The Association Between the Nature and Timing of Dental Visits and C-reactive Protein Levels

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BACKGROUND

- Chronic inflammation has been established as a cardiovascular disease (CVD) risk factor.
- The most commonly used biomarker is C-reactive protein (CRP), a marker of systemic inflammation that is an acute phase reactant.
- In most individuals, CRP rises and decreases in parallel with acute inflammation.
- An association between active periodontal disease and elevated CVD risk has been proposed in the literature.[1,2]
- To date, studies of the link between dental disease and CVD have focused primarily on active periodontal disease and CRP.[3]
  - The impact of dental preventive visits on CRP levels is less clear.
- Given the association between dental disease and CVD, and the significant public health concerns due to cardiovascular morbidity and mortality, better understanding of this relationship is needed.

OBJECTIVE

- The purpose of this study is to investigate the association between time since last dental visit, reason for the last dental visit, and the likelihood of having elevated CRP.

METHODS

Study Design

- This study was a retrospective analysis of data from the National Health and Nutrition Examination Survey (NHANES).
- The institutional review board at RTI International determined that the conduct of this study was exempt from review.

Data Source

- NHANES is a nationally representative, periodic survey of the noninstitutionalized US civilian population conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention.
  - NHANES collects an extensive range of participant-level information on demographic characteristics, health conditions and behaviors, and clinical measures.
  - Participants are interviewed to obtain information on health history, behaviors, and risk factors, and are asked to undergo a physical examination. Vital statistics such as body mass index (BMI) and specimen samples (e.g., CRP, glycosylated hemoglobin [HbA1c], and white blood cell counts [WBC]) are collected as part of the examination.
  - Questions regarding participants' dental care are asked, including time since last dental visit and reason for visit.
- Sampling weights allow for generating results representative of the US population.
- We combined data from the 1999-2000, 2001-2002, and 2003-2004 NHANES for this study.

Study Sample Selection Criteria

- We excluded the following from the original NHANES data:
  - Participants under 20 years of age
  - Participants who were pregnant at the time of the survey
  - Participants who did not take part in the examination component of the survey
  - Participants who were missing any of the measures included in the subsequent regression model
  - Participants who reported never visiting a dentist
- Additionally, participants without a history of any dental visits were excluded, as were those with laboratory evidence for an acute inflammatory process (i.e., CRP measure > 1 mg/dL).

Study Measures

- The main study measure of interest, elevated CRP, was defined as a measured value > 0.30 mg/dL, and a corresponding dichotomous variable was created using this threshold.
- Time since last dental visit was categorized as < 6 months, 6 months to < 1 year, and 1+ years.
- The reason for last dental visit was dichotomized into "preventive" and "symptom-driven," with the former including self-referral for routine checkup/examination/cleaning and provider-initiated reminders for checkup/examination/cleaning, and the latter including self-referral due to a dental symptom and provider-initiated revisits for a problem discovered earlier.
- Demographic (i.e., age, sex, race/ethnicity) and lifestyle characteristics (i.e., smoking status, alcohol consumption, cholesterol-lowering drug use, and BMI) were documented.
- Underlying comorbidity burden and recent illness was documented, including history of asthma, rheumatoid arthritis, cancer, chronic bronchitis, diabetes, recent illness (i.e., a head or chest cold, stomach or intestinal illness with vomiting or diarrhea, flu, pneumonia, or ear infection in the past 30 days), and elevated WBC counts.

Analytic Approach

- All data management and analyses were conducted using the SAS for Windows (version 9) and Stata (version 11) statistical software packages, respectively.
- Descriptive analyses summarized study population characteristics.
- A multivariable, weighted logistic regression model described the association between time since last dental visit, reason for the last dental visit, and the likelihood of having elevated CRP, accounting for the NHANES's complex survey design.
  - Covariates in the model included time since last dental visit, reason for last dental visit, two-way interactions between time since and reason for the last dental visit, age, sex, race/ethnicity, smoking status, cholesterol-lowering drug use, alcohol consumption, BMI, recent illness status, WBC count > 11 (1,000 cells/μL), diabetes, and history of asthma, cancer, rheumatoid arthritis, and chronic bronchitis.

RESULTS

Demographic and Clinical Characteristics (Table 1)

- A total of 5,365 participants (weighted N = 88,356,553) met all study selection criteria.
  - 1,495 participants (weighted N = 23,186,024; 26.24%) had elevated CRP; 3,870 participants (weighted N = 65,170,529; 73.76%) had normal CRP.
- Among the two-way interactions of time since last dental visit and the reason for the last dental visit, several statistically significant differences were observed.
- Statistically significant unadjusted (descriptive) differences in the distribution of age and sex between the elevated and normal CRP groups were found.
- Similarly, significant, unadjusted differences in lifestyle characteristics (i.e., BMI, smoking status, lipid-modifying drug use) and recent health and comorbid conditions (i.e., recently ill, WBC count, diabetes, rheumatoid arthritis, chronic bronchitis) between the elevated and normal CRP groups were observed.
- Mean (standard error [SE]) CRP was 0.52 (0.01) mg/dL among those with elevated CRP versus 0.12 (0.00) mg/dL among those with normal CRP ($P < 0.0001$).

Logistic Regression Model Results (Table 2)

- Holding all else constant, the time since last dental visit was not statistically significantly associated with the risk of elevated CRP.
- However, those whose last dentist visit was preventive were less likely to have elevated CRP compared to those whose last dentist visit was symptom-driven.
- There were no statistically significant associations between elevated CRP and the interaction between the timing of and reason for the last dental visit.
- Females were more likely than males to have elevated CRP.
- Those 50 to 59, 60 to 69, and ≥ 70 years of age were more likely to have elevated CRP, compared with those 20 to 29 years of age.
- Those with lower BMI (i.e., < 25 or 25-29) had a reduced likelihood of having elevated CRP.
- Being a current smoker increased the risk of elevated CRP.
- Being recently ill or having elevated WBC measure were associated with increased risk of having elevated CRP.
- Diabetes, rheumatoid arthritis, asthma, cancer, and chronic bronchitis were not found to have significant associations with elevated CRP, nor did being a heavy drinker or currently using a cholesterol-lowering drug.

LIMITATIONS

- There is a potential for recall bias as many of the covariates were measured by self-report.
- We did not include anti-inflammatory drug use. The effects of chronic versus acute use of these drugs on CRP cannot be reliably elucidated in this cross-sectional study design.
- We were unable to reliably discriminate between statins and other cholesterol-lowering agents, as other classes have also been shown to reduce CRP.[4,5]

CONCLUSIONS

- These results suggest a significant association between the reason for the last dental visit and the likelihood of elevated CRP.
  - Interestingly, the impetus for the last dental care received appears to be more important than the actual timing of the visit, with respect to the risk of elevated CRP.
- Currently there exist few formalized guidelines for dental preventive visits in the US. This study provides at least one evidence-based foundation on which routine dental preventive visits may be recommended in selected populations at risk for elevated CRP or CVD, if not for the general population.

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Table 1. Clinical, Lifestyle, and Demographic Characteristics: Summary Statistics

	Total		Elevated CRP (> 0.3 mg/dL)[a]		Normal CRP (≤ 0.3 mg/dL)[a]		*P* Value
	Weighted N (Unweighted n)	Weighted %[b]	Weighted N (Unweighted n)	Weighted %[b]	Weighted N (Unweighted n)	Weighted %[b]	
Total	88,356,553 (5,365)	100.00	23,186,024 (1,495)	100.00	65,170,529 (3,870)	100.00	—
Time since last dental visit							
< 6 months	40,327,794 (2,208)	45.64	9,919,059 (583)	42.78	30,408,735 (1,625)	46.66	0.0460
6 months to < 1 year	15,005,540 (918)	16.98	4,049,215 (256)	17.46	10,956,324 (662)	16.81	0.6689
1+ years	33,023,219 (2,239)	37.37	9,217,750 (656)	39.76	23,805,470 (1,583)	36.53	0.0885
What was the main reason for last visit to the dentist?							
Preventive visit[c]	53,088,838 (2,949)	60.08	12,169,409 (713)	52.49	40,919,429 (2,236)	62.79	< 0.0001
Symptom-driven visit[d]	35,267,715 (2,416)	39.92	11,016,615 (782)	47.51	24,251,100 (1,634)	37.21	< 0.0001
Interaction terms							
Last visit was preventive							
< 6 months ago	28,332,170 (1,475)	32.07	6,388,431 (357)	27.55	21,943,739 (1,118)	33.67	0.0009
6 months to < 1 year ago	10,252,896 (571)	11.60	2,510,615 (139)	10.83	7,742,281 (432)	11.88	0.4021
1+ years ago	14,503,771 (903)	16.42	3,270,363 (217)	14.10	11,233,408 (686)	17.24	0.0200
Last visit was symptom-driven							
< 6 months ago	11,995,623 (733)	13.58	3,530,628 (226)	15.23	8,464,996 (507)	12.99	0.0486
6 months to < 1 year ago	4,752,643 (347)	5.38	1,538,600 (117)	6.64	3,214,043 (230)	4.93	0.0697
1+ years ago	18,519,448 (1,336)	20.96	5,947,387 (439)	25.65	12,572,061 (897)	19.29	< 0.0001
Demographics[e]							
Race/ethnicity							
White	66,127,416 (2,912)	74.84	17,240,617 (791)	74.36	48,886,799 (2,121)	75.01	0.6090
Black	7,440,107 (890)	8.42	2,086,148 (262)	9.00	5,353,958 (628)	8.22	0.2231
Hispanic	11,400,841 (1,395)	12.90	3,030,406 (406)	13.07	8,370,434 (989)	12.84	0.8266
Other race	3,388,189 (168)	3.83	828,852 (36)	3.57	2,559,337 (132)	3.93	0.6289
Sex							
Male	52,991,804 (3,497)	59.97	12,034,320 (863)	51.90	40,957,484 (2,634)	62.85	< 0.0001
Age (years)							
20-29	20,043,468 (1,192)	22.68	4,343,145 (272)	18.73	15,700,323 (920)	24.09	0.0015
30-39	22,791,937 (1,218)	25.80	5,586,931 (298)	24.10	17,205,006 (920)	26.40	0.0986
40-49	23,058,258 (1,219)	26.10	6,316,531 (350)	27.24	16,741,726 (869)	25.69	0.2232
50-59	15,000,717 (805)	16.98	4,585,787 (266)	19.78	10,414,930 (539)	15.98	0.0062
60-69	4,111,559 (454)	4.65	1,324,042 (154)	5.71	2,787,518 (300)	4.28	0.0283
70+	3,350,614 (477)	3.79	1,029,588 (155)	4.44	2,321,026 (322)	3.56	0.0924
Lifestyle measures							
BMI < 25	34,770,240 (1,939)	39.35	5,012,038 (298)	21.62	29,758,202 (1,641)	45.66	< 0.0001
BMI 25 to 29	31,756,966 (2,025)	35.94	8,149,258 (530)	35.15	23,607,708 (1,495)	36.22	0.5258
BMI ≥ 30	21,829,347 (1,401)	24.71	10,024,729 (667)	43.24	11,804,618 (734)	18.11	< 0.0001
Never a smoker	40,290,494 (2,411)	45.60	9,598,776 (605)	41.40	30,691,718 (1,806)	47.09	0.0046
Current smoker	26,808,043 (1,581)	30.34	7,955,414 (491)	34.31	18,852,629 (1,090)	28.93	0.0023
Former smoker	21,258,016 (1,373)	24.06	5,631,834 (399)	24.29	15,626,182 (974)	23.98	0.8211
Heavy drinker	10,702,471 (717)	12.11	2,578,028 (191)	11.12	8,124,443 (526)	12.47	0.2406
Currently using a cholesterol-lowering drug	6,036,752 (427)	6.83	1,961,282 (141)	8.46	4,075,470 (286)	6.25	0.0336
Recent health							
Recently ill (i.e., within last 30 days)	24,415,544 (1,513)	27.63	7,701,354 (492)	33.22	16,714,190 (1,021)	25.65	0.0001
WBC > 11	3,755,909 (214)	4.25	1,849,923 (103)	7.98	1,905,986 (111)	2.92	< 0.0001
Medical conditions							
Diabetes	2,963,281 (281)	3.35	1,259,854 (124)	5.43	1,703,428 (157)	2.61	0.0051
Asthma	10,663,569 (582)	12.07	2,789,523 (170)	12.03	7,874,046 (412)	12.08	0.9615
Cancer	4,800,793 (314)	5.43	1,527,704 (105)	6.59	3,273,089 (209)	5.02	0.0735
Rheumatoid arthritis	2,853,801 (219)	3.23	1,215,407 (98)	5.24	1,638,394 (121)	2.51	0.0022
Chronic bronchitis	4,564,670 (250)	5.17	1,605,324 (88)	6.92	2,959,347 (162)	4.54	0.0082

[a] Mean (SE) CRP, mg/dL: 0.52 (0.01) among those with elevated CRP vs. 0.12 (0.00) among those with normal CRP; P < 0.0001.
[b] Within the column.
[c] Checkup, examination, or cleaning.
[d] Something was wrong, bothering, or hurting, or went for treatment of a condition that dentist discovered at earlier checkup or examination.
[e] Mean (SE) age, years: 42.9 (0.38) in elevated CRP vs. 40.4 (0.34) in normal CRP; P < 0.0001.

Table 2. The Association Between Dental Care and Elevated CRP: Logistic Regression Results

	OR	95% CI		*P* Value
Time since last dental visit				
< 6 months	0.911	0.720	1.152	0.4290
6 months to < 1 year	0.994	0.695	1.421	0.9730
1+ years	Reference category			
What was the main reason for last visit to the dentist?				
Preventive visit[a]	0.722	0.562	0.928	0.0120
Symptom-driven visit[b]	Reference category			
Interaction terms				
Last visit was preventive, < 6 months ago	1.036	0.740	1.452	0.8310
Last visit was preventive, 6 months to < 1 year ago	1.037	0.711	1.513	0.8470
Demographics				
Race/ethnicity				
White	Reference category			
Black	0.905	0.740	1.108	0.3260
Hispanic	0.951	0.759	1.191	0.6540
Other race	1.072	0.675	1.703	0.7640
Sex				
Female	2.058	1.692	2.502	< 0.0001
Male	Reference category			
Age				
20-29	Reference category			
30-39	1.073	0.832	1.384	0.5770
40-49	1.196	0.934	1.531	0.1520
50-59	1.449	1.067	1.967	0.0190
60-69	1.716	1.208	2.438	0.0030
70+	1.906	1.244	2.919	0.0040
Lifestyle measures				
BMI < 25	0.186	0.156	0.222	< 0.0001
BMI 25 to 29	0.437	0.362	0.526	< 0.0001
BMI ≥ 30	Reference category			
Current smoker	1.331	1.078	1.643	0.0090
Former smoker	1.001	0.815	1.228	0.9950
Never a smoker	Reference category			
Heavy drinker	0.971	0.758	1.243	0.8100
Not a heavy drinker	Reference category			
Currently using a cholesterol-lowering drug	1.023	0.747	1.399	0.8870
Not currently using a cholesterol-lowering drug	Reference category			
Recent health				
Recently ill (i.e., within last 30 days)	1.345	1.134	1.594	0.0010
Not recently ill	Reference category			
WBC ≤ 11	Reference category			
WBC > 11	2.422	1.771	3.311	< 0.0001
Medical conditions				
Diabetes	1.439	0.944	2.194	0.0890
Asthma	0.873	0.697	1.093	0.2290
Cancer	1.094	0.780	1.534	0.5940
Rheumatoid arthritis	1.478	0.953	2.292	0.0800
Chronic bronchitis	0.980	0.686	1.399	0.9080

CI = confidence interval; OR = odds ratio.
[a] Checkup, examination, or cleaning.
[b] Something was wrong, bothering, or hurting, or went for treatment of a condition that dentist discovered at earlier check-up or examination.