Cochrane for Clinicians

Putting Evidence into Practice

Coenzyme Q10 for Heart Failure

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Clinical Question

Does coenzyme Q10 decrease mortality and hospitalizations in patients with heart failure?

Evidence-Based Answer

In patients with chronic heart failure, supplementation with coenzyme Q10 may reduce all-cause mortality (absolute risk reduction [ARR] = 7.5%; 95% CI, 0.9% to 11.6%; number needed to treat [NNT] = 13; 95% CI, 9 to 111) and heart failure–related hospitalization (ARR = 10.5%; 95% CI, 6.1% to 14.1%; NNT = 10; 95% CI, 7 to 16).[1] (Strength of Recommendation [SOR]: B, based on inconsistent or limited-quality patient-oriented evidence.) Adverse effects are generally mild and may be only slightly increased with coenzyme Q10 supplementation.[1] (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Heart failure is associated with high rates of morbidity and mortality and is classified as systolic (reduced ejection fraction) or diastolic (preserved ejection fraction).[2] The prevalence of any heart failure classification in the United States in 2012 was 2.4% and is expected to be at least 3% by 2030.[3] Serum oxidants are elevated in persons with heart failure, are correlated with severity of disease, and predict mortality.[3] Coenzyme Q10 is a nutritional supplement with antioxidant properties. Low plasma concentrations of coenzyme Q10 have been found to be an independent predictor of mortality in patients with heart failure.[4] The authors of this Cochrane review sought to assess the safety and effectiveness of coenzyme Q10 supplementation, compared with placebo or conventional therapy, in persons with heart failure.[1]

This Cochrane review included 11 randomized controlled trials (RCTs) and 1,573 participants (1,535 adults; 38 children).[1] The follow-up time ranged from one to 26 months. Primary outcomes included all-cause mortality, risk of myocardial infarction and stroke, heart failure–related hospitalization, improvement in left ventricular ejection fraction, and adverse effects. Study participants included patients with any type of chronic heart failure regardless of severity. Acute heart failure was the only exclusion criterion. Significant variation in the dosing of coenzyme Q10 was noted in eight out of 11 included studies (range = 30 to 400 mg per day). Five studies were performed in Asia, two in Europe, one each in Russia, Australia, and the United States, and one study enrolled participants from Europe, Australia, and Asia. Data in this review regarding all-cause mortality, heart failure–related hospitalization, and adverse effects were derived primarily from the latter, a double-blind RCT.

Patients with New York Heart Association class III or IV heart failure who received coenzyme Q10 supplementation, 300 mg per day, had lower all-cause mortality after 26 months (ARR = 7.5%; 95% CI, 0.9% to 11.6%; NNT = 13; 95% CI, 9 to 111). However, this was based on a single double-blind RCT (n = 420 adults). Supplementation with coenzyme Q10 did not significantly decrease the risk of myocardial infarction or stroke.

Heart failure–related hospitalizations were reduced at 19 months in patients with New York Heart Association class III or IV heart failure who were treated with coenzyme Q10, 150 to 300 mg per day (ARR = 10.5%; 95% CI, 6.1% to 14.1%; NNT = 10; 95% CI, 7 to 16; two RCTs; n = 1,061

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CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 449.

adults). It is unclear how duration of treatment affected outcomes.

Common adverse effects of coenzyme Q10 include mild gastrointestinal symptoms, such as nausea, vomiting, and diarrhea. Only two of the 11 studies reported on adverse effects, but neither specified symptoms. In both studies, adverse effects were reported slightly more often in the coenzyme Q10 group vs. placebo or standard therapy; however, pooled analysis did not reveal a statistically significant greater risk.

Limitations of this review include the inconsistent daily dosage of coenzyme Q10 used in the studies. Most studies did not use an intention-to-treat analysis. There is questionable generalization to a U.S. population; most conclusions in this review are based on one RCT that did not enroll U.S. participants.

In 2013, the American College of Cardiology Foundation and the American Heart Association recommended against the use of nutritional supplements (including coenzyme Q10) for the treatment of heart failure.[5] The 2017 update to this practice guideline did not address coenzyme Q10. The approximate cost of a one-month supply of the 200-mg dose of coenzyme Q10 is $10.[6] At this time, there is insufficient evidence to support, or refute, the use of coenzyme Q10 in patients with heart failure.

The practice recommendations in this activity are available at http://www.cochrane.org/CD008684.

Editor's Note: The ARRs, NNTs, and their corresponding CIs reported in this Cochrane for Clinicians were calculated by the author based on raw data provided in the original Cochrane review.

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References

1. Al Saadi T, Assaf Y, Farwati M, et al. Coenzyme Q10 for heart failure. *Cochrane Database Syst Rev.* 2021;(1):CD008684.
2. Savarese G, Lund LH. Global public health burden of heart failure. *Card Fail Rev.* 2017;3(1):7-11.
3. Virani SS, Alonso A, Benjamin EJ, et al.; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics–2020 update: a report from the American Heart Association. *Circulation.* 2020;141(9):e139-e596.
4. Molyneux SL, Florkowski CM, George PM, et al. Coenzyme Q10: an independent predictor of mortality in chronic heart failure. *J Am Coll Cardiol.* 2008;52(18):1435-1441.
5. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation.* 2013;128(16):e240-e327.
6. GoodRx. Coq10. 2021. Accessed September 24, 2021. https://www.goodrx.com/coq10

Basal Cell Carcinoma: Comparison of Surgical and Nonsurgical Interventions

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Clinical Question

Which treatments for basal cell carcinoma (BCC) have the lowest recurrence rates and most favorable cosmetic outcomes?

Evidence-Based Answer

The recurrence rate after surgical management of BCC by standard surgical excision or Mohs micrographic surgery is very low (recurrence at five years = 5.2% vs. 3.2%, respectively; 95% CI, 0.9% to 10.7%). Recurrence after management with imiquimod (Aldara) is also low (recurrence at five years = 17.5%) and may result in more favorable cosmetic outcomes. (Strength of Recommendation [SOR]: B, based on moderate-quality patient-oriented evidence.) Other nonsurgical options may have acceptably low rates of recurrence but also have low certainty of evidence.[1] (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

According to one estimate, about one-half of the 5.4 million nonmelanoma skin cancers diagnosed in 2012 were BCC.[2] Numerous surgical and nonsurgical treatment options exist. This Cochrane review summarizes evidence for 15 treatments of BCC from 52 randomized controlled trials (RCTs) involving 6,690 participants.[1]

Most of the studies (48 of 52) included only low-risk superficial or nodular BCC, as defined by the National Comprehensive Cancer Network.[3] Although not further defined in the review, low-risk lesions were generally smaller, slower growing, and outside of cosmetically challenging areas such as the face or genitals. The review identified four treatments: Mohs micrographic surgery, imiquimod, photodynamic therapy, and radiation. Primary outcomes were recurrence at three to five years after diagnosis and favorable cosmetic result.

For low-risk BCC, radiation resulted in a higher recurrence rate than standard surgical excision at four years (relative risk [RR] = 11.06; 95% CI, 1.44 to 84.77). There were mixed results regarding the benefits of cryotherapy. Compared with patients treated with radiation, those treated with cryotherapy had significantly more recurrences at one year, yet compared with photodynamic therapy, cryotherapy was not shown to result in any statistically significant difference in recurrence rate. The difference between

SUMMARY TABLE

Recurrence Risk and Cosmetic Outcomes of Various Interventions to Treat Basal Cell Carcinoma

Intervention*	Absolute risk of recurrence (95% CI)	NNT or NNH for favorable cosmetic outcome reported by observers (95% CI)†
Mohs micrographic surgery	At 5 years: 3.2 (0.9 to 10.7)	Not reported
Imiquimod 5% (Aldara)	At 5 years: 17.5 (6.4 to 48.1)	NNT = 4 (2 to 8)
Photodynamic therapy	At 3 years: 36.4 (4.9 to 1,302.7)	NNT = 3 (2 to 4)
Radiation	At 4 years: 6.4 (0.8 to 48.7)	NNH = 3 (3 to 4)

NNH = number needed to harm; NNT = number needed to treat.

*—For all reported interventions, comparator group was standard (non-Mohs) surgical excision. †—Favorable cosmetic outcome was defined differently across studies. For imiquimod, favorable cosmetic outcome was defined as 5 or 6 on a 6-point Likert scale. For photodynamic therapy, favorable cosmetic outcome was defined as 3 or 4 on a 4-point scale. For radiation, favorable cosmetic outcome was defined as a score of 3 on a 3-point scale.

five-year recurrence rates after standard surgical excision (5.2%) and Mohs micrographic surgery (3.2%) was not statistically significant based on one small low-quality RCT, indicating similar effectiveness.

Although surgical management of BCC appeared to be most effective at preventing recurrence, conservative measures have reasonably low recurrence rates and may have more favorable cosmetic outcomes. Imiquimod 5% cream applied daily for six weeks (superficial BCC) or 12 weeks (nodular BCC) resulted in more patients achieving favorable observer-rated cosmetic results on a Likert scale compared with standard surgical excision three years after the treatments were administered (number needed to treat [NNT] for one additional patient to achieve good or excellent observer-rated cosmetic result = 4; 95% CI, 2 to 8). Study quality was considered low because the data came from a single study (n = 344), and there was a high risk of bias due to difficulty in blinding and the subjective nature of the cosmetic outcome. Within the same study group, recurrence at five years with imiquimod was 17.5% vs. 2.3% with standard surgical excision (RR for recurrence with imiquimod = 7.73; 95% CI, 2.81 to 21.30; n = 383).

Treatment with photodynamic therapy also yielded favorable cosmetic outcomes. Compared with patients undergoing standard surgical excision, those who had photodynamic therapy with two sessions separated by one week were more likely to have a favorable observer-rated cosmetic outcome (NNT for one additional patient to achieve a good or excellent observer-rated cosmetic result = 3; 95% CI, 2 to 4). Recurrence was only reported at three years and favored standard surgical excision over photodynamic therapy (RR for recurrence with photodynamic therapy = 26.47; 95% CI, 1.63 to 429.92). One RCT (n = 347) demonstrated that radiation therapy was inferior at achieving favorable cosmetic outcomes (rated by observers and participants) compared with surgery.

Limitations of this review include the heterogeneity of treatments and their outcomes. In addition, most of the studies of imiquimod were industry-funded and unblinded. The reported cosmetic outcomes were subjective, and in several of the included studies, observers performed the rating rather than participants, which may be considered a less patient-centered result. Finally, data on race-specific outcomes were not included because most of the studies either did not report or did not define race.

The American Academy of Dermatology recommends surgical excision for low-risk BCC but states that nonsurgical options are reasonable alternatives.[3] The Choosing Wisely Initiative recommends deferring Mohs micrographic surgery referral in patients with uncomplicated, nonmelanoma skin cancer less than 1 cm in size on the trunk or extremities.[4]

The practice recommendations in this activity are available at http://www.cochrane.org/CD003412.

Editor's Note: The NNTs, NNH, and their corresponding CIs reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

References

1. Thomson J, Hogan S, Leonardi-Bee J, et al. Interventions for basal cell carcinoma of the skin. *Cochrane Database Syst Rev*. 2020;(11):CD003412.
2. Rogers HW, Weinstock MA, Feldman SR, et al. Incidence estimate of nonmelanoma skin cancer (keratinocyte carcinomas) in the U.S. population, 2012. *JAMA Dermatol*. 2015;151(10):1081-1086.
3. Kim JYS, Kozlow JH, Mittal B, et al. Guidelines of care for the management of basal cell carcinoma. *J Am Acad Dermatol*. 2018;78(3):540-559.
4. American Academy of Dermatology. Don't treat uncomplicated, nonmelanoma skin cancer less than 1 centimeter in size on the trunk and extremities with Mohs micrographic surgery. Choosing Wisely. Updated June 20, 2019. Accessed January 9, 2021. https://www.choosingwisely.org/clinician-lists/american-academy-dermatology-mohs-micrographic-surgery-uncomplicated-melanoma/ ■