(11.1%) always did. The main factors influencing caution in using the loading dose were gastrointestinal side-effects and other toxicity. Some consultants had adopted a starting dose of 10 mg/day increasing to 20 mg/day if tolerated. Thirty-two (59.3%) advised patients that occasional alcohol consumption was acceptable, 12 (22.2%) advised no alcohol restriction, and only 10 (18.5%) followed the recommendation of the SPC of avoiding alcohol. Some consultants commented that patients may refuse leflunomide if there was an alcohol ban.

Against SPC recommendations, 26 (48.1%) never used a cholestryramine or activated charcoal washout for swapping leflunomide to another DMARD and 16 (29.6%) used one occasionally. Not all consultants indicated whether the full 11 days washout was used but some commented that they used shorter washout periods as few patients tolerated the 11 days. Although the SPC warns against combination therapy, 31 (57.4%) and 8 (14.8%) combined leflunomide with methotrexate occasionally and usually, respectively. Combination therapy was never used by 14 (25.9%) consultants. The main concern raised with combination therapy was the potential for liver toxicity.

Thirty-five (64.8%) monitored bloods fortnightly in the first 6 months, in keeping with SPC recommendations. The remainder had variable monitoring regimes, ranging from fortnightly for 2 months then monthly, to fortnightly for 2 months, monthly for 4 months, then 3-monthly. Blood pressure monitoring was conducted fortnightly and monthly in 23 (42.6%) and 22 (40.7%), respectively. One responder never checked the blood pressure.

In summary, this survey has demonstrated that for most rheumatologists in the Midlands leflunomide has established a firm footing in their clinical practice, and usually follows the failure of sulphasalazine and methotrexate. This survey confirmed the marked variation in the prescribing and monitoring of leflunomide. In some regards, the majority of consultants are disregarding the SPC and national guidelines [3]. This applies to the infrequent use of the loading dose, failure to ban alcohol, not using a washout to transfer patients from leflunomide to another DMARD, and combining the drug with methotrexate. The percentage of rheumatologists who were monitoring full blood counts less frequently than the SPC recommends was 35.2%, and one person was not checking blood pressure at all.

These discrepancies between clinical practice and the recommendations of the SPC can be interpreted in two ways. The first interpretation is that the SPC is too restrictive, and increasing experience with the drug is influencing confidence in deviating from recommendations. If this is the case, then information needs to be collected to be able to modify the SPC. The second interpretation is that consultants have become too relaxed in their approach to the prescribing and monitoring of leflunomide, and this may lead to medicolegal consequences. We would like to suggest that the former is closer to the truth than the latter, and that urgent attention needs to be given to modifying the SPC.

There are already data on the safe and efficacious use of combinations of leflunomide and methotrexate [4, 5], despite warnings about possible adverse liver reactions [6]. Full blood count abnormalities are infrequent [7–12], suggesting that fortnightly blood tests for 6 months is excessive. More information is required on the efficacy and toxicity of using or avoiding the loading dose [13]. More data are needed on the safety of alcohol with leflunomide, and the need for washing patients out prior to switching from leflunomide to another DMARD.

The difficulty with SPCs is that, once a recommendation has been made, evidence is needed before it can be modified with confidence. We believe that for leflunomide there is already enough data and a sufficient groundswell of clinical practice and experience to modify the SPC.

Conflict of interest: the authors have declared that this research was supported by a small unrestricted grant from Aventis Pharmaceuticals.
Electron beam computed tomography (EBCT) has emerged as a simple and non-invasive technique for the diagnosis of coronary atherosclerosis [1, 2]. It detects coronary artery calcification, which is a potential indicator of significant future coronary risk and also shows the wall morphology and patency of coronary arteries with contrast enhancement [1–3].

We investigated the frequency of coronary atherosclerosis, by using EBCT, in a group of male BS patients selected specifically for having major vessel disease and long disease duration. Our hypothesis was that coronary atherosclerosis would be frequent in this group of BS patients. We defined major vascular involvement as the presence of an aneurysm and/or arterial occlusion and/or thrombosis of the venae cavae. All patients were initially screened for cardiovascular risk factors. Total and individual coronary calcium scores were calculated according to the method described by Agatston et al. [3]. Coronary artery calcium scores were stratified as follows: (i) no calcification; (ii) 1–100, minimal to slight calcification; (iii) 101–400, intermediate calcification; (iv) score greater than 400, extensive calcification. The study was approved by the local ethics committee of Cerrahpaşa Medical Faculty and informed consent was obtained from all patients.

We studied 24 patients [mean age 37.8 ± 4.5 (s.d.) yr; duration of vascular involvement 10.1 ± 3.7 yr]. The main vessels involved were the pulmonary arteries (nine patients), abdominal aorta (four patients) and vena cava (nine patients). Seven patients had more than one diseased vessel. Fifteen patients (63%) had used corticosteroids previously, with a mean duration of 3.9 ± 3 yr. All patients were previous or current users of cyclophosphamide or azathioprine. The mean duration of treatment with these drugs was 4.3 ± 3 yr. The majority (88%) smoked and 42% had at least mild lipid abnormalities. One patient had diabetes mellitus. No patient had arterial hypertension or myocardial infarction. Coronary artery calcium scores were zero in 21 (88%) patients. Two patients had scores suggesting minimal or slight calcification (58 and 7) and one patient had a calcium score of 600, indicating extensive calcification. These three patients (12%) were also the only ones with abnormal imaging on EBCT coronary angiography, as shown in Fig. 1. One patient had total occlusion and calcified aneurysm in the proximal part of the left anterior descending artery (LAD) (Fig. 1, left panel). The second had mild stenosis with calcified plaque formations in the LAD (Fig. 1, middle panel), and the third had non-calcified aneurysm in the LAD (Fig. 1, right panel). Our results suggest that coronary artery abnormalities are not common in BS even in a selected group of male patients.

In a recent study using EBCT, coronary artery calcification (CAC) was described among 31% of 65 SLE patients with no history of coronary artery disease, compared with 9% of 69 controls. The patients and controls in this study were predominantly women and had an average age of approximately 40 yr [4]. The prevalence of CAC among women is estimated to be half that in men until the age of 60 yr [1]. Extrapolating from this, and not forgetting the limitations of indirect comparisons, especially among different ethnic groups, the frequency of CAC among our selected male patient population seems to be at least not increased when compared with what is found in the general population. Unfortunately, data on coronary calcification in the general population of Turkey are not available and our study did not include a formal control group.

Among 350 patients with BS who were followed up between 1974 and 1993 in France, three (0.09%) had coronary arterial involvement [5]. Furthermore, in a 20-yr outcome survey on 387 patients from our centre, only three of the 42 deaths (0.7%) were due to coronary artery disease [6]. In that study the mortality in BS was mainly due to extracardiac vascular or neurological disease, and these complications showed a tendency to decrease in frequency with the passage of time during the disease course. This mortality pattern is different from what is found in RA and SLE [7, 8], in which there is an increased or bimodal mortality pattern with increased atherosclerotic coronary artery disease with the prolonged disease course.

It is believed that the classical risk factors, such as smoking and high lipid levels, are important in the coronary atherosclerosis of inflammatory diseases. Disease duration, corticosteroid use and inflammatory activity are implicated as additional risk factors [9]. In our study, coronary atherosclerosis was lower than what we expected, although our patients carried most of these risk factors. The relatively young age of our patients or the immunosuppressive treatment employed might have played a role in
this outcome. Another explanation could be that the disease activity in BS is more short-lasting compared with other diseases characterized by chronic and long-lasting inflammation, such as SLE and RA [6].

In summary, our preliminary findings indicate a relatively low frequency of coronary atherosclerosis in BS even when studied under worst-case conditions. Further studies are needed, first to verify these preliminary observations in a controlled setting and secondly to elucidate their biological importance, if verified.

This study was supported by the Research Fund of the Istanbul University (Project No: 1529/16012001).

The authors have declared no conflicts of interest.

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Key messages
- EBCT is a suitable non-invasive method to detect coronary artery pathology in BS.
- Patients with BS seem to have a relatively low frequency of coronary atherosclerosis.

The authors have declared no conflicts of interest.

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