randomization, ascertained equal distribution of patients in the different recruiting hospitals for both treatment arms.

Study intervention

Center-based CR program. Both groups participated in the 12-week conventional center-based CR program, including 45 pluridisciplinary rehabilitation sessions with at least two training sessions per week.⁹ Patients were instructed to exercise for 45-60 min per session at a target heart rate and/or workload corresponding to an intensity between their first ventilatory threshold (VT_1) and respiratory compensation point (RCP).¹⁰ Endurance training consisted of walking/running, and/or cycling and arm cranking.

Telerehabilitation program. Intervention group patients received a 24-week internet-based, comprehensive telerehabilitation program in addition to the conventional center-based CR. The telerehabilitation program started at week six of the center-based CR, allowing the intervention group patients to become familiarized with the telerehabilitation's motion sensor (Yorbody accelerometer) and associated webservice during the 6-week overlap period. The program focused on multiple CR core components and used both physical activity telemonitoring and dietary/smoking cessation/physical activity telecoaching strategies. For the telemonitoring part, intervention group patients were prescribed with patient-specific exercise training protocols, based on achieved peak aerobic capacity (VO_2 peak) during initial maximal cardiopulmonary exercise testing (CPET)¹¹ and calculated body mass index (BMI).⁷ Intervention group patients were instructed to continuously wear the accelerometer and to weekly transmit their registered activity data to the telerehabilitation centre's local server. These data enabled a semi-automatic telecoaching system to provide the patients with feedback, encouraging them to gradually achieve predefined exercise training goals. In addition patients received e-mails

and/or SMS's with tailored dietary and smoking cessation recommendations, based on cardiovascular risk factor profiling at study start.

Cardiovascular rehospitalisations

Rehospitalisations were defined as both emergency visits (< 24 hours), hospital admissions (> 24 hours) and day procedures. All rehospitalisations (both cardiovascular and non-cardiovascular) were retrieved from the patients' electronic medical files in the recruiting hospitals by the study investigators. They were cross-checked with those on file in the patients' medical insurance records to ascertain accurateness. A Clinical Endpoint Committee (CEC), composed of three independent cardiologists blinded to treatment allocation, classified all rehospitalisations to (non-) cardiovascular and provided physician reported diagnoses. The time to first cardiovascular rehospitalisation was calculated as were the number of days lost due to cardiovascular rehospitalisations and the proportion of actual to theoretical maximal days alive and out of hospital.

Cost-effectiveness

The cost-effectiveness evaluation was conducted from a society and patient perspective, taking into account both intervention and health care resource costs. As the majority of patients was retired, productivity losses due to illness-related absence from the workplace were not estimated.

Intervention costs were those associated with delivering the center-based CR and telerehabilitation program. The National Sickness and Invalidity Insurance Institution (INAMI/RIZIV)'s (dd. 01/2015) nomenclature-based tariffs were employed to quantify the center-based CR costs (code nr. 771212). Expenditure records were used to determine the equipment and consumable resources for telerehabilitation. Health care costs were the aggregated costs of emergency visits, hospital admissions

and day procedures for cardiovascular reasons (together cardiovascular rehospitalisations) as also specialist visits and associated diagnostics. The cardiovascular rehospitalisations' related costs were derived from invoices retrieved from the recruiting hospitals' financial departments. INAMI/RIZIV's nomenclature-based tariffs defined specialist visits and diagnostics denominations.

Quality adjusted life years (QALY's) were used as generic measure of effectiveness. Estimates of QALY's were derived from the EQ-5D questionnaire¹², which was completed by participants at baseline, at 6 weeks and 24 weeks of follow-up period. The EQ-5D scores were converted to utility scores. The utility estimates were converted to adjusted mean QALY's by calculating the 'area under the curve' (AUC) utility estimates for all time intervals for each patient, weighed by the length of follow-up at that time interval. The change from baseline utility (adjusted differential incremental QALY's) was then calculated, using the multiple regression model to control for baseline utility differences.¹³

The incremental cost-effectiveness ratio (ICER) was calculated [$ICER = \frac{Cost_{intervention\ group} - Cost_{control\ group}}{Effectiveness_{intervention\ group} - Effectiveness_{control\ group}}$] to compare costs and outcomes (effectiveness) across both treatment groups. The incremental cost was determined by the difference in total average cost per patient between the intervention group and control group. The incremental effectiveness was estimated by the adjusted differential incremental QALY's.

Statistical analysis

Data analysis was performed using SPSS v. 22 according to the intention-to-treat principle, by assigned treatment group. The Shapiro-Wilk test was used to assess normality. Independent t-tests and Mann-Whitney U tests compared normally and not normally continuous variables between treatment groups respectively. Chi-square tests compared categorical variables between groups, Fisher's exact tests were used when expected frequencies were small. Cumulative survival curves for the time-to-first

rehospitalisation analyses were made according to the Kaplan-Meier method; the log-rank statistic evaluated the difference between the curves. The Cox regression model was used to estimate the hazard ratio (HR), treatment was the only covariate. Censoring was applied in case of dropout and when the study terminated before the first event of interest occurred. For the proportion of actual versus theoretical maximal days alive and out of hospital; the theoretical maximal days was defined from randomization to one year after study completion. In case of premature dropout, theoretical maximal days were defined up to the censoring date. The significance level for tests was 2-sided α of 0.05.

Results

A total of 140 patients were enrolled in Telerehab III (Figure 1). The numbers and reasons for dropout during study period were similar for both treatment groups; with the exception of one intervention patient (diagnosed with non-cardiac related pathology i.e. lung cancer) that was excluded from final analysis. Baseline demographics, clinical characteristics and cardiovascular medication use were similar between the two groups (Table 1).

Cardiovascular rehospitalisations

The proportional hazards assumption was valid as assessed using the log-log plot and comparing curves for the different strata. One year after study termination, 23 participants were rehospitalized for cardiovascular reasons (7 for intervention group, 16 for control group). The reasons for rehospitalisation were in-stent restenosis (n = 2), atypical thoracic pain (n = 1), ventricular arrhythmia (n = 1), supraventricular arrhythmia (n = 1), pericarditis (n = 1) and peripheral artery disease (n = 1) for the intervention group. In the control group, rehospitalisations were due to in-stent restenosis (n = 1), acute coronary syndrome (n = 2), stable angina (n = 6), atypical thoracic pain (n = 2), ventricular arrhythmia (n

= 1), supraventricular arrhythmia (n = 1), atrial fibrillation ablation (n = 1), CRT-D replacement (n = 1) and peripheral artery disease (n = 1). The average [95% CI] time to first cardiovascular rehospitalisation was 502 [469-535] days for the intervention group and 445 [400-491] days for the control group ($p = 0.045$; HR 0.415 [0.170-1.009]) (Figure 2). The number of days lost due to cardiovascular rehospitalisations in the intervention group (0.33 ± 0.15) was significantly lower than in the control group (0.79 ± 0.20), $U = 2127$, $z = -2.084$, $p = 0.037$, $r = -0.18$ (i.e. small to medium effect). The proportion of actual to theoretical maximal days alive and out of hospital was significantly higher in the intervention group, compared to the control group, $U = 2765$, $z = 2.038$, $p = 0.042$, $r = 0.17$ (i.e. small to medium effect).

Cost-effectiveness

The total average cost per patient (intervention plus health care costs) was significantly lower in the intervention group (2156 ± 126 €) than in the control group (2720 ± 276 €, $U = 3068$, $z = 2.582$, $p = 0.01$, $r = 0.22$ (i.e. small to medium effect) (Table 2). In the intervention group quality of life improved (average $\Delta QALY$ 0.06), in the control group quality of life deteriorated (average $\Delta QALY$ -0.09) during study period. The cost-effectiveness analysis demonstrated that overall, the addition of the telerehabilitation program to center-based CR (intervention group) was both cost-saving and more effective than the center-based CR alone (control group). Dividing the overall incremental average cost per patient (-564.40 €) by the baseline adjusted differential incremental QALY's (0.026 QALY's) yielded an ICER of -21,707 €/QALY. The distribution of the points in the cost-effectiveness scatter plot (Figure 3) further illustrated aforementioned findings.

Discussion

This cost-effectiveness study showed that overall, the addition of the cardiac telerehabilitation program to conventional center-based CR, was more effective and efficient as compared to center-based CR alone. The additional health benefits provided by the telerehabilitation program, reflected in the intervention group's reduced cardiovascular rehospitalisation rate, may have been responsible for the additional quality of life gained over the trial period.

As reported by several recently published clinical trials, including the TIM-HF trial¹⁴, the Telerehab II trial¹⁵, the CHOICE trial¹⁶, the COACH trial¹⁷, the eOCR trial¹⁸, the TeleIntermed trial¹⁹ and the TEMA-HF trial²⁰, cardiac tele-interventions showed favorable results regarding feasibility, safety and effectiveness (such as effect on adherence to physical activity guidelines, VO2 peak). However trials including profound cost-utility assessment are less prevalent. *Kortke et al.*²¹ were one of the first groups to report on cost-effectiveness in a non-randomized controlled trial assessing a transtelephonic guide for ambulatory rehabilitation in cardiac surgery patients. They concluded the total cost of an ambulant telemedicine CR program to be lower compared to conventional in-hospital CR.

It is clear however that, from an economical point of view, current restrictions on health care budgets impose great difficulties for CR centers to expand center-based CR services in order to cope with the increasing CVD epidemic. There is a need for alternative care strategies, exemplified by remote cardiac tele-intervention programs, that prove to be cost-effective. This paper provided promising cost-utility assessment results, but given the contradicting findings with other trial(s), also indicates the necessity for future large clinical randomized controlled trials to further assess the potential cost-effectiveness of cardiac telerehabilitation programs.

Strengths of this study were that data on use of health care services were derived from administrative records, rather than patient self-report, thereby eliminating recall bias. The quality of life data were

collected directly from participants using a tool validated in a cardiac patient population¹¹ similar to the one in this trial. The follow-up period of one year allowed a reasonable time frame to assess cardiovascular rehospitalisation rate. A limitation of this study is that it did not take into account a full societal approach, potentially resulting in an underestimation of productivity gains for those patients still professionally active. However, given the study population was mostly retired, any such underestimation was likely to be minimal. This study compared the addition of a cardiac telerehabilitation program to conventional CR; with conventional center-based CR alone. A comparative study between cardiac telerehabilitation per se and conventional CR would enable a more direct cost-effectiveness analysis of the tele-intervention program. Lastly, the Telerehab III trial was initially designed to assess the effectiveness of the implemented intervention on physical fitness improvement (as defined by improved peak oxygen uptake (VO₂peak) on maximal cardiopulmonary exercise testing (CPET)), rather than cost-utility possibly underestimating current findings.

Conclusion

This paper showed the addition of a cardiac telerehabilitation program to conventional center-based CR to be more effective and efficient than center-based CR alone. At one year follow-up, it resulted in a reduced number of days lost due to cardiovascular rehospitalisations and an increased proportion of actual to theoretical maximal days alive and out of hospital. These results are useful for policy makers charged with deciding how limited health care resources should best be allocated in the era of an ever increasing CVD epidemic.

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Declaration of Conflicting Interests

The author(s) declare(s) that there is no conflict of interest.

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