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Pre-diagnosis dietary pattern and survival in patients with multiple myeloma

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Abstract

Inflammation and endogenous growth factors are important in multiple myeloma (MM) pathogenesis. Although diets that modulate these biologic pathways may influence MM patient survival, studies have not examined the association of dietary pattern with MM survival. We conducted pooled prospective survival analyses of 423 MM patients from the Nurses' Health Study (1986–2016) and the Health Professionals Follow-up Study (1988–2016) using Cox regression models. We used data from repeated food frequency questionnaires (FFQ) to compute dietary patterns as of the last pre-diagnosis FFQ, including the Alternate Healthy Eating Index (AHEI)-2010, alternate Mediterranean Diet, Dietary Approaches to Stop Hypertension, Prudent, Western and empirical dietary inflammatory patterns and empirical dietary indices for insulin resistance and hyperinsulinemia. During follow-up, we documented 295 MM-related deaths among 345 total deaths. MM-specific mortality was 15% to 24% lower per one standard deviation (SD) increase (e.g., towards healthier habits) in favorable dietary pattern scores. For example, the

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multivariable-adjusted hazard ratio [HR] and 95% confidence interval [CI] per 1-SD increase in AHEI-2010 score were 0.76, 0.67 to 0.87 (P<.001). In contrast, MM-specific mortality was 16% to 24% higher per 1-SD increase (e.g., towards less healthy habits) in "unhealthy" diet scores; for example, the multivariable-adjusted HR, 95% CI per 1-SD increase in Western pattern score were 1.24, 1.07 to 1.44 (P=0.005). Associations were similar for all-cause mortality. In conclusion, our consistent findings for multiple dietary patterns provide the first evidence that MM patients with healthier pre-diagnosis dietary habits may have longer survival than those with less healthy diets.

Keywords

Multiple myeloma; survival; dietary pattern; Healthy Eating Index; Western diet; Prudent diet; Mediterranean diet; empirical dietary index

Introduction

Multiple myeloma (MM) is an incurable malignancy of plasma cells. In 2019, MM is expected to account for 32,110 new cancer diagnoses and 12,960 deaths in the US.[1] Although recent advances in therapy have improved survival, MM remains incurable, with 5- and 10-year survival rates of 51.6% and 26.8%, respectively.[2–7] Moreover, the role of modifiable factors in MM etiology and survival is unclear; at present, obesity is the only established modifiable risk factor,[8, 9] and its association with survival is uncertain.[10, 11]

Evidence suggests that inflammation and endogenous growth factors, including insulin-like growth factors (IGF)-1 and interleukin (IL)-6, play an important role in MM pathogenesis.[12–18] However, it is unknown whether modifiable factors that modulate these biological pathways influence survival in MM patients. Identifying modifiable risk factors for MM survival is crucial to develop evidence-based guidelines for MM patients.

Dietary factors may affect inflammatory and endogenous growth factor pathways. Several case-control studies have reported that lower intake of vegetables and fish and higher intake of dairy products may be associated with increased MM incidence.[19–21] Assessing overall diet quality rather than individual foods or nutrients has advantages because dietary patterns provide more comprehensive and intuitive public health messages with feasible clinical applications.[22–25] In a recent large prospective cohort study, we have provided evidence that diets with higher inflammatory or insulinemic potential may increase MM incidence, particularly in men.[26] However, to our knowledge, no study has yet examined the association of individual diet or dietary pattern with survival in MM patients.[27] Moreover, current dietary guidelines for cancer survivors from the World Cancer Research Fund/ American Institute for Cancer Research (WCRF/AICR) recommend generally healthy diets based on limited studies, none of which included MM patients.[28]

Therefore, we utilized data from two large prospective cohort studies, the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS), to examine whether dietary pattern is associated with survival in MM patients.

Methods

Study Population

The NHS enrolled 121,700 female registered nurses aged 30 to 55 years in 1976. The HPFS enrolled 51,529 male health care professionals aged 40 to 75 years in 1986. The cohort design and methods have been described elsewhere[29, 30] and are similar for both cohorts. Briefly, participants have completed a mailed questionnaire on lifestyle and medical factors at enrollment and biennially thereafter. Follow-up rates have typically exceeded 90%. Food frequency questionnaires (FFQ) were administered approximately every four years beginning in 1980 (NHS) and 1986 (HPFS); those with sufficient detail to permit derivation of dietary patterns (see below) were first administered in 1984 (NHS) and 1986 (HPFS). To reduce the potential influence of preclinical MM on diet habits, we applied a two-year lag and defined the study baseline as 1986 (NHS) and 1988 (HPFS). After applying this lag, the baseline sample included 116,777 women (NHS) and 49,019 men (HPFS) (Supporting Information Figure S1). Informed consent was obtained from all participants. The study protocol was approved by the institutional review boards of the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health and those of participating registries as required.

Ascertainment of MM Cases

We identified most MM diagnoses (over 94%) by self-report on the biennial questionnaires. We then obtained the corresponding medical records (with participant permission) for review by a trained reviewer blinded to exposure history to confirm the diagnosis and diagnosis date.[31] When the medical records were unavailable, we confirmed MM diagnoses via linkage to state tumor registries. In the present study, we included a pooled total of 423 patients (233 women, 190 men) with confirmed incident first diagnoses of MM (without a history of other cancer) from baseline through 2014 and with a completed pre-diagnosis FFQ (Supporting Information Figure S1). Of note, distributions of covariates such as age, BMI and number of comorbidities were similar between patients who completed a pre-diagnosis FFQ and those who did not.

Measurement of Mortality

Deaths were identified by next of kin, the postal system or routine searches of the National Death Index, methods which have shown greater than 98% sensitivity in the NHS and HPFS.[32, 33] Reviewers blinded to exposures reviewed the corresponding medical records to assign the cause of death, including MM-specific death.

Dietary Assessment

For the present analysis, we used data from the validated FFQs (those with approximately 130 items) administered every four years starting from 1984 (NHS) or 1986 (HPFS),[34–36] as noted above. In each FFQ, participants were asked how often, on average, they consumed each food item during the past year, based on an indicated standard portion size, with 9 response options ranging from 'never or less than once per month' to '6 or more times per day.' We used repeated FFQ returned prior to MM diagnosis to compute pre-diagnosis

dietary patterns, as described briefly below and in detail elsewhere.[26] We focused on pre-diagnosis dietary habits because the median survival of MM (~3.5 years) was shorter than the 4-year interval between FFQ administrations in the NHS and HPFS. However, for MM patients with at least one post-diagnosis FFQ available (n=348), we also used the first post-dx FFQ to assess the correlation of pre- and post-diagnosis diets.

Dietary Patterns

We used three *a priori*-defined dietary scores. We calculated the Alternate Healthy Eating Index (AHEI)-2010 from 11 dietary components that have been identified as associated with reduced risk of chronic disease.[37] Higher AHEI-2010 scores represent a healthier diet. We calculated the alternate Mediterranean diet (aMED) score from 9 foods/nutrients that reflect a typical Mediterranean diet.[38] Higher aMED scores represent higher adherence to a ("healthy") Mediterranean diet. We based the Dietary Approach to Stop Hypertension (DASH) score on 8 foods/nutrients that were associated with lower risk of hypertension in the DASH trial.[39] Higher DASH scores indicate more favorable habits with regard to hypertension prevention.

We also derived two *a posteriori*-defined diet patterns based on approximately 40 food groups using principle component analysis with orthogonal transformation.[40, 41] The "Prudent pattern" featured a high intake of vegetables, fruits, legumes, whole grains, and fish, whereas the "Western pattern" was characterized by a high intake of red/processed meats, high-fat dairy products, refined grains, and sweets/desserts.

Lastly, we calculated three empirical hypothesis-oriented dietary indices using 39 predefined food groups from the FFQ. The development and validation of these indices have been described in detail previously.[42, 43] Briefly, the empirical dietary inflammatory pattern (EDIP) was derived using reduced rank regression and stepwise linear regression to identify food groups that are most predictive of three inflammatory markers including interleukin-6, C-reactive protein, and tumor necrosis factor-alpha receptor-2.[42] Similarly, the empirical dietary index for insulin resistance (EDIR) and empirical dietary index for hyperinsulinemia (EDIH) were derived using stepwise linear regression to identify food groups most predictive of insulin resistance (triglyceride to high-density lipoprotein cholesterol ratio) and hyperinsulinemia (C-peptide).[43] Higher scores represent a greater inflammatory or insulinemic potential of those diets.

Covariate Assessment

We collected information on adult height in 1976 for the NHS and in 1986 for the HPFS, and current weight and history of chronic diseases were obtained from each of the biennial questionnaires. Pre-diagnosis body mass index (BMI) was calculated as weight divided by height squared (kg/m^2) using the current weight reported on the last pre-diagnosis questionnaire. A comorbidity score was calculated by summing the number of prevalent diseases including high blood pressure, high cholesterol, diabetes, cardiovascular disease, and pulmonary disease.[44] The comorbidity score was updated throughout follow-up and included applicable pre-baseline information.

MM Clinical Characteristics

Additional clinical disease characteristics were available in a subgroup (≤35%) of MM patients. We used hospital medical records and pathology reports to abstract information on selected disease characteristics at the time of MM diagnosis prior to therapy. A summary of the abstraction protocol is provided in the Supporting Information Methods.

Statistical Analysis

We calculated person-time from the date of MM diagnosis until the earliest among date of death or the end of follow-up (January 2016). We utilized Cox proportional hazard regression models to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) of death associated with pre-diagnosis dietary patterns. The primary outcome of interest was death from MM; the secondary outcome was death from any cause. For the main analysis, we modeled the two-year lagged pre-diagnosis dietary patterns assessed closest to the MM diagnosis as continuous variables (i.e., in one standard deviation (SD) increasing increments) after testing for non-linearity by including polynomial terms of dietary patterns in the models and finding no evidence of non-linear relationships (all $P>0.05$). The main analyses were conducted on a pooled data set (NHS and HPFS combined), with stratification of the Cox models by cohort (sex), after finding no significant interaction between dietary patterns and sex in relation to MM-specific or all-cause mortality (all $P>0.05$). The simplest models adjusted for age at diagnosis and pre-diagnosis total calorie intake (both as continuous variables); additionally, we conducted multivariable-adjusted models which further included pre-diagnosis BMI (<22, 22 to 24.9, 25 to 29.9, ≥30 kg/m^2), time between FFQ return date and MM diagnosis (<median or ≥median), year of MM diagnosis (<2000 or ≥2000, e.g., approximating the periods before and after marked advancements in therapies for MM[4–6]), and comorbidity score (continuous). For comparison with the continuous terms for the dietary patterns, we examined associations with mortality using tertile of pre-diagnosis dietary patterns and generated tertile-specific survival curves using Kaplan-Meier methods, testing their statistical significance with the log-rank test.

In the absence of data on first-line therapy, we explored potential effect modification by therapy by conducting additional multivariate analyses that examined whether the association between dietary patterns and mortality differed by calendar period of MM diagnosis (<2000, ≥2000).[4–6] We also conducted stratified analyses by pre-diagnosis BMI (<25 or ≥25 kg/m^2), which has been associated with MM incidence and mortality.[45] We tested for interaction by including product terms of dietary patterns and diagnosis period or category of BMI in the models. Additionally, as a sensitivity analysis, we compared findings for MM-specific and all-cause mortality based on the cumulative average of repeated measures of pre-diagnosis dietary pattern rather than the dietary pattern based on only the most recent pre-diagnosis FFQ. Other sensitivity analyses included adjustment of the multivariable models for alcohol intake or exclusion of the alcohol component from relevant dietary pattern scores (e.g., AHEI and aMED). To explore the implications of our focus on pre-diagnosis dietary patterns, and specifically on the most recent pre-diagnosis FFQ available, we calculated Spearman correlation coefficients between the most recent and the cumulative average pre-diagnosis dietary patterns, and between the most recent pre-diagnosis and the first post-diagnosis dietary patterns. Lastly, we compared distributions of

available clinical indicators of disease severity at diagnosis by tertile of dietary pattern and by availability (returned/missing) of the last pre-diagnosis FFQ.

All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC). All tests were two-sided, with P<0.05 considered statistically significant.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Results

The analysis included 423 MM patients, with a mean age at MM diagnosis of 70 years for women and 72 years for men (Table 1). The mean BMI at MM diagnosis was 27 kg/m^2, and the mean time between FFQ return and MM diagnosis was approximately 25–27 months for both women and men. The pairwise Spearman correlations among AHEI-2010, aMED, DASH and Prudent patterns ranged from 0.45 to 0.75 (Supporting Information Table S1). These dietary patterns generally showed inverse correlations with the Western pattern, EDIP, EDIR and EDIH. The correlations among empirical dietary indices ranged from 0.44 and 0.72.

During a mean follow-up of 4.5 years (median of 3.5 years), we ascertained 295 MM-specific and 345 total deaths. In the multivariable-adjusted pooled models, “healthier” dietary patterns, as captured by higher pre-diagnosis AHEI-2010, aMED, DASH, and Prudent pattern scores and lower pre-diagnosis Western pattern, EDIR and EDIH scores, were significantly associated with a lower risk of MM-specific mortality (Table 2). MM-specific mortality decreased by 24%, 15%, 15% and 24% per 1-SD increase in AHEI-2010 (fully-adjusted HR, 95% CI: 0.76, 0.67 to 0.87; P<.001), aMED (0.85, 0.75 to 0.97; P=0.01), DASH (0.85, 0.76 to 0.95; P=0.006), and Prudent pattern scores (0.76, 0.66 to 0.87, P<.001). MM-specific mortality increased by 24%, 16% and 17% per SD increase in Western pattern (fully-adjusted HR, 95% CI: 1.24, 1.07 to 1.44; P=0.005), EDIR (1.16, 1.02 to 1.33; P=0.03), and EDIH scores (1.17, 1.01 to 1.35; P=0.03). We observed a statistically non-significant but suggestive positive association of EDIP with MM-specific mortality. The Kaplan-Meier survival curves suggested that associations with MM-specific mortality corresponded to modest increases in survival after MM diagnosis for patients in the highest (healthiest) tertile of favorable dietary pattern scores and modest decreases in survival for those in the highest (least healthy) tertile of the “unhealthy” dietary pattern scores (Supporting Information Figure S2; unadjusted for covariates). We observed similar associations of pre-diagnosis dietary patterns with all-cause mortality and overall survival (Table 3 and Supporting Information Figure S3). When we modeled dietary patterns by tertile, the overall results did not change (Supporting Information Tables S2 and S3).

In the analyses stratified by year of MM diagnosis (<2000 or ≥2000), we found generally consistent associations for MM-specific and all-cause mortality in both strata (all $P_{interaction}$>0.05, except for the Prudent pattern and MM-specific mortality; $P_{interaction}$=0.04) (Supporting Information Table S4). In the pre-diagnosis BMI-stratified analyses, with a few

exceptions, the associations tended to be somewhat stronger for overweight and obese persons than those with a lower BMI (Supporting Information Table S5). However, not all stratum-specific associations were markedly different in magnitude, and only the Western pattern associations showed statistically significant heterogeneity by BMI (MM-specific mortality, $P_{interaction}$=0.002; all-cause mortality, $P_{interaction}$=0.006) (Supporting Information Table S5).

When we modeled the cumulative average of pre-diagnosis dietary pattern scores across repeated FFQs instead of the most recent pre-diagnosis patterns, we observed similar but somewhat weaker associations (Supporting Information Tables S6 and S7). In contrast, additional adjustment for alcohol intake or exclusion of alcohol intake from applicable dietary pattern derivations (e.g., from the derivation of the AHEI and aMED patterns) did not materially alter the results. For example, the HR (95% CI) for the association of the AHEI score with MM-specific mortality after adjustment for the original covariates plus alcohol intake was 0.74 (0.65 to 0.85 per 1-SD increase in AHEI score. The association based on an AHEI score derived without the alcohol intake component was also 0.74 (0.65–0.85) with adjustment for all the covariates. There were high correlations between the cumulative average and the most recent pre-diagnosis dietary patterns (r=0.71–0.91), as well as between the most recent pre- and post-diagnosis dietary patterns (r=0.73–0.89) (Supporting Information Table S8). In the MM patients with available clinical data, we found no evidence of systematic differences in clinical prognostic factors by tertile of dietary pattern or missingness of the most recent pre-diagnosis FFQ (data not shown).

Discussion

In two large prospective cohorts of US adults, MM patients with healthier pre-diagnosis dietary patterns had superior survival to those with less healthy diets. Specifically, higher pre-diagnosis AHEI-2010, aMED, DASH, and Prudent pattern scores and lower pre-diagnosis Western pattern, EDIR, and EDIH scores were significantly associated with lower MM-specific and all-cause mortality in MM patients. Our findings provide the first evidence that healthy pre-diagnosis dietary habits may offer survival benefits among MM patients. Whether the increased mortality from presumably unhealthy diets is even greater in overweight or obese patients, as suggested by the pre-diagnosis BMI-stratified findings, requires further evaluation in larger populations, as the lower-BMI stratum had fewer patients overall and thus less statistical precision.

The current understanding of effects of diet on cancer survival is limited. Recently, the WCRF/AICR noted that both quantity and quality of evidence are insufficient to provide evidence-based dietary guidelines for most types of cancer patients and advised cancer survivors to follow the general dietary recommendations for cancer prevention.[28] A number of cohort studies have examined the association of food intake and various dietary patterns with mortality in cancer survivors.[27, 46] These studies suggested that adherence to a higher quality diet (e.g., AHEI, aMED, DASH and Prudent patterns) was inversely associated with overall mortality, while greater adherence to a Western pattern was positively associated with overall mortality in cancer survivors. Additionally, studies of individual food intakes suggested that higher intake of vegetables and fish and lower intake of alcohol may be

associated with decreased mortality in cancer survivors. These results were consistent when the analyses were restricted to studies that examined post-diagnosis dietary pattern rather than pre-diagnosis dietary pattern. However, the majority of the studies examined patients with breast or colorectal cancers; very limited evidence exists for patients with other cancer types.

To our knowledge, no other studies have examined the association of individual foods or dietary patterns with survival in MM patients. In the current study, we found that healthier pre-diagnosis dietary habits, as indicated by higher adherence to the AHEI-2010, aMED, DASH, and Prudent patterns and lower adherence to the Western pattern, were significantly associated with lower MM-specific and overall mortality in MM patients. In addition, we found that empirically derived dietary indices predictive of inflammatory or insulin resistance-related biomarkers were marginally or significantly associated with poor MM survival. These novel dietary indices, which capture diets with inflammatory or insulinemic potential, have not been examined previously in relation to cancer survival. However, in a recent analysis of the association between dietary pattern and MM incidence, we observed that diets with inflammatory or insulinemic potential may also have an etiologic role in MM.[26]

Interestingly, we consistently observed that a healthier pre-diagnosis dietary pattern was associated with lower mortality in MM patients regardless of the year of MM diagnosis. This finding suggests that healthier pre-diagnosis dietary habits may have survival benefits that complement those of even the more advanced therapies that have emerged for MM treatment in the past two decades.

Plausible biological mechanisms link diet and MM survival. For example, inflammation and endogenous growth factors are important in MM cell growth, proliferation and survival.[12–18] Previous studies have shown that adherence to healthier dietary patterns, such as the AHEI-2010, aMED, DASH, and Prudent patterns, were inversely associated with biomarkers of inflammation (e.g., CRP, IL6) and insulin response (e.g., fasting insulin),[47–49] while adherence to a Western pattern was positively associated with biomarkers of fasting insulin, C-peptide, CRP and leptin.[49] Moreover, the indices EDIP, EDIR and EDIH were each a strong predictor of inflammation, insulin resistance and hyperinsulinemia, respectively.[42, 43] Our findings on these dietary patterns and survival were consistent with our initial hypothesis that pro-inflammatory and insulin-modulating diets increase the risk of mortality in MM patients by promoting a physiologic milieu favorable to disease progression.

Strengths of the present study include the prospective design, detailed information on diet and other covariates and long follow-up period. There are several limitations as well. First, although we had detailed collection of pre-diagnosis diet, we could not feasibly examine the association between post-diagnosis dietary pattern and survival in MM patients without introducing a survival bias (e.g., because the median survival of MM patients was 3.5 years, whereas FFQs were collected every 4 years). Because of the moderate to strong correlations we observed between pre- and post-diagnosis diets, we cannot conclude whether the observed associations truly reflect a distinct benefit of pre-diagnosis diet or whether pre-

diagnosis diet acted as a surrogate for post-diagnosis diet. However, the finding of stronger associations for the most recent than for a cumulative average of all pre-diagnosis dietary pattern scores suggests that relatively recent dietary habits had the strongest influence on MM survival. Second, we cannot rule out an influence of residual confounding by unknown or unmeasured factors. Most notably, we did not have comprehensive medical data with which to adjust directly for severity of disease or first-line therapy. The lack of a clear difference in clinical prognosis factors in the small subgroup of patients with available clinical data was reassuring, but the limited number and scope of those data fall short of conclusive elimination of concerns over selection bias or residual confounding. Lastly, our study cohorts were primarily comprised of white health professionals; thus, our findings may not be generalizable to all MM patients, although the homogenous study population strengthens the internal validity of the study.

In conclusion, our results support the current general dietary recommendations for cancer survivors[28] and provide the first evidence that healthy diets may enhance survival of MM patients even in the era of improved therapies. Additional cohort studies are warranted to confirm these associations in larger and diverse populations, including in population strata that frequently demonstrate a lesser benefit from modern therapies. If confirmed, our findings could inform clinical recommendations and/or the design of dietary interventions to enhance survival in MM patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

AHEI	alternate healthy eating index
aMED	alternate Mediterranean diet
BMI	body mass index
CI	confidence interval
DASH	dietary approaches to stop hypertension
EDIH	empirical dietary index for hyperinsulinemia
EDIP	empirical dietary inflammatory pattern

EDIR	empirical dietary index for insulin resistance
FFQ	food frequency questionnaire
HPFS	Health Professionals Follow-up Study
HR	hazard ratio
MM	multiple myeloma
NHS	Nurses' Health Study
SD	standard deviation

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA: a cancer journal for clinicians 2019;69: 7–34. [PubMed: 30620402]
2. Bosetti C, Bertuccio P, Malvezzi M, Levi F, Chatenoud L, Negri E, La Vecchia C. Cancer mortality in Europe, 2005–2009, and an overview of trends since 1980. Annals of oncology 2013;24: 2657–71. [PubMed: 23921790]
3. Kaya H, Peressini B, Jawed I, Martincic D, Elaimy AL, Lamoreaux WT, Fairbanks RK, Weeks KA, Lee CM. Impact of age, race and decade of treatment on overall survival in a critical population analysis of 40,000 multiple myeloma patients. International journal of hematology 2012;95: 64–70. [PubMed: 22160833]
4. Pozzi S, Marcheselli L, Bari A, Liardo EV, Marcheselli R, Luminari S, Quaresima M, Cirilli C, Ferri P, Federico M. Survival of multiple myeloma patients in the era of novel therapies confirms the improvement in patients younger than 75 years: A population-based analysis. British journal of haematology 2013;163: 40–6. [PubMed: 23889344]
5. Pulte D, Gondos A, Brenner H. Improvement in survival of older adults with multiple myeloma: results of an updated period analysis of SEER data. The oncologist 2011;16: 1600–3. [PubMed: 21968047]
6. Pulte D, Redaniel MT, Brenner H, Jansen L, Jeffreys M. Recent improvement in survival of patients with multiple myeloma: variation by ethnicity. Leukemia & lymphoma 2014;55: 1083–9. [PubMed: 23879201]
7. Howlader N, Noone A, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis D. SEER Cancer Statistics Review, 1975–2016, National Cancer Institute Bethesda, MD: National Cancer Institute. Bethesda, MD, 2019:https://seer.cancer.gov/csr/1975_2016/, based on November SEER data submission, posted to the SEER web site, April 7.
8. Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K, International Agency for Research on Cancer Handbook Working G. Body Fatness and Cancer--Viewpoint of the IARC Working Group. The New England journal of medicine 2016;375: 794–8. [PubMed: 27557308]
9. Marinac CR, Birmann BM, Lee I-M, Rosner BA, Townsend MK, Giovannucci E, Rebbeck TR, Buring JE, Colditz GA. Body mass index throughout adulthood, physical activity, and risk of multiple myeloma: a prospective analysis in three large cohorts. British journal of cancer 2018;118: 1013. [PubMed: 29527008]
10. Beason TS, Chang S-H, Sanfilippo KM, Luo S, Colditz GA, Vij R, Tomasson MH, Dipersio JF, Stockerl-Goldstein K, Ganti A. Influence of body mass index on survival in veterans with multiple myeloma. The oncologist 2013;18: 1074–9. [PubMed: 24048366]
11. Jung S-H, Yang D-H, Ahn J-S, Lee S-S, Ahn S-Y, Kim Y-K, Kim HJ, Lee J-J. Decreased body mass index is associated with poor prognosis in patients with multiple myeloma. Annals of hematology 2014;93: 835–40. [PubMed: 24310866]
12. Bataille R, Robillard N, Avet-Loiseau H, Harousseau J-L, Moreau P. CD221 (IGF-1R) is aberrantly expressed in multiple myeloma, in relation to disease severity. Haematologica 2005;90: 706–7. [PubMed: 15921396]

13. Ge N-L, Rudikoff S. Insulin-like growth factor I is a dual effector of multiple myeloma cell growth. Blood 2000;96: 2856–61. [PubMed: 11023522]
14. Interleukin Hirano T. 6 (IL-6) and its receptor: Their role in plasma cell neoplasias. Stem Cells 1991;9: 166–84.
15. Kawano M, Hirano T, Matsuda T, Taga T, Horii Y, Iwato K, Asaoku H, Tang B, Tanabe O, Tanaka H. Autocrine generation and requirement of BSF-2/IL-6 for human multiple myelomas. Nature 1988;332: 83–5. [PubMed: 3258060]
16. Qiang Y-W, Kopantzev E, Rudikoff S. Insulinlike growth factor–I signaling in multiple myeloma: downstream elements, functional correlates, and pathway cross-talk. Blood 2002;99: 4138–46. [PubMed: 12010818]
17. Qiang Y-W, Yao L, Tosato G, Rudikoff S. Insulin-like growth factor I induces migration and invasion of human multiple myeloma cells. Blood 2004;103: 301–8. [PubMed: 14504085]
18. Sprynski AC, Hose D, Kassambara A, Vincent L, Jourdan M, Rossi J-F, Goldschmidt H, Klein B. Insulin is a potent myeloma cell growth factor through insulin/IGF-1 hybrid receptor activation. Leukemia 2010;24: 1940. [PubMed: 20844560]
19. Hosgood HD, Baris D, Zahm SH, Zheng T, Cross AJ. Diet and risk of multiple myeloma in Connecticut women. Cancer Causes & Control 2007;18: 1065–76. [PubMed: 17694422]
20. Brown LM, Gridley G, Pottern LM, Baris D, Swanson CA, Silverman DT, Hayes RB, Greenberg RS, Swanson GM, Schoenberg JB. Diet and nutrition as risk factors for multiple myeloma among blacks and whites in the United States. Cancer Causes & Control 2001;12: 117–25. [PubMed: 11246840]
21. Caini S, Masala G, Gnagnarella P, Ermini I, Russell-Edu W, Palli D, Gandini S. Food of animal origin and risk of non-Hodgkin lymphoma and multiple myeloma: A review of the literature and meta-analysis. Critical reviews in oncology/hematology 2016;100: 16–24. [PubMed: 26921971]
22. Sacks FM, Obarzanek E, Windhauser MM, Svetkey LP, Vollmer WM, McCullough M, Karanja N, Lin P-H, Steele P, Proschan MA. Rationale and design of the Dietary Approaches to Stop Hypertension trial (DASH): a multicenter controlled-feeding study of dietary patterns to lower blood pressure. Annals of epidemiology 1995;5: 108–18. [PubMed: 7795829]
23. Wirfält AE, Jeffery RW. Using cluster analysis to examine dietary patterns: nutrient intakes, gender, and weight status differ across food pattern clusters. Journal of the American Dietetic Association 1997;97: 272–9. [PubMed: 9060944]
24. Neuhouser ML. The importance of healthy dietary patterns in chronic disease prevention Nutrition research (New York, NY) 2018.
25. Randall E, Marshall JR, Brasure J, Graham S. Dietary patterns and colon cancer in western New York. Nutr Cancer 1992;18: 265–76. [PubMed: 1296200]
26. Lee DH, Fung TT, Tabung FK, Colditz GA, Ghobrial IM, Rosner BA, Giovannucci EL, Birmann BM. Dietary pattern and risk of multiple myeloma in two large prospective US cohort studies. JNCI cancer spectrum 2019.
27. Jochems SH, Van Osch FH, Bryan RT, Wesselius A, van Schooten FJ, Cheng KK, Zeegers MP. Impact of dietary patterns and the main food groups on mortality and recurrence in cancer survivors: a systematic review of current epidemiological literature. BMJ open 2018;8: e014530.
28. World Cancer Research Fund/American Institute for Cancer Research. Diet, Nutrition, Physical Activity and Cancer: a Global Perspective. Continuous Update Project Expert Report 2018 Available at dietandcancerreport.org.
29. Colditz GA, MANSON JE, HANKINSON SE. The Nurses' Health Study: 20-year contribution to the understanding of health among women. Journal of women's health 1997;6: 49–62.
30. Rimm EB, Giovannucci EL, Willett WC, Colditz GA, Ascherio A, Rosner B, Stampfer MJ. Prospective study of alcohol consumption and risk of coronary disease in men. The Lancet 1991;338: 464–8.
31. Rajkumar SV, Dimopoulos MA, Palumbo A, Blade J, Merlini G, Mateos MV, Kumar S, Hillengass J, Kastritis E, Richardson P, Landgren O, Paiva B, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. The lancet oncology 2014;15: e538–e48. [PubMed: 25439696]

32. Rich-Edwards JW, Corsano KA, Stampfer MJ. Test of the national death index and Equifax nationwide death search. American journal of epidemiology 1994;140: 1016–9. [PubMed: 7985649]
33. Stampfer MJ, Willett WC, Speizer FE, Dysert DC, Lipnick R, Rosner B, Hennekens CH. Test of the National Death Index. American journal of epidemiology 1984;119: 837–9. [PubMed: 6720679]
34. Willett WC, Sampson L, Stampfer MJ, Rosner B, Bain C, Witschi J, Hennekens CH, Speizer FE. Reproducibility and validity of a semiquantitative food frequency questionnaire. American journal of epidemiology 1985;122: 51–65. [PubMed: 4014201]
35. Salvini S, Hunter DJ, Sampson L, Stampfer MJ, Colditz GA, Rosner B, Willett WC. Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. International journal of epidemiology 1989;18: 858–67. [PubMed: 2621022]
36. Feskanich D, Rimm EB, Giovannucci EL, Colditz GA, Stampfer MJ, Litin LB, Willett WC. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. Journal of the American Dietetic Association 1993;93: 790–6. [PubMed: 8320406]
37. Chiuve SE, Fung TT, Rimm EB, Hu FB, McCullough ML, Wang M, Stampfer MJ, Willett WC. Alternative dietary indices both strongly predict risk of chronic disease. The Journal of nutrition 2012: jn. 111.157222.
38. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. The New England journal of medicine 2003;2003: 2599–608.
39. Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller ER, Simons-Morton DG. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. New England journal of medicine 2001;344: 3–10. [PubMed: 11136953]
40. Moeller SM, Reedy J, Millen AE, Dixon LB, Newby P, Tucker KL, Krebs-Smith SM, Guenther PM. Dietary patterns: challenges and opportunities in dietary patterns research. Journal of the American Dietetic Association 2007;107: 1233–9. [PubMed: 17604756]
41. Schulze MB, Hoffmann K, Kroke A, Boeing H. An approach to construct simplified measures of dietary patterns from exploratory factor analysis. British Journal of Nutrition 2003;89: 409–18. [PubMed: 12628035]
42. Tabung FK, Smith-Warner SA, Chavarro JE, Wu K, Fuchs CS, Hu FB, Chan AT, Willett WC, Giovannucci EL. Development and validation of an empirical Dietary Inflammatory Index. The Journal of nutrition 2016;146: 1560–70. [PubMed: 27358416]
43. Tabung FK, Wang W, Fung TT, Hu FB, Smith-Warner SA, Chavarro JE, Fuchs CS, Willett WC, Giovannucci EL. Development and validation of empirical indices to assess the insulinaemic potential of diet and lifestyle. British Journal of Nutrition 2016;116: 1787–98.
44. Downer MK, Kenfield SA, Stampfer MJ, Wilson KM, Dickerman BA, Giovannucci EL, Rimm EB, Wang M, Mucci LA, Willett WC. Alcohol Intake and Risk of Lethal Prostate Cancer in the Health Professionals Follow-Up Study. Journal of Clinical Oncology 2019;37: 1499–511. [PubMed: 31026211]
45. Abar L, Sobiecki J, Cariolou M, Nanu N, Vieira A, Stevens C, Aune D, Greenwood D, Chan D, Norat T. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Annals of Oncology 2019;30: 528–41. [PubMed: 30753270]
46. Schwedhelm C, Boeing H, Hoffmann G, Aleksandrova K, Schwingshackl L. Effect of diet on mortality and cancer recurrence among cancer survivors: a systematic review and meta-analysis of cohort studies. Nutrition reviews 2016;74: 737–48. [PubMed: 27864535]
47. Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. Archives of internal medicine 2008;168: 713–20. [PubMed: 18413553]
48. Fung TT, McCullough ML, Newby P, Manson JE, Meigs JB, Rifai N, Willett WC, Hu FB. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction–. The American journal of clinical nutrition 2005;82: 163–73. [PubMed: 16002815]

49. Fung TT, Rimm EB, Spiegelman D, Rifai N, Tofler GH, Willett WC, Hu FB. Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk–. The American journal of clinical nutrition 2001;73: 61–7. [PubMed: 11124751]

Novelty and impact:

Most studies of survival of multiple myeloma focus on treatment or other clinical variables. In 423 multiple myeloma patients, we prospectively examined pre-diagnosis diet quality and survival and found that patients who adhered to healthier pre-diagnosis dietary patterns had 15–24% lower mortality from multiple myeloma (with similar findings for all-cause mortality). If confirmed, this novel evidence for an association of dietary habits with multiple myeloma survival may empower patients and inform clinical practice.

Table 1.

Age-standardized baseline characteristics of patients with multiple myeloma[a]

	NHS (1986; 233 women)[a]	HPFS (1988; 190 men)[a]
Age at diagnosis, year[b]	69.6 (7.8)	72.3 (9.2)
BMI at diagnosis, kg/m^2	27.0 (5.8)	26.5 (4.0)
Time between FFQ return and diagnosis, month	25.1 (14.2)	26.9 (14.9)
Comorbidity score, number of diseases	1.0 (1.1)	1.2 (1.3)
Diet intake		
Calorie intake, kcal/d	1665 (523)	2027 (613)
Alcohol, g/d	6.0 (10.4)	9.9 (13.8)
Processed meat, servings/wk	2.2 (2.3)	2.9 (5.2)
Red meat, servings/wk	4.4 (2.9)	4.2 (2.9)
Poultry, serving/wk	2.1 (1.5)	2.8 (2.4)
Fish, serving/wk	2.3 (1.8)	3.2 (2.4)
Whole grain, serving/wk	6.5 (7.3)	10.2 (9.5)
Refined carbohydrates, servings/wk	7.6 (6.0)	8.9 (7.8)
Fruits, serving/wk	10.2 (6.7)	12.4 (9.0)
Vegetables, serving/wk	16.3 (9.3)	21.1 (14.5)
Nuts, serving/wk	2.1 (3.1)	2.7 (3.6)
Coffee, servings/wk	16.0 (12.9)	26.6 (19.3)
Sugar sweetened beverage, servings/wk	1.9 (3.7)	2.3 (3.9)

Abbreviation: NHS, Nurses' Health Study; HPFS, Health Professionals Follow-up Study; BMI, body mass index; FFQ, food frequency questionnaire.

[a]Data were presented as mean (SD). Baseline years were defined from the application of a 2-year lag to the first years when food frequency questionnaires had sufficient data to derive the dietary patterns.

[b]Age was not standardized.

Table 2.

Association between pre-diagnosis dietary pattern and multiple myeloma-specific mortality in patients with multiple myeloma (NHS, 1986–2016 and HPFS, 1988–2016) *

	HR (95% CI) per 1-SD increase[c,d]			
	Women (NHS)	Men (HPFS)	Pooled[e]	P-value
Presumed healthy dietary patterns (higher score=healthier dietary habits)				
AHEI-2010				
Age and energy adjusted[a]	0.73 (0.62 to 0.85)	0.79 (0.66 to 0.94)	0.75 (0.67 to 0.85)	<.001
Multivariable adjusted[b]	0.71 (0.60 to 0.84)	0.82 (0.68 to 1.00)	0.76 (0.67 to 0.87)	<.001
aMED				
Age and energy adjusted[a]	0.88 (0.75 to 1.04)	0.87 (0.72 to 1.05)	0.88 (0.78 to 0.99)	0.04
Multivariable adjusted[b]	0.86 (0.72 to 1.02)	0.84 (0.69 to 1.02)	0.85 (0.75 to 0.97)	0.01
DASH				
Age and energy adjusted[a]	0.89 (0.77 to 1.03)	0.92 (0.78 to 1.10)	0.90 (0.80 to 1.00)	0.06
Multivariable adjusted[b]	0.84 (0.72 to 0.98)	0.87 (0.73 to 1.05)	0.85 (0.76 to 0.95)	0.006
Prudent				
Age and energy adjusted[a]	0.75 (0.63 to 0.90)	0.77 (0.62 to 0.96)	0.76 (0.66 to 0.87)	<.001
Multivariable adjusted[b]	0.74 (0.61 to 0.89)	0.79 (0.63 to 1.00)	0.76 (0.66 to 0.87)	<.001
Presumed unhealthy dietary patterns (higher score=less healthy dietary habits)				
Western				
Age and energy adjusted[a]	1.10 (0.92 to 1.32)	1.21 (0.96 to 1.52)	1.13 (0.98 to 1.31)	0.09
Multivariable adjusted[b]	1.30 (1.07 to 1.59)	1.21 (0.95 to 1.53)	1.24 (1.07 to 1.44)	0.005
EDIP[f]				
Age and energy adjusted[a]	1.17 (0.99 to 1.38)	1.07 (0.91 to 1.25)	1.11 (0.99 to 1.25)	0.06
Multivariable adjusted[b]	1.15 (0.96 to 1.37)	1.05 (0.89 to 1.24)	1.09 (0.97 to 1.23)	0.15
EDIR[f]				
Age and energy adjusted[a]	1.24 (1.04 to 1.48)	1.05 (0.85 to 1.28)	1.17 (1.03 to 1.33)	0.02
Multivariable adjusted[b]	1.21 (1.01 to 1.46)	1.08 (0.88 to 1.34)	1.16 (1.02 to 1.33)	0.03
EDIH[f]				
Age and energy adjusted[a]	1.25 (1.03 to 1.53)	1.13 (0.93 to 1.37)	1.20 (1.04 to 1.38)	0.01
Multivariable adjusted[b]	1.20 (0.99 to 1.47)	1.11 (0.90 to 1.36)	1.17 (1.01 to 1.35)	0.03

Abbreviation: NHS, Nurses' Health Study; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; CI, confidence interval; SD, standard deviation; AHEI, alternate healthy eating index-2010; aMED, alternate Mediterranean diet; DASH, dietary approaches to stop hypertension; EDIP, empirical dietary inflammatory pattern; EDIR, empirical dietary index for insulin resistance; EDIH, empirical dietary index for hyperinsulinemia.

* We applied a 2-year lag to the pre-diagnosis dietary patterns assessed closest to MM diagnosis.

[a] Adjusted for age at diagnosis in years (continuous) and pre-diagnosis energy intake (continuous).

[b] Additionally adjusted for pre-diagnosis body mass index (<22, 22 to 24.9, 25 to 29.9, ≥30 kg/m^2), time between food frequency questionnaire return date and multiple myeloma diagnosis (<median or ≥median), year of diagnosis (<2000 or ≥2000), comorbidity score (continuous).

[c] Sex-specific standard deviation was used.

[d] Case/total participants: 166/233 for women and 129/190 for men.

[e] The pooled analysis was additionally stratified by sex. P values for interaction between dietary pattern and sex in the multivariable adjusted models were: AHEI, P-interaction=0.19; aMED, P-interaction =0.70; DASH, P-interaction=0.90; Prudent, P-interaction=0.87; Western, P-interaction=0.21; EDIP, P-interaction=0.40; EDIR, P-interaction=0.38; EDIH, P-interaction=0.39.

[f] Empirically derived dietary indices, which were derived using biomarkers to capture dietary inflammatory (EDIP) or insulinemic (EDIR, insulin resistance; EDIH, hyperinsulinemia) potential (Tabung et al. J Nutr 2016;146: 1560–70; Tabung et al. Br J Nutr 2016;116: 1787–98). Higher scores indicate a higher inflammatory or insulinemic potential of the diet.

Table 3.

Association between pre-diagnosis dietary pattern and all-cause mortality in patients with multiple myeloma (NHS, 1986–2016 and HPFS, 1988–2016) *

	HR (95% CI) per 1-SD increase[c,d]			
	Women (NHS)	Men (HPFS)	Pooled[e]	P-value
Presumed healthy dietary patterns (higher score=healthier dietary habits)				
AHEI-2010				
Age and energy adjusted[a]	0.76 (0.65 to 0.88)	0.81 (0.69 to 0.95)	0.78 (0.70 to 0.87)	<.001
Multivariable adjusted[b]	0.74 (0.63 to 0.87)	0.84 (0.71 to 1.00)	0.80 (0.71 to 0.89)	<.001
aMED				
Age and energy adjusted[a]	0.91 (0.78 to 1.07)	0.88 (0.74 to 1.03)	0.89 (0.80 to 1.00)	0.05
Multivariable adjusted[b]	0.90 (0.76 to 1.05)	0.85 (0.71 to 1.00)	0.87 (0.78 to 0.98)	0.02
DASH				
Age and energy adjusted[a]	0.90 (0.78 to 1.03)	0.92 (0.79 to 1.08)	0.90 (0.81 to 1.00)	0.05
Multivariable adjusted[b]	0.85 (0.74 to 0.99)	0.89 (0.76 to 1.05)	0.86 (0.77 to 0.96)	0.006
Prudent				
Age and energy adjusted[a]	0.79 (0.67 to 0.94)	0.80 (0.66 to 0.97)	0.79 (0.69 to 0.89)	<.001
Multivariable adjusted[b]	0.78 (0.65 to 0.93)	0.81 (0.66 to 0.99)	0.79 (0.69 to 0.90)	<.001
Presumed unhealthy dietary patterns (higher score=less healthy dietary habits)				
Western				
Age and energy adjusted[a]	1.06 (0.89 to 1.26)	1.23 (1.00 to 1.52)	1.12 (0.98 to 1.28)	0.09
Multivariable adjusted[b]	1.24 (1.02 to 1.51)	1.20 (0.96 to 1.49)	1.19 (1.04 to 1.37)	0.01
EDIP[f]				
Age and energy adjusted[a]	1.18 (1.00 to 1.38)	1.10 (0.96 to 1.26)	1.13 (1.02 to 1.26)	0.02
Multivariable adjusted[b]	1.16 (0.98 to 1.38)	1.07 (0.93 to 1.24)	1.11 (0.99 to 1.24)	0.06
EDIR[f]				
Age and energy adjusted[a]	1.22 (1.03 to 1.44)	1.07 (0.89 to 1.28)	1.16 (1.03 to 1.31)	0.01
Multivariable adjusted[b]	1.19 (0.99 to 1.42)	1.08 (0.90 to 1.31)	1.16 (1.03 to 1.32)	0.02
EDIH[f]				
Age and energy adjusted[a]	1.24 (1.03 to 1.51)	1.15 (0.96 to 1.37)	1.21 (1.06 to 1.37)	0.005
Multivariable adjusted[b]	1.21 (0.99 to 1.46)	1.11 (0.93 to 1.33)	1.18 (1.03 to 1.34)	0.02

Abbreviation: NHS, Nurses' Health Study; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; CI, confidence interval; SD, standard deviation; AHEI, alternate healthy eating index-2010; aMED, alternate Mediterranean diet; DASH, dietary approaches to stop hypertension; EDIP, empirical dietary inflammatory pattern; EDIR, empirical dietary index for insulin resistance; EDIH, empirical dietary index for hyperinsulinemia.

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[c] Sex-specific standard deviation was used.

[d] Case/total participants: 181/233 for women and 164/190 for men.

[e] The pooled analysis was additionally stratified by sex. P values for interaction between dietary pattern and sex in the multivariable adjusted models were: AHEI, P-interaction=0.20; aMED, P-interaction=0.56; DASH, P-interaction=0.83; Prudent, P-interaction=0.82; Western, P-interaction=0.12; EDIP, P-interaction=0.36; EDIR, P-interaction=0.35; EDIH, P-interaction=0.32.

[f] Empirically derived dietary indices, which were derived using biomarkers to capture dietary inflammatory (EDIP) or insulinemic (EDIR, insulin resistance; EDIH, hyperinsulinemia) potential (Tabung et al. J Nutr 2016;146: 1560–70; Tabung et al. Br J Nutr 2016;116: 1787–98). Higher scores indicate a higher inflammatory or insulinemic potential of the diet.