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Cochrane Corner

Is Exercise-based cardiac rehabilitation for adults with atrial fibrillation effective? A Cochrane Review summary with commentary

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The aim of this commentary is to discuss from a rehabilitation perspective the recently published Cochrane Review "Exercise-based cardiac rehabilitation for adults with atrial fibrillation"[1] by Buckley et al.,[a] published on the Cochrane Library. This Cochrane Corner is produced in agreement with Turkish Journal of Physical Medicine and Rehabilitation by Cochrane Rehabilitation with views* of the review summary authors in the "implications for practice" section.

Atrial fibrillation (AF) is the most common sustained form of arrythmia, which is seen in 2-4% of the general population.[2] Since its incidence increases with age, its incidence is expected to increase in the near future as the population gets older.[3] Atrial fibrillation can cause symptoms of palpitations, shortness of breath, dizziness, fatigue and syncope. It is associated with a higher risk of mortality and morbidities such as stroke, heart failure and other thromboembolic events.[4] Its negative impact on health-related quality of life (HRQoL) has been well-documented, making AF a significant burden for patients. well-documented, making AF a significant burden for patients.[5] It has five subtypes: first-diagnosed AF, paroxysmal AF, persistent AF, long-standing persistent AF and permanent AF.[2]

Exercise based cardiac rehabilitation (ExCR) can be described as a comprehensive intervention that centers around exercise training but also contains interventions for life-style changes, risk assessment and management, health education and psychosocial evaluation and management.[6] It is currently not recommended by major guidelines for patients with AF, but both ESC and ACC/AHA/ACCP/HRS guidelines recommend moderate intensity physical activity and to remain active for secondary prevention in these patients.[2]

Exercise and therefore ExCR can help improving traditional cardiovascular risk factors such as abdominal obesity and high levels of blood lipid levels and in turn, reduce AF burden.[7] It also helps preventing thrombogenesis, by upregulating fibrinolysis, suppressing pro-inflammatory cytokine production and inducing the production of anti-inflammatory mediators and antioxidants.[8]Endothelial function is also positively affected by exercise by the increase in endothelial production of nitric oxide.[9] Lastly, exercise training may enhance autonomic nervous system (ANS) adaptation and potentially improve heart rate variability.[10] Therefore, ExCR has significant physiological basis and may be helpful for patients with AF in decreasing AF symptomatology and burden. Various observational studies and

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* *The views expressed in the summary with commentary are those of the Cochrane Corner author (different than the original Cochrane Review authors) and do not represent the Cochrane Library or Wiley.*

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randomized controlled studies also support this assumption.[11]

Exercise-based cardiac rehabilitation for adults with atrial fibrillation (Buckley et al., 2024)

What is the aim of this Cochrane review?

The aim of this Cochrane Review was to assess the benefits and harms of ExCR in patients with AF.

What was studied in the Cochrane review?

The population addressed in this review was patients with AF. To keep a broad approach, patients with all five subtypes of AF were included in this review. The interventions studied were all ExCR programs, regardless of its scope. Exercise based cardiac rehabilitation was defined in this review as or exercise-based interventions any rehabilitation program in an inpatient, outpatient, community, or home- based setting that included an exercise training component and may also have included a psycho-educational component. No restrictions on the length, intensity, or content of the exercise training program were applied. The intervention was compared to treatment as usual, no intervention or any other rehabilitation program that does not count as ExCR, depending on the design of the study. Studies that used other exercise-based measures for control groups were excluded. The primary outcomes studied were mortality, serious adverse events (SAEs), AF recurrence, AF symptom severity and burden. Secondary outcomes were HRQoL and exercise capacity.

Search methodology and up-to-dateness of the Cochrane review?

The review authors searched for studies that had been published from inception up to 24 March 2024 in Cochrane Central Register of Controlled Trials, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE Daily, and MEDLINE, Embase Classic and Embase, PsycINFO, CINAHL, Web of Science Core Collection, LILACS, clinicaltrials.gov and The World Health Organization International Clinical Trials Registry Platform to identify all relevant randomized controlled trials.

What are the main results of the Cochrane review?

The review included 20 randomized controlled trials with a total of 2,039 patients with AF. All trials were conducted between 2006 and 2024. Most trials were small, single-center studies. None of the trials are exclusively cited within this paper due to reference limitations. Please refer to the original paper for further information.

The review shows that:

- There may be little to no difference in mortality between ExCR versus controls (risk ratio (RR) 1.06, 95% confidence interval (CI) 0.76 to 1.49; I^2= 0%). The evidence for mortality was deemed to be of low certainty.
- ExCR may have little to no effect on SAEs (RR 1.30, 95% CI 0.63 to 2.67; I^2= 0%). Ten trials reported this outcome with four trials reporting zero SAEs. The evidence for SAEs was assessed to be of low certainty.
- ExCR likely reduces AF recurrence (RR 0.70, 95% CI 0.56 to 0.88; I^2= 2%). Four trials reported AF recurrence dichotomously measured with Holter monitors worn for various lengths of time. The evidence for AF recurrence were assessed to be of moderate certainty.
- Low certainty evidence suggests that ExCR may improve AF symptom severity mean difference (MD) −1.59, 95% CI −2.98 to −0.20; I^2= 61%) and reduce AF episode frequency (MD −1.29, 95% CI −2.50 to −0.07; I^2= 75%).
- Moderate certainty evidence shows that ExCR likely reduces AF symptom burden (MD −1.61, 95% CI −2.76 to −0.45; I^2= 0%) and AF episode duration (MD −0.58, 95% CI −1.14 to −0.03; I^2= 0%).
- Eleven trials utilized 36-item short form health survey (SF-36) for evaluation of HRQoL. According to the analyses of SF-36, ExCR likely improves mental component measures of SF-36 but its effect on physical component measures is uncertain.
- Low certainty evidence suggests that ExCR may increase exercise capacity, as measured by six-minute walking test or Vo2 peak levels. This increase can be clinically meaningful in decreasing premature mortality as previously shown in the literature.[12]

How did the authors conclude on the evidence?

The authors concluded that benefits of ExCR seem to be reduction of AF recurrence and burden and the improvement in mental health components of HRQoL. It may also improve AF severity, AF

episode frequency and exercise capacity. The authors also mention that the impact of ExCR on mortality and SAEs is uncertain. The authors state that this is one of the most comprehensive reviews that include RCT evidence, but it may still fail to adequately represent all patient groups, since females, elderly individuals, and those with specific comorbidities are commonly excluded from RCTs. still leave out less represented patient populations such as females, elderly patients and patients with specific co-morbidities, since these populations are usually excluded from the RCTs. Also, they state that included trials were relatively small, had short-term follow-up periods and clinically heterogenous.

What are the implications of the Cochrane evidence for practice in rehabilitation?

This Cochrane review indicates that while the positive effects of ExCR is limited in patients with AF, it may still help in reducing AF related symptom burden and recurrence while improving mental health related quality of life. It also documents that the risk of mortality and SAEs are low when these patients undergo ExCR.

As previously mentioned, regular exercise has significant positive physiological effects for all patients with cardiac diseases. Therefore, implementing regular exercise regimens is crucial for all these patients. The lack of solid evidence still hinders routine referrals to and use of ExCR worldwide. The various difficulties in reaching these centers are also a major limiting factor for patients.[13] Increasing the reach and availability of these centers worldwide would be both helpful for patients and for practitioners who are unable to track down the effects of ExCR.

The majority of the studies' included in this review had regimens that included a form of aerobic exercise but not all of them included strength exercises. The majority of the studies included in this review had regimens that incorporated some form of aerobic exercise; however, not all of them included strength training. Two studies implemented a form of yoga and one implemented QiGong. Therefore, when evaluating the results of this review, it must be kept in mind that the authors kept a very wide range of exercise interventions for increasing inclusion and the results cannot be considered as the outcome of a single type of intervention. This review does not comment on the safest or the most efficient way of ExCR, due to lack of sufficient studies, nor is asking these questions. Therefore, any appropriate exercise program available for the patient should be constructed by a rehabilitation specialist. The scope of all ExCR programs can and must be individualized and tailored according to the needs of the patient in real life settings, so all practitioners should evaluate the patients' needs and conditions and determine accordingly.

Uncontrolled arrythmias are among contraindications for ExCR.[13] However, once diagnosed and uncontrolled atrial fibrillation ceases to be a contraindication for patients with ExCR. However, rehabilitation professionals may be reluctant to include those patients in regular cardiac rehabilitation programs due to the risk of increasing symptoms. Before the initiation of any exercise-based program, it is crucial to determine the current state of AF. Once controlled, patients with AF can safely be referred to such programs. It must be kept in mind that continuous monitoring during ExCR helps keep the patients within a safe zone and determines the appropriate intensity for exercise outside of these programs, so that the patients can continue doing their exercises without supervision after the program ends. This helps the patients overcome their fears regarding regular exercise, preventing further complications of immobilization such as loss of mean muscle mass and may help them to gain beneficial habits. The absence of documented SAEs in these reviews supports the safe inclusion of patients with controlled AF in ExCR programs, encouraging broader implementation in clinical practice. It is still crucial to adjust the programs of the patients accordingly to prevent any unwanted occurrences and they should be closely monitored throughout the program.

As a result, ExCR, regardless of the content of actual exercise, can be a helpful adjunct to all patients with AF. Educational campaigns for healthcare professionals about the benefits of ExCR can increase awareness within the medical community and decrease the reluctance for patient referral. As the reach and the referrals of these patients increase, both researchers and practitioners will have more insight into the effects and SAEs that occur with these interventions. Community-based or home-based programs, with the help of telemedicine, mobile apps and wearable devices can increase the access of cardiac rehabilitation for geographically or economically disadvantaged patients. However, current data regarding the effectiveness and safety of such programs are still scarce.

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