

# Males With Rheumatoid Arthritis Often Evidence Carotid Atheromas on Panoramic Imaging: A Risk Indicator of Future Cardiovascular Events

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**Purpose:** Males with rheumatoid arthritis (RA) are at an exceedingly high risk of adverse intraoperative ischemic events, given the role of systemic inflammation in the atherogenic process. We hypothesized that their panoramic images would demonstrate calcified carotid artery atheromas (CCAPs) significantly more often than those from a general population of similarly aged men.

**Patients and Methods:** We implemented a retrospective observational study. The sample was composed of male patients older than 55 years of age who had undergone panoramic imaging studies. The predictor variable was the diagnosis of RA confirmed by a positive rheumatoid factor (RF) titer, and the outcome variable was the prevalence rate of CCAPs. The other major study variable was the level of RF among the patients evidencing CCAPs. The prevalence of CCAPs among the patients with RA was then compared with that of a historical general population of similarly aged men. Descriptive and bivariate statistics were computed, and the *P* value was set at .05.

**Results:** Of the 100 men (mean age  $69.89 \pm 8.927$  years) with RA, 29 (29%; mean age  $72.10 \pm 7.68$  years) had atheromas (CCAP+). Of these 29 men, 25 (86%; mean age  $71.88 \pm 7.43$  years) had a RF titer of  $\geq 41$  IU/mL, twice that of normal. A statistically significant ( $P < .05$ ) association was found between a diagnosis of RA and the presence of an atheroma on the panoramic image compared with the 3% rate found in the historical cohort.

**Conclusions:** The results of the present study suggest that CCAP, a risk indicator of future adverse cardiovascular events, is frequently seen on panoramic images of male patients with RA and that these individuals routinely manifest high titer levels of RF, a biologic marker of inflammation. Oral and maxillofacial

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113 surgeons planning surgery for male patients with RA must be uniquely vigilant for the presence of these  
114 lesions.

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119 Rheumatoid arthritis (RA), an autoimmune disease  
120 caused by a combination of genetic and environmental  
121 factors, is characterized by inflammation and swelling  
122 of the synovium, most frequently of the finger and  
123 wrist joints.<sup>1</sup> The diagnosis of RA, arrived at by the  
124 findings from history, clinical examination, and imag-  
125 ing studies, is often further substantiated by testing  
126 for rheumatoid factor (RF), a biologic marker of inflam-  
127 mation and a risk indicator of generalized atheroscle-  
128 rosis.<sup>2</sup> The disease in men is encountered far less  
129 frequently (1:3) than in women but confers on men  
130 an exceedingly high risk of premature cardiovascular  
131 death, which is far greater than in women with the  
132 disorder and almost twice that of similarly aged men  
133 without the autoimmune disease.<sup>3-9</sup>  
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135 Clinical studies conducted among male patients  
136 with RA have consistently documented an ~70%  
137 increased incidence of fatal myocardial infarction  
138 (MI) and ischemic stroke (cerebrovascular accident  
139 [CVA]), independent of traditional risk factors (eg, hy-  
140 pertension).<sup>10,11</sup> For inexplicable reasons, the  
141 premorbid identification of such patients, however,  
142 can be missed because the symptoms of ischemic  
143 disease can be silent or atypical.<sup>12</sup> These ischemic car-  
144 diovascular events are believed to arise from disease-  
145 associated (RA), persistent, systemic inflammation,  
146 mediated through proinflammatory cytokines, in  
147 particular, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and  
148 interleukin-6 (IL-6). These initiate C-reactive protein  
149 synthesis and stimulate a proatherogenic lipid profile,  
150 foster insulin resistance, and impair endothelial func-  
151 tion, thereby accelerating the development of calcified  
152 atherosclerotic plaques in the coronary and carotid  
153 vasculature.<sup>13-15</sup>

154 Carotid artery ultrasound studies conducted among  
155 RA cohorts in Hong Kong<sup>16,17</sup> have consistently  
156 documented the presence of calcified plaques in the  
157 bifurcation area. These findings are consistent with  
158 the increased cardiovascular incident rates and in  
159 accordance with that these lesions as a validated  
160 "risk factor" for both future stroke and MI.<sup>18</sup>

161 Calcified carotid artery plaques (CCAPs) can also be  
162 demonstrated on panoramic imaging studies. Fried-  
163 lander and Baker<sup>19</sup> reported a prevalence of 3% (posi-  
164 tive for CCAPs) after evaluating more than 300  
165 panoramic images from older (age  $\geq 55$  years) Amer-  
166 ican military veterans (96% male) presenting to  
167 the outpatient oral surgery clinic in 1994. The prog-  
168 nostic significance of CCAPs on panoramic images

169 has likewise been confirmed by a separate study of  
170 46 multiethnic American male military veterans,  
171 which documented that such lesions significantly her-  
172 alded future adverse cardiovascular and cerebrovascu-  
173 lar events.<sup>20</sup>  
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175 Given that no studies evaluating panoramic images  
176 for the presence of CCAP among men with RA have  
177 been any previously reported, we undertook the pre-  
178 sent project. Our specific purpose was to determine  
179 the prevalence rate of CCAPs among older male mili-  
180 tary veterans with a diagnosis of RA determined by a  
181 rheumatologist. The prevalence rate of CCAPs in this  
182 cadre of patients was hypothesized to be significantly  
183 greater than that previously reported (3%) among  
184 older male military veterans.<sup>19</sup>  
185

## 186 Patients and Materials

### 187 STUDY DESIGN AND PATIENT SAMPLE

188 To address these research questions, we designed  
189 and implemented a retrospective observational study.  
190 The study was conducted in accordance with the  
191 Declaration of Helsinki guidelines. The institutional re-  
192 view board of the Veterans Affairs Greater Los Angeles  
193 Healthcare System approved the study protocol, and  
194 the need for informed consent from each subject  
195 was waived, given the retrospective nature of the proj-  
196 ect, its use of de-identified patient data, anonymous  
197 coding of information with the key known only to  
198 the primary investigator, and the use of a secure data-  
199 base. The medical center's electronic medical records  
200 (EMRs) and digital dental image library data from  
201 January 1, 2000 to December 31, 2016 were accessed  
202 and reviewed. Chosen for further scrutiny were the  
203 medical records and images of all male patients aged  
204 55 years or older, with a diagnosis of RA, and a classi-  
205 cally positioned panoramic imaging study obtained  
206 to diagnose dental disease.  
207

208 To be included as a case subject, the patient's EMRs  
209 had to 1) document a diagnosis of RA that was predi-  
210 cated on the individual fulfilling the classification  
211 criteria for RA developed by the American College of  
212 Rheumatology/European League Against Rheuma-  
213 tism,<sup>1</sup> which specify at least 5 inflamed joints, elevated  
214 erythrocyte sedimentation rate and/or serum  
215 C-reactive protein concentration, positive RF and/or  
216 anti-cyclic citrullinated peptides, and evidence of  
217 inflammation on plain radiographs of the hands, wrists,  
218 or feet; 2) a positive RF test result (RF  $\geq 20$  IU/mL); 3)  
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