Does altering diet affect progression of prostate cancer? The MEAL study

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Can modifications in dietary intake affect survival in men with prostate cancer? Despite robust data indicating that dietary constituents may be substantially associated with the natural history of prostate cancer, there remains a paucity of Level I evidence on which to base clinical recommendations.¹

Randomized clinical trials of dietary supplements have failed to yield demonstrable benefits. For example, the Selenium and Vitamin E Cancer Prevention Trial (SELECT)—a randomized, placebo-controlled study of more than 34,000 men randomized to once daily vitamin E (400 IU), selenium (200 mcg/day), both, or placebo—showed that neither vitamin E nor selenium had any observable benefit in preventing incident prostate cancer. In fact, the study showed a nonsignificant increased risk of prostate cancer and diabetes for patients taking those amounts of vitamin E (p=0.06) and selenium (p=0.06), respectively.² Other studies have yielded similar results for selenium, vitamin E, and vitamin C.²³

A new approach

These disappointing observations have prompted researchers to reassess the prior micronutrient models of prostate cancer therapy and refocus their efforts on developing viable interventions based on broad patterns of dietary practice. Epidemiological studies suggest that altering nutritional intake—specifically, switching to a diet that emphasizes vegetable intake and de-emphasizes meat and fat intake—may inhibit prostate cancer initiation and clinical progression.⁴⁻⁶ Experimental studies in prostate cell line and animal models demonstrate that components of cruciferous vegetables (such as kale, broccoli, and turnips) and carotenoids (such as tomatoes and carrots) induce apoptosis of prostate cancer cells, inhibit carcinogenesis, and promote the expression of cytoprotective enzymes in prostate tissue.⁷⁻⁹

Clinical evidence supporting these observational and preclinical data, however, is limited. Three small studies have evaluated diet change as a therapy for prostate cancer, one of which suggested a beneficial effect for a vegetable-intense diet in a small number of patients with low-stage, low-grade disease.¹⁰⁻¹² However, whereas this intensive lifestyle intervention also included dietary supplements, exercise, stress management, and support group participation, more definitive studies, testing feasible yet robust diet-based interventions capable of being implemented and sustained on a larger scale, are needed.¹¹
Active surveillance for prostate cancer and dietary interventions

Nearly 50 percent of newly diagnosed prostate cancer patients in the U.S. present with localized, early stage, relatively indolent disease. A substantial proportion of these patients receive unnecessarily aggressive treatment with surgery, radiation, or hormone-based treatments. These therapies produce considerable urinary, bowel, and sexual morbidities, and their impact on prostate cancer-specific or overall mortality in patients with less aggressive cancers is not clear.

MEAL flowchart

Active surveillance, which entails careful monitoring of selected patients with early stage prostate cancer, may provide a viable and safe alternative to more aggressive treatments. Approximately 35 percent of patients on active surveillance will progress within five years, while many others will opt for intervention even though they do not meet the objective criteria for progression. Reducing the number of active surveillance patients who progress or choose treatment represents an important opportunity to minimize treatment-associated morbidity, improve quality of life, and contain health care costs among appropriate prostate cancer patients.

Dietary interventions represent an opportunity to potentially reduce the number of prostate cancer patients who progress on active surveillance. We have designed and successfully pilot-tested a dietary intervention for prostate cancer patients based on well-established sociological principles. This intervention, which involves telephone-based counseling, produced robust diet changes and led to increased plasma carotenoid levels—biomarkers for vegetable intake—in patients with localized prostate cancer on active surveillance.

CALGB 70807: The Men’s Eating and Living (MEAL) Study

The MEAL Study is a randomized clinical trial testing the effect of a high-vegetable diet on disease progression in prostate cancer patients on active surveillance (see figure and table). It is the first national trial of a nonsupplement dietary intervention for prostate cancer and one of the first major studies of an intervention targeted for active surveillance patients. A total of 464 patients will be enrolled and monitored, each for up to two years. MEAL uses the same telephone-based counseling intervention validated in the pilot study. Patients will be randomized to a telephone counseling program to assist with their dietary change.

Selected inclusion criteria for CALGB 70807

- Biopsy-proven adenocarcinoma of the prostate, clinical stage ≤ T2a diagnosed within 24 months
- < 25% of biopsy tissue cores positive for cancer
- ≤ 50% of any one biopsy tissue core positive for cancer
- PSA < 10 ng/mL
- Aged 50 to 80 years
For men ≤ 70 years, biopsy Gleason score must be ≤ 6; for men > 70 years, biopsy Gleason score must be ≤ (3 + 4) = 7

Patients who have had prior treatment for prostate cancer by surgery, irradiation, local ablative, or androgen deprivation therapy are not eligible

The primary goal of MEAL will be to measure disease progression defined by total prostate-specific antigen (PSA), PSA doubling time, and pathology on repeat prostate biopsy. Secondary measures will include treatment seeking, patient anxiety, health-related quality of life, and tissue biomarkers.

Therapeutic dietary modification would potentially promulgate a novel paradigm for lower-risk prostate cancer akin to diet alterations for non–insulin-dependent diabetes: medical management, without curative intent, of a chronic disease state. There is widespread interest in diet as a possible factor in disease risk and progression. The limited data available suggest that a diet emphasizing plant products and de-emphasizing animal products protects against carcinogenesis and cancer progression. Experimental consideration confirming or refuting the impact of diet, however, is needed. The MEAL study, which will follow prostate cancer patients under expectant management, will provide important data on the actual, short-term impact of the adoption of a diet that increases vegetable intake and limits meat and dairy intake.

References


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