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ORIGINAL ARTICLE

Effects of Glucocorticoids on Weight Change During the Treatment of Wegener's Granulomatosis

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Objective. **Weight gain is a side effect of glucocorticoid (GC) use, but the natural history and health implications of changes in weight that occur during the treatment of inflammatory disease are not understood.**

Methods. **We evaluated data from the Wegener's Granulomatosis Etanercept Trial. Patients were categorized according to clinical outcome at 1 year: remission (no disease flares), single flare, or multiple flares. Risk factors for gaining ≥10 kg were examined in multivariate models.**

Results. **Weights at baseline and 1 year were available for 157 (93%) of the 168 patients analyzed. During year 1, the mean cumulative prednisone dosage in the multiple flares subgroup was 7.9 gm, compared with 6.0 gm and 3.9 gm in the single flare and remission subgroups, respectively ($P < 0.001$). Patients in these subgroups gained an average of 2.6 kg, 4.1 kg, and 5.8 kg, respectively ($P = 0.005$). Weight gain did not correlate with cumulative GC dose (R = 0.10, $P = 0.25$). Thirty-five patients (22.3%) gained and maintained ≥10 kg in the first year. New diagnosis of Wegener's granulomatosis at baseline was an independent predictor of gaining ≥10 kg at 1 year (odds ratio 19.7, 95% confidence interval 2.4–162.6, $P = 0.006$). Among the 78 patients in the remission subgroup, 40 sustained remissions through the 2-year time point. For these 40 patients, the mean weight gained at year 1 did not regress by the end of year 2, despite the absence of continued GC use.**

Conclusion. **Disease control was associated with lower cumulative GC doses but greater weight gain. More than one-fifth of patients gained >10 kg in the first year of treatment. The quantity of weight gained by patients during treatment has potential future health implications.**

INTRODUCTION

Glucocorticoids (GCs) are integral to the treatment of inflammatory diseases, many of which are characterized by recurrent disease flares that require repeated GC courses or continuous use. Common conditions such as obstructive and reactive airway diseases are frequently treated with intermittent, short courses of GCs to maintain disease control (1,2). Other conditions such as inflammatory bowel disease, systemic lupus erythematous, and systemic vasculitis require prolonged courses of GCs to induce remission or prevent relapses (3–6). In developed countries, the prevalence of GC use is nearly 1% (7–9).

Despite their unquestionable benefits in many diseases,

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GCs also have numerous well-recognized side effects, including weight gain. However, the natural history of weight gain associated with GC use is not well understood. To our knowledge, no study has investigated the amount, duration, and course of weight change caused by GC use. Wegener's granulomatosis (WG), one of the most common forms of systemic vasculitis, is the paradigm of diseases associated with antineutrophil cytoplasmic antibodies. GCs, combined with other immunosuppressive agents such as cyclophosphamide or methotrexate, are the mainstay of therapy for WG (6,10,11). The GC regimen used to treat WG is typical of that used in the therapy of many inflammatory conditions, i.e., high initial doses followed by a tapering course over many months. For patients who experience disease flares during or after the period of remission induction, additional courses of GC are required. For some patients with persistently active disease, maintenance therapy with the lowest effective dose of GC is necessary.

In this study, we assessed the quantity, duration, and progression of weight change in patients who received GCs for active WG under a clinical trial protocol. Our study had 3 objectives. First, we tested the hypothesis that a stepwise increase in weight gain across 3 study subgroups would be observed. We anticipated that patients who achieved remission and required no more prednisone after 6 months (the remission subgroup) would gain less weight than those who experienced single disease flares over the first year of treatment (the single flare subgroup), who in turn would gain less weight than those who experienced multiple disease flares over that period (the multiple flare subgroup). Second, we hypothesized that patients who achieved disease remission and maintained the remission state would lose the weight gained during the period of GC treatment. Finally, we performed a multivariate analysis to determine risk factors for gaining and maintaining a minimum of 10 kg from baseline over the first year of treatment.

PATIENTS AND METHODS

Data from the Wegener's Granulomatosis Etanercept Trial (WGET) formed the basis of this study (10). Members of the WGET are listed in Appendix A. The WGET population was well suited for studying the impact of GCs on weight gain because of the tendency of many patients with WG to experience disease flares and because of the requirement for repeated GC courses to treat such flares. Moreover, data from the WGET cohort included detailed evaluations of disease status, e.g., disease activity (12), damage (13,14), quality of life, and medication use at sequential time points during the trial.

WGET design. The WGET was a randomized, double-blind, placebo-controlled trial designed to test the efficacy of etanercept (Enbrel; Amgen Corporation, Thousand Oaks, CA), a soluble inhibitor of tumor necrosis factor, in combination with conventional therapy for the maintenance of remission (15). Details of the trial design, the baseline evaluation of the cohort, and the overall trial results have been published (10,15,16). The primary outcome in the WGET was the ability of the experimental medication to maintain disease remissions as conventional immunosuppressive agents were tapered. A total of 180 patients with active WG either newly diagnosed or recurrent at the time of trial entry (previously diagnosed) were enrolled and followed for a median of 27 months.

Treatment regimen. Patients with severe WG, defined as disease posing an immediate threat to the patient's life or the function of a vital organ (15), were treated with cyclophosphamide and prednisone (0.5–1 mg/kg/day). Methylprednisolone (1 gm/day for 3 days) could be administered at the investigator's discretion at the start of therapy. The initial prednisone regimen and its taper are shown in Figure 1. Patients with limited WG at enrollment, defined as disease that did not pose an immediate threat to either life or vital organ function, were treated with methotrexate and the same GC regimen as those with severe disease, except that patients with limited disease did not receive methylprednisolone pulses. Following 1 month of high-dose GC treatment, a taper was initiated with the goal of discontinuing prednisone within 6 months of randomization.

Disease flare led to the resumption of systemic therapy (15). Patients with severe flares were treated with regimens of GCs and cyclophosphamide identical to those received by patients who presented initially with severe disease. Patients who experienced limited flares received increased doses of GCs, methotrexate, or both. After 4 weeks at the increased GC dose, the tapering regimen was resumed.

Baseline data collection. At enrollment, data on demographics, clinical characteristics, treatment history, and selected medical history items were collected. Disease-specific information (i.e., onset and diagnosis, specific or-

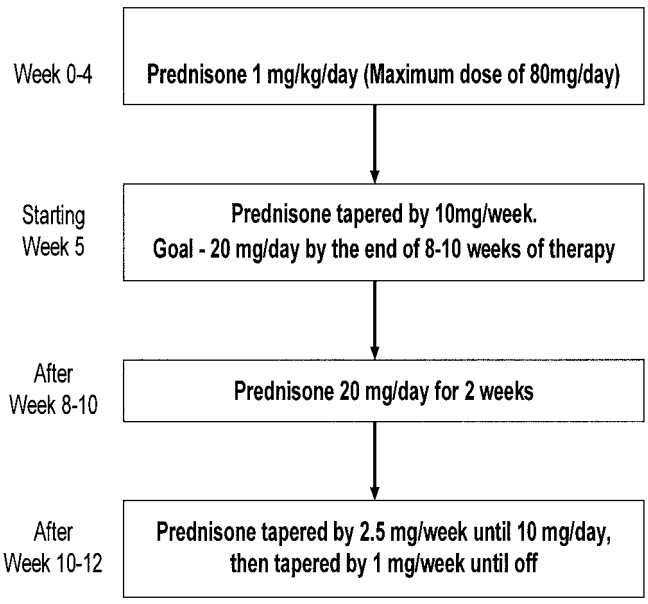

Figure 1. Prednisone tapering regimen. Patients with severe disease could receive intravenous methylprednisone (1 gm/day for 3 days) at the start of treatment.

gan involvement, and disease flare history) was also collected. The duration of use and maximum doses of all medications used to treat WG were recorded.

Followup. Followup evaluations were scheduled at 6 weeks, 12 weeks, and every 3 months thereafter. At each trial visit, interim medical events were captured on standardized followup history forms. At followup visits, patients' weight, medications, and medication doses were recorded. Patients were followed to a common closeout date, designated to be 1 year after the last patient was enrolled.

Body mass index. Patients' height measured at baseline and weight recorded at each trial visit were used to calculate body mass index (BMI; kg/m^2). We classified patients at baseline into 1 of 6 National Heart, Lung, and Blood Institute–defined categories for BMI (17): underweight (BMI $\leq$18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), obesity class I (BMI 30–34.9 kg/m^2), obesity class II (BMI 35–39.9 kg/m^2), and obesity class III (BMI $\geq$40 kg/m^2).

Study subgroups. We defined 3 patient subgroups: remission (patients who achieved disease control and tapered off GC therapy without having to resume it during the first year of therapy [n = 78]), single flare (patients who experienced 1 disease flare during the first year of treatment [n = 42]), and multiple flares (patients who experienced more than 1 disease flare during the first year of therapy [n = 37]).

Statistical analysis. All GC doses administered during the trial including methylprednisolone pulses were converted to prednisone equivalents for the purposes of tabulating cumulative doses. In initial analyses, univariate differences between the study subgroups in categorical variables were evaluated using either chi-square tests or Fisher's exact sign test. Continuous variables were evaluated by the nonparametric Kruksal-Wallis test.

We selected 1 year, the minimum length of time in the trial for any patient, as the point at which to evaluate our primary weight change outcome. Because of the importance of longer-term followup studies in obesity, we also evaluated time points beyond 1 year for patients for whom such data were available. The change in absolute weight from visit to visit was calculated by subtracting patients' weight at every visit from the weight at baseline. The significance of mean changes in weight was evaluated by either the Mann-Whitney test (for comparisons of 2 subgroups) or the Kruksal-Wallis test (for comparisons of 3 subgroups).

Multiple logistic regression analysis was used to identify odds ratios for gaining and maintaining at least 10 kg more than baseline weight during the first year of treatment. The 10-kg weight gain is an arbitrary cutoff that most patients can relate to and would deem significant. Variables examined in the multivariate analysis included baseline weight; age; sex; smoking history; disease severity; new diagnosis of WG at enrollment; treatment with etanercept; hypertension; serum creatinine ($\geq$1.4 mg/dl or $<$1.4 mg/dl); and baseline disease activity (12), damage (13,14), and quality of life scores (18).

RESULTS

Baseline characteristics of patients as a function of disease course. Among the 180 patients with WG originally enrolled in the trial, 6 died and 6 were lost to followup during the first year. Thus, baseline and 1-year followup data related to weight and BMI were available for 157 (93%) of the 168 patients. The baseline characteristics of all 157 patients and the 3 subgroups are shown in Table 1.

The mean $\pm$ SD BMI at trial entry was 29 $\pm$ 7 kg/m^2. Thirty-eight percent of all patients were obese (BMI $\geq$30 kg/m^2) at baseline. There were significantly fewer patients in the multiple flares group who had severe WG, and significantly fewer who were newly diagnosed. In addition, patients in the multiple flares group had lower disease activity scores (Birmingham Vasculitis Activity Score for WG) at baseline, but higher damage scores (Vasculitis Damage Index).

Doses of GCs in the remission, single flare, and multiple flare subgroups. The cumulative dose of GCs increased as a function of the number of disease flares in the first year (Figure 2). At the first followup visit (6 weeks), all 3 subgroups had received similar cumulative doses of GCs (mean $\pm$ SD prednisone dosage 1.92 $\pm$ 1.00 gm). However, at the 1-year interval, patients in the multiple flares subgroup had received 7.90 $\pm$ 3.50 gm of prednisone, compared with 6.00 $\pm$ 2.70 gm and 3.90 $\pm$ 2.30 gm for patients in the single flare and remission subgroups, respectively, over the same period ($P \leq 0.001$) (Figure 2).

Weight gain among all patients and the 3 subgroups. The 3 subgroups had similar baseline weights (Table 1). For the entire cohort, the mean $\pm$ SD weight gain at 1 year was approximately 3.9 $\pm$ 6.9 kg, representing a 4.4% increase from the mean baseline weight. Thirty-eight (24%) of the 157 patients gained $\geq$10 kg over the first year of treatment, with a mean increase in body weight of 11.2 kg (13.5% over their mean baseline weight).

The weight gained by all patients and the 3 subgroups at sequential time points is shown in Figure 3. Between the 3- and 6-month followup visits, patients in the multiple flare, single flare, and remission subgroups reached mean $\pm$ SD maximum weight gains of 2.6 $\pm$ 4.9 kg, 4.1 $\pm$ 4.4 kg, and 5.8 $\pm$ 5.8 kg, respectively ($P = 0.011$). The mean percent gains in weight at 1 year by patients in the multiple flares, single flare, and remission subgroups were 3.2%, 4.3%, and 5.1%, respectively. Weight gain did not correlate with cumulative GC dose ($R = 0.10$, $P = 0.25$).

Weight gain in newly and previously diagnosed patients. The quantities of weight gained by patients who were newly diagnosed with WG compared with those who

Table 1. Baseline features of the remission, single flare, and multiple flares subgroups*

Feature	Overall (n = 157)	Remission (n = 78)	Single flare (n = 42)	Multiple flares (n = 37)	*P*
Age, mean ± SD years	49 ± 15	51 ± 16	48 ± 12	45 ± 15	0.13†
Male sex	58	63	57	49	0.35
White race	92	95	86	92	0.22
Height, mean ± SD cm	173 ± 11	173 ± 10	173 ± 11	171 ± 12	0.37†
Weight, mean ± SD kg	87 ± 22	86 ± 21	93 ± 25	82 ± 21	0.89†
BMI, mean ± SD kg/m^2	29 ± 7	29 ± 7	31 ± 7	28 ± 6	0.89†
BMI categories, kg/m^2					
Underweight (BMI <18.5)	1.9	3.8	0	0	0.23‡
Normal weight (BMI 18.5–24.9)	26	31	12	32	0.05
Overweight (BMI 25–29.9)	34	33.3	43	27	0.32
Obese (BMI ≥30)	38.1	31.6	45	40.1	0.25
Newly diagnosed	45	56	45	19	0.014
Severe disease	68	74	71	51	0.041
Mean serum creatinine, mg/dl	1.5	1.7	1.5	1.2	0.33†
Serum creatinine <1.5 mg/dl	76	72	76	86	0.22
Never smoked	56	59	45	62	0.24
Menopause (% of women)	55	62	44	53	0.49
Hypertension	31	27	45	22	0.13
BVAS/WG, mean ± SD	6.8 ± 3.6	7.4 ± 3.8	6.8 ± 3.5	5.6 ± 2.7	0.03†
VDI, mean ± SD	1.3 ± 1.7	1.0 ± 1.6	1.4 ± 1.7	2.0 ± 1.8	0.004†
SF-36, mean ± SD	49 ± 28	46 ± 28	57 ± 29	45 ± 26	0.10†
PCS	33 ± 10	33 ± 10	34 ± 9	33 ± 11	0.85†
MCS	44 ± 12	44 ± 12	46 ± 12	42 ± 11	0.18†
Etanercept group	49	50	55	41	0.44

* Values are the percentage unless otherwise indicated. BMI = body mass index; BVAS/WG = Birmingham Vasculitis Activity Score for Wegener's Granulomatosis; VDI = Vasculitis Damage Index; SF-36 = Short Form 36; PCS = Physical Component Score; MCS = Mental Component Score.
† Kruksal-Wallis test.
‡ Fisher's exact test.

were previously diagnosed at baseline are depicted in Figure 4. Seventy (45%) of the 157 patients had new diagnoses of WG at baseline; 87 (55%) had undergone courses of treatment for WG prior to the disease flare leading to trial entry. The baseline weights were lower in patients with new diagnoses of WG compared with patients who entered the trial with a previous diagnosis of WG (mean ± SD 82.8 ± 21.6 kg versus 88.9 ± 22.2 kg; $P = 0.043$). Although the peak weight gain occurred at 6 months for both groups, the newly diagnosed patients gained 6.3 ± 6.8 kg (7.3% increase from baseline weight) over the first year, compared with only 1.9 ± 6.4 kg (3.1% increase from baseline weight) for the previously diagnosed patients ($P < 0.0001$).

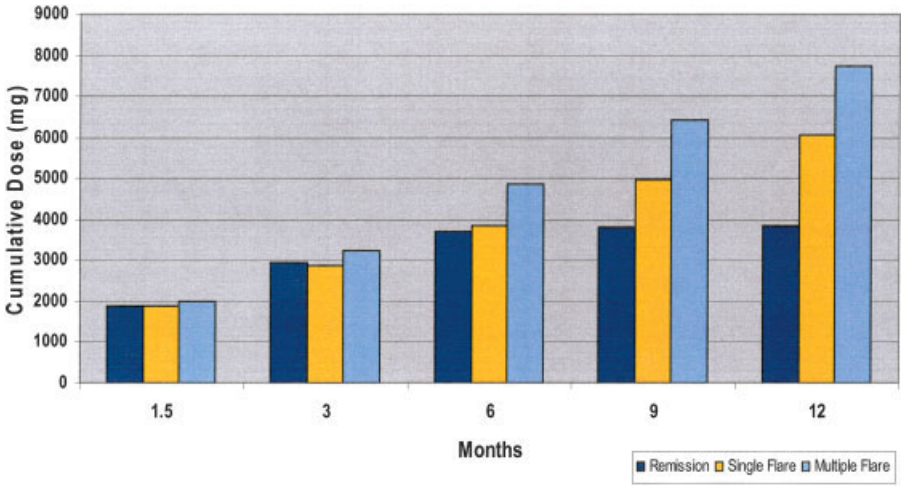

Figure 2. Cumulative glucocorticoids used from baseline. At 6, 9, and 12 months, *P* values were < 0.001.

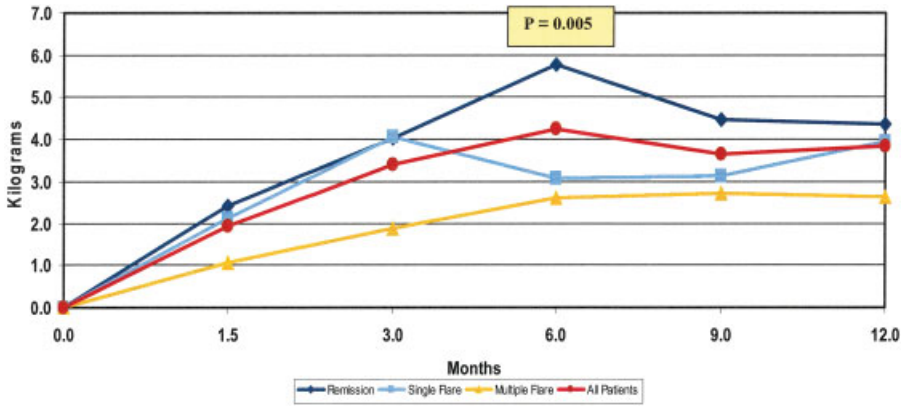

Figure 3. Average weight gain of all patients and 3 study subgroups.

Retention of weight at 2 years and beyond. Among the 103 patients in the cohort with at least 2 years of followup, the mean weight gain at 6 months was 4.2 ± 7.2 kg. Forty patients achieved and maintained disease remissions through the 2-year visit. Among these 40 patients, the mean weight gained by 1 year was maintained through the end of the second year (mean ± SD weight 5.6 ± 7.0 kg), despite the absence of additional GC use after month 6. Among the 25 patients with followup at 2 years who had experienced multiple disease flares, the mean weight gained at the 2-year time point was 1.03 ± 5.22 kg (P = 0.014 compared with sustained remission group).

Multivariate analysis. Results of the multivariate analysis are shown in Table 2. New diagnosis of WG at baseline had the strongest association with a 10-kg weight gain (odds ratio 19.7, 95% confidence interval 2.4–162.6, P = 0.006) and was the only significant risk factor for this complication. Etanercept treatment was not associated with weight gain, either in univariate or multivariate analyses (data not shown). Although male patients gained more weight at 1 year than did female patients (mean ± SD 4.9 ± 6.6 kg versus 2.4 ± 7.1 kg; P = 0.02), sex was not predictive of gaining and maintaining at least 10 kg more than baseline weight.

DISCUSSION

Despite the role of GCs as the cornerstone of therapy for a broad array of illnesses, to our knowledge this study is the first to analyze the degree and duration of weight change over the course of high-dose GC treatment for inflammatory disease. Our findings indicate points of concern related to the quantities of weight gained by many patients treated with GCs and the long-term health implications of GC use. Twenty-two percent of the patients treated with GCs in this study gained a minimum of 10 kg and maintained this weight at the time of their 1-year followup. In these patients, the mean weight gained (11.2 kg) constituted a 13.5% increase over their baseline weight. Even patients who required no additional GC courses for up to 2 years after entry failed to lose the weight they had gained during the first 6 months of treatment.

We hypothesized that the patients who achieved and maintained disease remissions would lose any weight gained during the initial treatment of their disease flare once they stopped taking GCs. In fact, patients tended to retain the weight gained during GC treatment for the entire duration of followup. The 40 patients who achieved and maintained disease remissions over the first 2 years of followup were actually heavier at year 2 than they were upon completion of their GC taper (4.2 kg at month 6

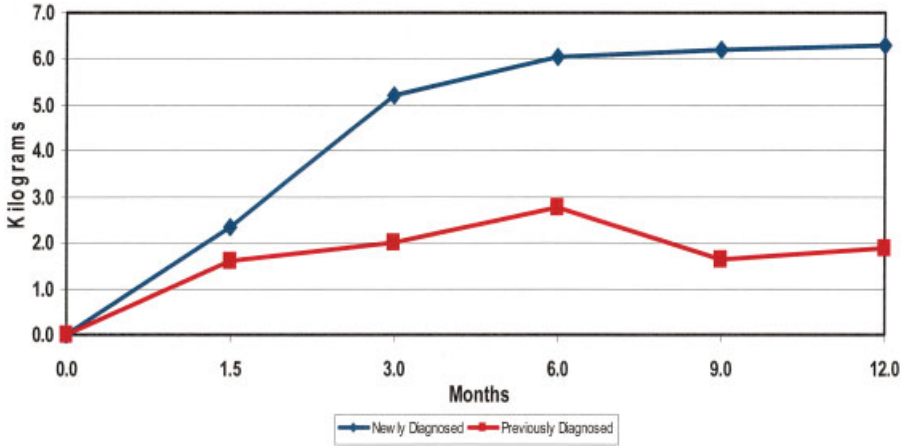

Figure 4. Average weight gain in patients with newly diagnosed versus previously diagnosed Wegener's granulomatosis at baseline. P values at 3, 6, 9, and 12 months all < 0.0001.

Table 2. Multivariate model risk factors for predicting 10-kg weight gain*

Risk factors	OR	95% CI	*P*
Severe	1.6	0.3–7.7	0.54
Limited	1.0		
New diagnosis	19.7	2.4–162.7	0.006
Previous diagnosis	1.0		
Male	1.3	0.3–4.6	0.72
Female	1.0		
No history of smoking	0.3	0.1–1.0	0.06
History of smoking	1.0		
Placebo	0.99	0.3–3.4	0.98
Etanercept	1.0		
Hypertension	1.0	0.3–3.9	0.99
No hypertension			
Age	1.02	0.9–1.1	0.35
Baseline weight	0.99	0.9–1.0	0.45
Serum creatinine	1.4	0.8–2.4	0.22
BVAS/WG	0.917	0.8–1.1	0.35
VDI	0.84	0.5–1.3	0.47
SF-36			
PCS	1.023	0.9–1.1	0.52
MCS	1.01	0.9–1.1	0.61

* OR = odds ratio; 95% CI = 95% confidence interval; see Table 1 for additional definitions.

versus 5.6 kg at year 2), despite the absence of any interim GC therapy. Thus, patients who achieved and sustained disease remission through year 2 were 12 pounds heavier than when they entered the study. As noted, 38% of patients were already obese when they entered the study. The tendency to maintain the weight gain during the treatment of active inflammation is particularly concerning in view of the proclivity of WG (and other inflammatory illnesses) to recur and to require further GC treatment.

The results of this study suggest complex relationships between disease control, cumulative GC dose, and weight gain. We had hypothesized that more disease flares would be associated with higher GC use and greater weight gain, leading to a stepwise increase in weight gain across the 3 subgroups (multiple flares > single flare > remission). Indeed, patients in the multiple flares subgroup received 32% more prednisone than those in the single flare subgroup and 100% more than those in the remission subgroup. Paradoxically, by the end of the first year, patients in the multiple flares subgroup had gained the least amount of weight among the 3 subgroups.

The relationships between GC use and weight gain observed in this trial have several potential explanations. First, weight loss caused by chronic inflammation has been demonstrated in a number of disorders, including cancer, rheumatoid arthritis, and the frailty syndrome (sarcopenia) (19–28). The results of our study suggest that this is also true in WG. Such an effect of inflammation on the observed weight changes in this study is suggested by the association of multiple disease flares with the least amount of weight gain despite the highest cumulative doses of GC. Second, the fact that previously diagnosed patients gained less weight than newly diagnosed patients may be related to behavioral modification: patients with previous diagnoses of WG and familiarity with the effects of GCs may have altered their dietary habits or increased their exercise patterns to avoid excess weight gain from GC use. The fact that a new diagnosis of WG emerged as the strongest predictor of large weight gain in our multivariate analysis lends indirect support to this explanation. These data suggest that providing patients with behavioral strategies pertaining to exercise and diet might help diminish the impact of GC treatment on their weight.

An alternative explanation for part of the weight change observed in this study is that the weight gained was physiologic: weight gained over the course of treatment may represent a compensation for weight lost prior to the start of therapy. However, dramatic weight loss occurs in only a small minority of patients with WG (6,16). Moreover, the baseline weights in our cohort did not suggest that a substantial proportion of our patients had cachexia. On the contrary, 72% of the patients in our cohort were overweight or obese at trial entry, and only 2% were underweight at baseline (Table 1). Future studies that scrutinize the pattern of weight change from premorbid weights following a period of active disease will help address this question.

Weight gain, especially to the levels that constitute obesity, is strongly linked to a variety of diseases with major public health impact: type 2 diabetes, cardiovascular disease, knee osteoarthritis, sleep apnea, and many forms of cancer (29). Obesity decreases lifespan (30), reduces quality of life (31), diminishes work productivity (32), and has a substantial economic impact on society (33). Consequently, GC-associated weight gain has implications for the overall health of patients with inflammatory diseases, especially in light of the maintenance of this weight gain over time. The development of comorbidities prompted by GC-associated weight gain could complicate patients' future clinical care.

This study has several important strengths as well as potential weaknesses. First, although many complications of GC therapy have been evaluated thoroughly (34,35), the adverse effect of weight gain—the effect most obvious to patients—has been relatively neglected. Thus, our study opens a line of investigation into a neglected area not only for WG, but for a host of conditions associated with inflammation. Second, the clinical trial setting in which these data were collected permitted detailed analyses of the degree, timing, and duration of weight gain in a population of patients treated with a standardized regimen of GCs. The GC regimen used in this trial was comparable with standard therapy for many serious inflammatory illnesses. Therefore, it is likely that these data are relevant for populations of patients with other inflammatory illnesses whose treatment regimens are similar.

With regard to weaknesses, the number of patients studied in this investigation remains relatively small compared with the size of other disease cohorts even though the parent clinical trial is the largest prospective study of patients with WG performed to date. Confirmation of these findings in groups of patients with other systemic inflammatory illnesses will be important. Future analyses of such patterns may yield knowledge related to clinical interventions designed to mitigate GC-related weight gain.

In conclusion, we have quantified the degree and course of weight gain over the course of treatment with high-dose GCs. We observed a complex relationship between cumulative GC dose and weight gain, and documented an inverse correlation between disease activity and weight gain: patients with the best disease control had the lowest cumulative GC doses, yet gained the most weight. New diagnosis at the time of trial entry was the strongest risk factor for dramatic weight gain, suggesting that education at the start of therapy about the effects of GC may be an important prophylactic intervention. The retention of weight gained during treatment may have significant future health implications, even if the inflammatory disease remains in remission and no further GC therapy is required.

AUTHOR CONTRIBUTIONS

Dr. Stone had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study design. Wung, Davis, St.Clair, Stone.

Acquisition of data. Wung, Hoffman, Specks, Merkel, Spiera, Davis, St.Clair, McCune, Stone.

Analysis and interpretation of data. Wung, Anderson, Fontaine, Merkel, Davis, St.Clair, Stone.

Manuscript preparation. Wung, Anderson, Fontaine, Hoffman, Specks, Merkel, Spiera, Davis, St.Clair, McCune, Stone.

Statistical analysis. Wung, Anderson, Stone.

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APPENDIX A: THE WEGENER'S GRANULOMATOSIS ETANERCEPT TRIAL RESEARCH GROUP

Members of the Wegener's Granulomatosis Etanercept Trial are as follows: John H. Stone (Chairman, The Johns Hopkins Vasculitis Center); Gary S. Hoffman (Co-Chairman, Cleveland Clinic Foundation Center for Vasculitis Research and Care); Janet T. Holbrook, Curtis L. Meinert, John Dodge, Jessica Donithan, Nancy Min, Laurel Murrow, Maria Oziemkowska, Jacki Smith, Andrea K. Tibbs, Mark Van Natta (The Johns Hopkins University Center for Clinical Trials); Robert Spiera, Iresha Abeynayake, Rosanne Berman, Sandy Enuha (The Beth Israel Medical Center, New York); Peter A. Merkel, Rondi Gelbard, Melynn Nuite, Aileen Schiller (Boston University); David Blumenthal, Debora Bork, Tiffany Clark, Sonya L. Crook, Leonard H. Calabrese, Sharon Farkas, Sudhakar Sridharan, Kimberly Strom, William Wilke (The Cleveland Clinic Foundation); E. William St.Clair, Nancy B. Allen, Karen Rodin, Edna Scarlett (Duke University); David B. Hellmann, Matthew A. Marriott, Amanda M. Moore, Lourdes Pinachos, Michael J. Regan, Misty L. Uhlfelder (Johns Hopkins University); Ulrich Specks, Kristin Bradt, Kimberly Carlson, Susan Fisher, Boleyn Hammel, Kathy Mieras, Steven Ytterberg (The Mayo Clinic); John C. Davis, Anne Marie Duhme, Maureen Fitzpatrick, Ken Fye, Steve Lund (University of California, San Francisco); Joseph McCune, Billie Jo Coomer, Barbara Gilson, Hilary Haftel, Ana Morrel-Samuels, Sandra Neckel (University of Michigan); Noel R. Rose, C. Lynne Burek, Jobert Barin, Monica Talor (The Johns Hopkins University Immune Diseases Laboratory); Paul L. Canner (Maryland Medical Research Institute); Doyt L. Conn (Emory University); John H. Klippel (Arthritis Foundation); J. Richard Landis (University of Pennsylvania).