Response

We thank Dr. Nyberg for his interest in our recent correspondence to the Journal (1). In 1993, we reported a pronounced effect of saturated fat intake on risk of lung cancer (2). In that analysis, we entered both saturated fat and total calories as categoric variables in a standard multivariate model. Subsequently, we were persuaded that the standard multivariate model exaggerates the true variation in fat intake when data are modeled as quantile-categoric variables (3,4). Nyberg has asked us to address two questions. Was energy adjustment necessary for dietary constituents other than saturated fat? If we had not adjusted for total calories or used a different method of adjustment, would we have arrived at different conclusions?

Nyberg suggested that we examine risk estimates unadjusted for energy for a variety of dietary variables presented in two tables. The data are provided in Table 1 for selected dietary constituents. First, we examined energy-providing nutrients, all of which were highly correlated with total calories (Spearman correlations between .8 and .9). Unadjusted for total calories, both fats and carbohydrate were directly related to risk of lung cancer. When we examined fat and carbohydrate as a percent of total calories consumed, the fat and saturated fat associations persisted, but carbohydrate was inversely associated with risk of the disease (odds ratios across increasing quintiles 1.0, 1.19, 0.87, 0.80, 0.75; two-sided P for trend .09), suggesting that these macronutrients should be energy adjusted. By use of the standard multivariate approach, risk associated with fat was increased, whereas risk associated with intake of carbohydrate disappeared (2). Two food group variables—1) beans and peas and 2) citrus fruit and juice—were independently associated with risk of the disease; neither was affected by energy adjustment. Spearman correlations with total calories were .2 for beans and peas and .3 for citrus fruit and juice. In the present study, we also included yellow and green leafy vegetables, because the protective effect of this food group is well established for lung cancer. We saw no clear benefit of frequent consumption of these foods either with or without energy adjustment. Similarly, β-carotene was not protective or affected by method of energy adjustment.

In our original report (2), the analytic strategy was to identify dietary constituents (nutrients and food groups) independently associated with lung cancer risk. Since we had used the standard multivariate approach for energy adjustment, Nyberg was interested to know if we would have arrived at the same final model had we used different methods of energy adjustment. Saturated fat, beans and peas, and citrus fruit and juice were independently associated with risk, regardless of the method of energy adjustment (data not shown). The strength of the associations was not materially altered, and the test for trend remained statistically significant.

The issue of energy adjustment remains controversial. In our experience, the nutrient residual approach and the nutrient density approach provide comparable results. However, it is not clear whether energy adjustment is needed for all dietary constituents or whether one method is necessarily superior.

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References


Notes

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Long-Term Follow-up of Untreated Stage T1a Prostate Cancer

Stage T1a prostate cancer is defined as incidental adenocarcinoma detected at the time of the transurethral resection of the prostate (TURP), involving 5% or less of the resected prostatic tissue (1). It is estimated that 6.5% of men undergoing TURP will have stage T1a adenocarcinoma of the prostate (2). The biologic potential of stage T1a adenocarcinoma is uncertain (2). Some studies (3,4) have suggested that a significant proportion of patients (16%–26%) with stage T1a carcinoma will have clinically aggressive disease. However, our knowledge is limited with regard to the long-term outcome for untreated patients with stage...
T₁a cancer. A recent study (5) indicated that 8% of men with untreated, clinically occult, and incidental cancer have metastatic progression with up to 15 years’ follow-up.

In this study, we sought to determine the natural history of untreated stage T₁a prostate cancer after long-term follow-up.

The study group consisted of 102 consecutive case subjects who were diagnosed with stage T₁a prostate cancer at Mayo Clinic during the period from 1960 through 1970. None of these men were treated until there was evidence of disease progression. The ages of the case subjects at diagnosis ranged from 48 to 91 years (mean, 69 years). All histologic slides were reviewed by two pathologists (L. Cheng and D. G. Bostwick) and fulfilled the American Joint Committee on Cancer criteria for stage T₁a cancer (1). The weight of resected prostatic tissue ranged from 3 g to 115 g (mean, 24 g). Cancer volume, determined by the grid method, ranged from 0.01 cm³ to 0.22 cm³ (mean, 0.06 cm³). The mean Gleason score was 5 (range, 2–7), and the mean number of cancer foci was 1.6 (range, 1–5).

The mean follow-up after initial diagnosis was 9.5 years (range, 0.3–31 years). One case subject was alive without evidence of disease. Fifty-five case subjects died of intercurrent diseases, four case subjects died of prostate cancer, and 14 died of unknown causes. Twenty-eight subjects were lost to follow-up. During the follow-up of 9.5 years, 14 men (14%) developed clinical progression of disease. In summary, men with untreated stage T₁a prostate cancer are at risk of clinical progression of cancer.

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References


(3) Blute ML, Zincke H, Farrow GM. Long-term

Table 1. Characteristics of 14 patients with progression*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, y</th>
<th>Weight of TURP, g</th>
<th>Gleason score</th>
<th>No. of cancer foci</th>
<th>Cancer volume, cm³ †</th>
<th>Disease progression</th>
<th>Time to disease progression, y</th>
<th>Follow-up, y</th>
<th>Current status</th>
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<tr>
<td>1</td>
<td>64</td>
<td>11</td>
<td>2 + 3 = 5</td>
<td>2</td>
<td>0.16</td>
<td>Gleason 4 + 3 = 7 cancer on needle biopsies †</td>
<td>12</td>
<td>13</td>
<td>Died of renal failure</td>
</tr>
<tr>
<td>2</td>
<td>69</td>
<td>22</td>
<td>3 + 2 = 5</td>
<td>1</td>
<td>0.04</td>
<td>Gleason 4 + 4 = 8 cancer on needle biopsies †</td>
<td>13</td>
<td>21</td>
<td>Died of unknown causes</td>
</tr>
<tr>
<td>3</td>
<td>72</td>
<td>25</td>
<td>2 + 2 = 4</td>
<td>4</td>
<td>0.16</td>
<td>Gleason 4 + 4 = 8 cancer on TURP</td>
<td>3</td>
<td>3</td>
<td>Died of acute renal failure</td>
</tr>
<tr>
<td>4</td>
<td>69</td>
<td>7</td>
<td>3 + 2 = 5</td>
<td>2</td>
<td>0.05</td>
<td>Gleason 3 + 4 = 7 cancer on needle biopsies †</td>
<td>5</td>
<td>9</td>
<td>Unknown</td>
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<tr>
<td>5</td>
<td>70</td>
<td>15</td>
<td>3 + 3 = 6</td>
<td>2</td>
<td>0.05</td>
<td>Gleason 4 + 3 = 7 cancer on needle biopsies †</td>
<td>8</td>
<td>11</td>
<td>Unknown</td>
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<tr>
<td>6</td>
<td>76</td>
<td>20</td>
<td>2 + 3 = 5</td>
<td>1</td>
<td>0.09</td>
<td>Gleason 5 + 4 = 9 cancer on TURP</td>
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<td>5</td>
<td>Died of thrombocytopenic purpura</td>
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<td>7</td>
<td>73</td>
<td>14</td>
<td>3 + 2 = 5</td>
<td>1</td>
<td>0.01</td>
<td>Gleason 4 = 3 = 6 cancer on needle biopsies †</td>
<td>2</td>
<td>10</td>
<td>Died of cardiac failure</td>
</tr>
<tr>
<td>8</td>
<td>70</td>
<td>10</td>
<td>3 + 2 = 5</td>
<td>2</td>
<td>0.17</td>
<td>Gleason 5 + 4 = 9 cancer on needle biopsies †</td>
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<td>7</td>
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<td>1 + 2 = 3</td>
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<td>0.03</td>
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<td>16</td>
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<tr>
<td>10</td>
<td>73</td>
<td>14</td>
<td>3 + 2 = 5</td>
<td>3</td>
<td>0.10</td>
<td>Distant metastasis</td>
<td>2</td>
<td>6</td>
<td>Died of congestive heart failure</td>
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<tr>
<td>11</td>
<td>73</td>
<td>40</td>
<td>3 + 3 = 6</td>
<td>2</td>
<td>0.08</td>
<td>Died of prostate cancer</td>
<td>23</td>
<td>23</td>
<td>Died of prostate cancer</td>
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<tr>
<td>12</td>
<td>59</td>
<td>12</td>
<td>3 + 3 = 6</td>
<td>1</td>
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<td>73</td>
<td>9</td>
<td>3 + 3 = 6</td>
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<td>Died of prostate cancer</td>
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<td>9</td>
<td>Died of prostate cancer</td>
</tr>
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<td>68</td>
<td>26</td>
<td>3 + 3 = 6</td>
<td>1</td>
<td>0.02</td>
<td>Died of prostate cancer</td>
<td>12</td>
<td>12</td>
<td>Died of prostate cancer</td>
</tr>
</tbody>
</table>

*TURP = transurethral resection specimens.
†Cancer volume was measured by the grid method.
‡Needle biopsies were directed against clinically palpable nodules.


Notes

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Outcome Research After Radical Retropubic Prostatectomy for Prostate Cancer

Recent reports (1,2) describing outcome research after nerve-sparing radical retropubic prostatectomy showed only about 40% of men totally continent of urine and only about 30% of men potent without penile injections or penile prostheses.

Additional outcome research after nerve-sparing radical retropubic prostatectomy showed organ-confined disease (pT1–2) in 51% (4339 of 8477) of the surgical specimens (3). That report by Garnick and Fair was a summary of six series of patients who had undergone a nerve-sparing radical prostatectomy procedure at one of six different academic medical centers; the number of patients in each series ranged from 415 to 3170.

Outcome research from The Johns Hopkins Medical Center, Baltimore, MD (4), where the nerve-sparing radical prostatectomy procedure was initially developed, showed that, of 586 patients who had undergone a nerve-sparing radical prostatectomy procedure and from whom pathology specimens were obtained, 328 (56%) had organ-confined disease (pT1–2), 123 (21%) had specimen-confined disease (pT3), and 135 (23%) had non-specimen-confined disease (pT4). With a median follow-up of 4 years, there were prostate-specific antigen (PSA) failures (detectable PSA) in 20 (6%), 32 (26%), and 107 (79%) patients with pT1–2, pT3, and pT4 disease, respectively. At a median follow-up of 4 years, there were clinical failures in 10 (3%), 12 (10%), and 51 (38%) patients with disease at stages pT1–2, pT3, and pT4, respectively.

Outcome research at the Mayo Clinic, Rochester, MN (5), showed that, after standard radical retropubic prostatectomy with maximal surgical margins, clinical recurrence was seen in 20% (52 of 261) of the patients with organ-confined disease (pT1–2) who were followed for a median of 9.4 years. These recurrences were local in 12% (31 of 261) of the patients and systemic in 12% (31 of 261) of the patients.

The biology of prostate cancer and the anatomy of the prostate gland dictate these surgical outcomes—50% organ-confined disease (pT1–2) (3), 40% urinary continence (1,2), 30% potency (1,2), and 20% clinically recurrent cancer in patients with organ-confined disease (pT1–2) with a median follow-up of 9.4 years (5). Any apparent “cure” of prostate cancer by surgery will happen despite the surgery and be the result of the biology of the cancer and/or lead time bias.

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References


Notes


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