Individually tailored cardiac rehabilitation - will the dream come true by identifying sex and age-related differences by assessing health-related quality of life at entry?

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Awareness of sex differences in medical diagnosis, treatment, secondary prevention of cardiovascular disease (CVD) and cardiac rehabilitation (CR) has been in focus of the scientific community for more than two decades, (1-4) resulting in a significant improvement in knowledge and therapeutic treatment of CVD in women. (1-4) Nevertheless, a recently published comprehensive review of sex differences in CR (5) still reveals numerous gaps regarding the optimal referral, enrollment, implementation and effectiveness of CR in women. The authors identify numerous gender-specific differences in the administration of core components of CR, that must be taken into account in CR-implementation to meet the particular preferences, expectations and needs of female patients. (5) In this context, the authors highlight, among others, the higher prevalence of psychosocial burden in female patients at CR entry compared to men, which requires special attention and treatment strategy during CR. (5) The authors point out that gender differences in CR and their impact on CR outcomes are still insufficiently studied. (5) Interestingly, sex differences in health-related quality of life (HRQOL) were not included into the discussion in this review. (5) It remains unclear, why the authors did not address this issue in their review.

Very recently, HRQOL outcomes during CR were analyzed for the first time by meta-analysis specifically for women. (6) In this systematic review (6) the authors found 11 studies (n=1,237 women; mean age 61-70 yrs), eligible for inclusion. Only three of these studies were randomized controlled trials (RCT), six prospective observational studies, and two quasi-experimental studies. In six out of these 11 studies, only women were included, and in five studies, the proportion of women was low (16-47%). The authors point out that due to lack of good-quality RCT including sufficient women, data do not allow outcome analysis between sexes. (6) Seven pre/post-studies used 36-item Short Form Health Survey to assess HRQOL and were integrated in to the meta-analysis. One study was excluded from the meta-analyses due to unavailable data, three due to use of a unique HRQOL tool (MacNew Questionnaire; Quality of Life After Acute Myocardial Infarction: Cardiac Quality of Life Index). (6) However, this meta-analysis revealed significant and clinically meaningful improvements in multiple domains of HRQOL within women attending CR. The greatest improvements were observed in the domains Role Physical, Physical Functioning, and Vitality. (6) Importantly, the meta-analysis of two RCT offering additional psychosocial support during CR revealed statistically significant and clinically important pre-post-differences in HRQOL for women in the intervention group compared to control group receiving traditional CR. (6) In addition, in the intervention group several HRQOL domains remained significantly better until 3 months after CR completion, when compared to
control group. Thus, the use of specially tailored CR strategies including psychosocial support
can increase the benefit of a CR in female patients. (6) An important general finding of the
systematic review by Chung et al. (6) is the fact that HRQOL data for women participating in CR
as well as high quality RCTs including sufficient numbers of women, are lacking so far. The
authors (6) emphasize that this lack of data does not allow for a differentiated and in particular
sex-differentiated evaluation. As a consequence, the question of whether women exhibit
different HRQOL than men yet at entry of CR or as a result of participation in CR cannot be
answered by the data available so far.
In this context, the recently published study by Jellestada et al. (7) is an important addition to
the existing literature, allowing for the first time a sex-differentiated analysis of pre and post CR
HRQOL results in a large cohort. Jellestada et al. (7) evaluated HRQOL in a large cohort of
participants at entry and discharge of an in-patient CR program in both sexes (n=8,286; 69.21 ±
11.47; male n=5,581 (67.4%), 67.8 ±11.3 years; women 2,705 (32.6%), 72.2±11.3 years). HRQOL
was assessed using the disease-specific Mac New HRQOL questionnaire (8) and all patient
groups significantly improved in their HRQOL during CR. Since the analyses did not include a
control group, conclusions about causal effects of CR on HRQOL, cannot be drawn from the
results. More interestingly, Jellestada et al. (7) focused on highlighting the age- and sex-specific
effects of inpatient CR on HRQOL and performed multivariable analyses to estimate, sex- and
age-specific changes in HRQOL throughout CR, adjusting for baseline HRQOL and clinical
characteristics. This analysis revealed numerous new and valuable results that might help to
close the gaps of knowledge concerning sex differences in CR outcomes. At CR-entry women
scored significantly lower in social and emotional HRQOL, when compared to men. On the
other hand, women exhibited more pronounced benefit of CR in all HRQOL-subdomains, as
compared to men. (7) Higher age (>75 years) predicts less improvement in social, emotional
and physical HRQOL, in both sexes. Female patients, however, showed greater improvements
in emotional and physical HRQOL, but not in social HRQOL in this subgroup of the elderlies (>75
years). (7) These results are notable since they help to better understand the sex and age-
related difference in CR. They clearly point out the need for a more individually tailored
approach to meet the special needs of elderly and female patients admitted to CR. Their need
for emotional and social support during CR is considerable. In female patients, especially in elderly women, the lack of emotional and social support is known to be an important barrier, not only to CR enrollment and completion but also to the adherence to therapeutic interventions during CR. (5) Furthermore, lack of emotional and social support is negatively linked to depressive mood (5), to adherence to cardiovascular risk factor management (9), CV-prognosis (10) and development of frailty in patients with CVD (11). As a consequence, the need of emotional and social support should be implemented in assessments at the beginning of CR (at least in women), in order to tailor this specific support to the individual needs, i.e. in counseling and/or woman/elderly-only educational or psychosocial support groups. This could decisively influence CR outcomes, thus the further course of the disease and improve the patient’s self-effectiveness. An additional finding of Jellestada et al. (7) is that exercise capacity, measured as 6-minute walking distance (6MWD) at CR entry and its changes throughout CR significantly predicted baseline HRQOL and its improvements across all subdomains. This means that in the total sample and in all subgroups, a longer 6-minute walking distance at the beginning of CR was significantly associated with higher HRQOL score in all domains at CR-entry. In addition, the extent of improvements in 6MWD during CR was significantly correlated with improvements in HRQOL in all domains. This was seen in the total sample as well as in all subgroups and for both sexes. Independent of age, women and men significantly benefited from CR with regard to their 6-minutes walking distance, men more than women. Exercise training is a core component of CR. Its multiple beneficial effects on the symptomology and progression of various cardiac diseases are well documented. (12) Exercise capacity is a powerful predictor of prognosis in women with CVD. Higher exercise capacity (VO$_2$peak ml/kg/min) have been demonstrated to be associated with reduction in cardiac mortality and all-cause mortality. (2,5,12) Numerous studies revealed that women exhibit significantly lower exercise capacity when entering CR as compared to men. (2,5) In addition, women often achieve lower improvements in exercise capacity during CR as compared to men, even participating in exactly the same exercise intervention. (5) It has been discussed whether women need a different approach to exercise training, with respect to program duration, exercise intensity and/or duration in order to achieve similar results. (5) On the other hand,
women are usually integrated into male-dominated programs that often do not meet their expectations and special needs. (2) Women need intense, individualized motivation and instruction to meet their expectations and needs in terms of exercise options, that also meet women’s needs for emotional support, and social interaction. (2)

In summary, the results of Jellestada et al. (7) underscore the use of HRQOL measurements as part of the baseline assessment before patients enter any CR-program in order to identify patients' specific deficits and needs at admission. Thus, enabling more personalized therapeutic interventions to increase the effectiveness of CR. The results demonstrate that CR provider have to pay more attention to the specific strengths and weaknesses of individual patients and patient groups participating in CR, especially with regard to age and gender. It is time to take consequences and translate this knowledge into the CR-praxis.
References


