# Framingham, ACC/AHA or QRISK3: which is the best in systemic lupus erythematosus cardiovascular risk estimation?

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## Abstract

### Objective

*TOur objective was to compare three algorithms for cardiovascular (CV) risk estimation, namely Framingham, ACC/AHA and QRISK3, in a cohort of patients with systemic lupus erythematosus (SLE).*

### Methods

*Consecutive patients with SLE according to the ACR criteria were enrolled. Traditional risk factors, ongoing therapies, comorbidities and SLE-specific evaluations were assessed. In those without previous myocardial infarction or stroke, Framingham, ACC/AHA and QRISK3 algorithms were then used to estimate the individual risk of developing a CV disease over the next 10 years.*

### Results

*Patients eligible for CV risk estimation were 123 out of 135 enrolled. Framingham index reported a median risk score of 4.7% (IQR 9.5–2.2), considering 29 patients (23.6%) at high CV risk. ACC/AHA index showed a median risk score of 1.4% (IQR 4.5–0.7), with 17 patients (13.8%) at high-risk. QRISK3 revealed a median risk score of 6.2% (IQR 12.5–2.8), making it possible to classify 44 patients (35.8%) at high CV risk. The subgroup analysis of subjects older than 40 years confirmed the same number of high-risk patients for both Framingham and ACC/AHA, while QRISK3 instead considered 38 subjects at high CV risk.*

### Conclusion

*QRISK3 classifies a greater number of SLE patients at high-risk of developing CV diseases over the next 10 years in comparison with classic algorithms as Framingham and ACC/AHA. If its predictive accuracy were confirmed by longitudinal data, QRISK3 could become an important tool in the early detection of a considerable part of CV high-risk SLE patients that would be underestimated when applying classic algorithms.*

**Key words**

systemic lupus erythematosus, cardiovascular diseases, risk factors

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*Received on April 6, 2016; accepted in revised form on July 22, 2019.*



*Competing interests: none declared.*

## Introduction

It is well documented in the literature that systemic lupus erythematosus (SLE) patients have a higher risk of developing cardiovascular (CV) diseases (CVD) as compared to the general population (1). Moreover, several studies have demonstrated that CVD are one of the leading causes of death during the years after SLE diagnosis, and this is especially relevant for patients under 50 years old (2-5). More specifically, SLE patients are at greater risk for major CV events (6), which are myocardial infarction (MI) (7) and stroke (8).

Taking this increased morbidity and mortality into account, both European and American guidelines recommend evaluating the CV risk status in SLE patients, for an early identification of patients at high risk and subsequent application of preventive strategies (9, 10). Among the many algorithms available for CV risk evaluation, the Framingham score (11) and the ACC/AHA score (12) are two of the most widespread and validated for all kinds of patients. Based on traditional risk factors (TRF), they allow estimating the 10-year individual risk of developing CVD. Another algorithm recently validated is the QRISK3, which is the first that takes into account specific items in addition to TRF, such as the presence of SLE and the use of glucocorticoids (13).

The aim of this study is to evaluate the prevalence of traditional cardiovascular risk factors and to compare the three aforementioned algorithms for CV risk estimation by applying them to our cohort of SLE patients.

## Methods

*Patients*

Adult consecutive patients with SLE according to the ACR criteria (14) attending a routine visit at the Lupus Clinic of the Rheumatology Unit of the University of Pisa between May 2017 and September 2017 were enrolled in this study. Full ethical approval was obtained from the local ethics committee (Comitato etico Area Vasta Nord Ovest). Each patient voluntarily agreed to participate and gave their written informed consent to publish the material. At enrolment time, data were collected through questions, medical records and physical examination. Each patient was asked about previous CV events including: stable and unstable angina, MI, transient ischaemic attack, stroke, deep vein thrombosis, pulmonary embolism, acute limb ischaemia and peripheral artery disease. Family history of early CVD was also investigated: the presence of MI or stroke in first-degree relatives before the age of 55 in men and 65 in women were considered. Patients were asked about smoking habits, further differentiating between current and non-current smokers. Comorbidities were investigated for the presence of diabetes mellitus and systemic arterial pressure; patients with systemic arterial hypertension (SAH) were also assessed for the intake of an antihypertensive treatment. Anthropometric evaluations, including body mass index (BMI) for the detection of overweight (BMI between 25 and 30) and obesity (BMI ≥30), and the circumferences of waist and hips were made. Central obesity was defined as waist circumference >88 cm for women and >102 cm for men.

Laboratory tests were investigated for the presence of hyperhomocysteinaemia (>11.1 μmol/L), hyperuricaemia (>7 mg/dL) and alterations in total cholesterol (normal value <200 mg/dL), HDL-cholesterol (nv ≥40 mg/dL for men and ≥50 mg/dL for women), LDL-cholesterol (nv <130 mg/dL) and triglycerides (nv <150 mg/dL). Patients were also assessed for the presence of metabolic syndrome as defined by AHA/NHLBI (15).

Regarding SLE-specific evaluations, patients were assessed for disease duration, cumulative organ involvement, cumulative serology and ongoing therapy. Then disease activity was evaluated as defined by the SLEDAI-2K (16, 17). Patients were furthermore assessed for chronic damage as defined by the SLICC/ACR damage index (18).

*10-year CV risk estimation*

Three different algorithms were used to estimate the individual risk of developing CVD over the next 10 years. Framingham risk score analyses TRF and, on account of the percentage result, allows stratifying patients into three groups: low-risk (score <10%),

intermediate-risk (score ≥10% and <20%) and high-risk (score ≥20%). For the purposes of this work, in accordance with the NICE guidelines (19), high-risk was considered for Framingham scores ≥10%. Also, ACC/AHA risk score is based on TRF (with the addition of ethnicity but with a lower reliability for patients less than 40 years of age), and classifies patients for the 10-year CVD risk in low-risk (score <7.5%) and high-risk (≥7.5%). QRISK3 risk score is an algorithm validated in 2017 that, together with TRF, takes into account the presence of: rheumatoid arthritis, SLE, chronic glucocorticoid treatment, chronic kidney disease (stage ≥3), atrial fibrillation, migraines, severe mental illness, therapy with atypical antipsychotics, erectile dysfunction and its treatment. Patients with a score ≥10% are considered at high-risk of developing CVD in the next 10 years (19). QRISK3 also gives other outputs like the score of a healthy person of the same age, sex and ethnicity, the relative risk (patient's risk divided by the healthy person's risk) and the "QRISK3 healthy heart age", the age at which a healthy person has patient's 10-year QRISK3 score.

Previous major CV events (MI and stroke) were considered exclusion criteria for CV risk estimation.

*Statistical analysis*

Variables were described in terms of mean and standard deviation or median and 25th–75th percentiles depending on variable distribution. T-test and the non-parametric Wilcoxon test were used to investigate differences between groups of patients. Cross-tabulated data were analysed by chi-square or Fisher's test when the expected cell count was less than five.

Statistics were performed using the STATA software. *p*-values less than 0.05 were considered statistically significant.

## Results

One hundred and thirty-five patients were enrolled in this study. Thirty-two patients (23.7%) had already had a CV event and, among those, 12 (8.9%) had suffered a MI or a stroke and were therefore excluded from CV risk estimation. Among the remaining 123 patients eligible for the study, 111 were female (90.2%) and 119 (96.7%) Caucasian, with a median age at enrolment of 44 years (IQR 52–34.5). The median disease duration was 11 years (IQR 20-6). Clinical characteristics of the cohort are reported in Table I.

Briefly, 91 of them (74%) had a history of joint involvement, 64 (52%) skin manifestations, 63 (51.2%) haematological abnormalities, 53 (43.1%) kidney involvement, 23 (18.7%) serositis, and 7 (5.7%) neuropsychiatric manifestations. Regarding serology, antinuclear antibodies (ANA) were present in all the patients, and extractable nuclear antigens (ENA) were found to be positive in 70 (56.9%) of them. Positivity for double-stranded DNA (ds-DNA) was present in 84 patients (68.3%), and 60 (48.8%) had antiphospholipid antibodies.

At the time of our evaluation, active disease (SLEDAI ≥4) was present in 30 patients (24.4%).

As far as organ damage is concerned, 44 patients (35.8%) had at least one permanent organ damage (SLICC ≥1): among them, the median SLICC was 2 (IQR 3–1).

Regarding therapy, at enrolment, 70 patients (56.9%) were on chronic glucocorticoids (prednisone or 6-methylprednisolone; median daily intake of 2 mg, IQR 4–0). Moreover, 95 patients (77.2%) were taking hydroxychloroquine (HCQ), 19 (15.4%) mycophenolate mofetil (MMF), 11 (8.9%) azathioprine (AZA), 8 (6.5%) methotrexate (MTX), 7 (5.7%) belimumab, 6 (4.9%) cyclosporine (CyA), 4 (3.2%) tacrolimus, 2 (1.6%) leflunomide, 1 (0.8%) rituximab (RTX) and 1 (0.8%) cyclophosphamide (CYC).

*Traditional CV risk factors*

The prevalence of CV risk factors is reported in Table II. Among the 123 patients who never had major CV events, 17 (13.8%) were overweight and 5 (4.1%) were obese. Central obesity was present in 17 female patients (13.8%) and in 4 male patients (3.2%). Evaluating family history of early CVD, 18 patients (14.6%) reported the presence of MI or stroke; 3 (2.4%) did not know. Sixty patients (48.8%) had a history of smoking: among them, 31 (25.2%) were current smokers at enrolment. Therefore, there were were 92 (74.8%) non-current smokers (including both those who quit smoking and those who have never smoked). Thirty-three patients (26.8%) presented SAH, which was kept under pharmacological control in 30 (24.4%) of them, whereas 7 patients (5.7%) had diabetes mellitus. Twenty-five patients (20.3%) were found to have hyperhomocysteinaemia, and 5 (4.1%) hyperuricaemia. Analysing lipid profiles, patients with lipid levels out of range were 38 (30.9%) for high total cholesterol, 40 (32.5%) for low HDL-cholesterol, 28 (22.8%) for high LDL-cholesterol, and 21 (17.1%) for high triglycerides. Fourteen patients (11.4%) were under treatment for dyslipidaemia and, among those with hypercholesterolaemia at enrolment, 10 (8.1%) were taking a specific therapy for it (statin or

**Table 1.** Epidemiological and clinical characteristics of patients at enrolment time.

| | | |
|---|---|---|
| Number of patients (%) | 123 | (100) |
| Female (%) | 111 | (90.2) |
| Caucasian (%) | 119 | (96.7) |
| Age (yrs) median (IQR) | 44 | (52-34.5) |
| Disease duration (yrs) median (IQR) | 11 | (20-6) |
| *Cumulative organ involvement and serology* | | |
| Joint involvement (%) | 91 | (74) |
| Skin involvement (%) | 64 | (52) |
| Haematological involvement (%) | 63 | (51.2) |
| Kidney involvement (%) | 53 | (43.1) |
| Serositic involvement (%) | 23 | (18.7) |
| Neuropsychiatric involvement (%) | 7 | (5.7) |
| ANA (%) | 123 | (100) |
| ENA (%) | 70 | (56.9) |
| - Ro/SSA (%) | 37 | (30.1) |
| - La/SSB (%) | 7 | (5.7) |
| - Sm (%) | 17 | (13.8) |
| - RNP (%) | 29 | (23.6) |
| ds-DNA (%) | 84 | (68.3) |
| Antiphospholipid antibodies (%) | 60 | (48.8) |
| SLICC median (IQR) | 0 | (1-0) |
| SLICC ≥1 (%) | 44 | (35.8) |
| SLICC ≥1 median (IQR) | 2 | (3-1) |
| *Ongoing therapy* | | |
| Corticosteroids (%) | 70 | (56.9) |
| - Daily intake (mg) median (IQR) | 2 | (4-0) |
| HCQ (%) | 95 | (77.2) |
| Other immunosuppressants | 53 | (43.1) |
| - MMF (%) | 19 | (15.4) |
| - AZA (%) | 11 | (8.9) |
| - MTX (%) | 8 | (6.5) |
| - Belimumab (%) | 7 | (5.7) |
| - CyA (%) | 6 | (4.9) |
| - Tacrolimus (%) | 4 | (3.2) |
| - Leflunomide (%) | 2 | (1.6) |
| - RTX (%) | 1 | (0.8) |
| - CYC (%) | 1 | (0.8) |

**Table II.** Traditional CV risk factors of patients at enrolment.

| | |
|---|---|
| BMI (kg/m$^2$) median (IQR) | 22 (23.7-20.1) |
| Waist circumference (cm) median (IQR) | 76 (85-70) |
| Hip circumference (cm) median (IQR) | 95.5 (101-90) |
| Central obesity (%) | 21 (17.1) |
| Family history of early CVD (%) | 18 (14.6) |
| Smoking habit (%) | 60 (48.8) |
| - Current smokers (%) | 31 (25.2) |
| SAH (%) | 33 (26.8) |
| Diabetes mellitus (%) | 7 (5.7) |
| Hyperhomocysteinaemia (%) | 25 (20.3) |
| Hyperuricaemia (%) | 5 (4.1) |
| Total cholesterol high values (%) | 38 (30.9) |
| HDL-cholesterol low values (%) | 40 (32.5) |
| LDL-cholesterol high values (%) | 28 (22.8) |
| Triglycerides high values (%) | 21 (17.1) |
| Metabolic syndrome (%) | 18 (14.6) |

ezetimibe). Metabolic syndrome was diagnosable in 18 patients (14.6%).

*CV risk estimation*

With the exclusion of 12 patients who had already experienced MI or stroke, the 10-year risk of CV events was evaluated in 123 patients with the aforementioned algorithms (Fig. 1). Framingham index revealed a median risk score of 4.7% (IQR 9.5–2.2). According to this algorithm, 94 patients (76.4%) were classified as low-risk (score <10%) and 29 (23.6%) as high-risk (score ≥10%). ACC/AHA index showed a median risk score of 1.4% (IQR 4.5–0.7). Based on ACC/AHA results, 106 patients (86.2%) were considered at low-risk (score <7.5%), and 17 patients (13.8%) at high-risk (score ≥7.5%). QRISK3 revealed a median risk score of 6.2% (IQR 12.5–2.8). According to QRISK3, 79 patients (64.2%) were classified as low-risk (score <10%), and 44 (35.8%) as high-risk (score ≥10%). By comparison, according to the same algorithm, the estimated risk score in an age-, sex- and ethnicity-matched healthy ideal population would be 1.5% (IQR 3–0.5) in median and 2.9% in mean. Median relative risk was 3.6 (IQR 7–2.1), and "QRISK3 healthy heart age" showed a median of 62 years (IQR 71–53), with a mean of 61.9 years.

Since ACC/AHA is not validated in subjects under the age of 40 (n=39 in our cohort), the three algorithms were recalculated in 84 patients over 40 years of age (Fig. 2). In this subgroup, the

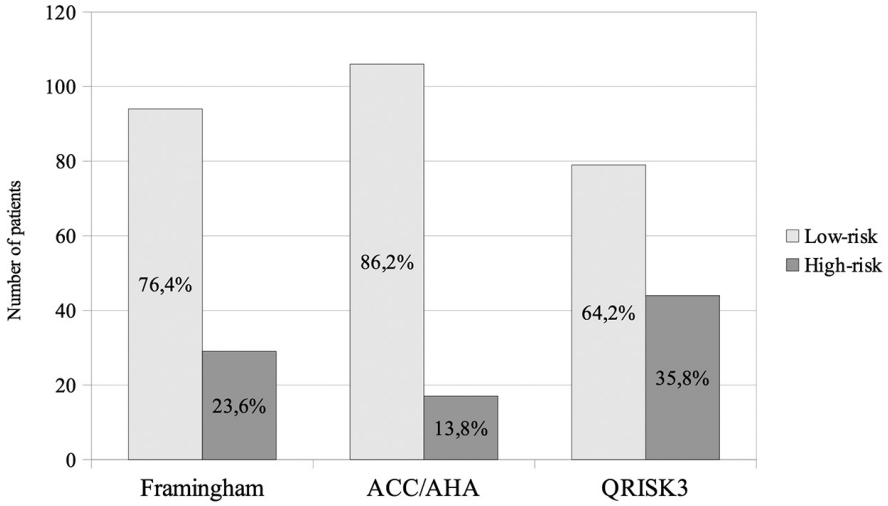


**Fig. 1.** Differences in numbers and percentages of 123 SLE patients classified in risk classes by three algorithms.

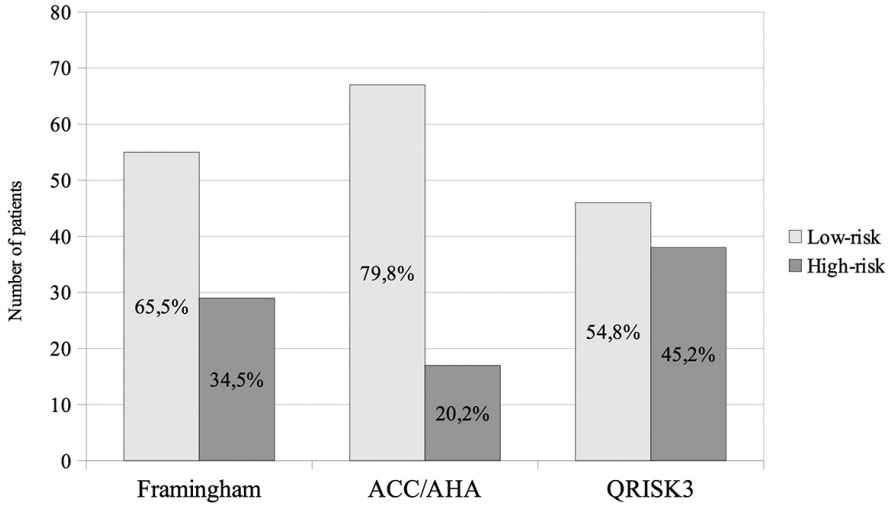


**Fig. 2.** Differences in numbers and percentages of 84 SLE patients over 40 years of age classified in risk classes by three algorithms.

Framingham index revealed a median risk score of 6.6% (IQR 11–4), classifying 55 (65.5%) patients as low-risk (score <10%) and 29 (34.5%) as high-risk (score ≥10%). The ACC/AHA index showed a median risk score of 2.7% (IQR 5.8–1.3). Based on the ACC/AHA results, 67 patients (79.8%) were considered at low-risk (score <7.5%), and 17 patients (20.2%) at high-risk (score ≥7.5%). QRISK3 revealed a median risk score of 9% (IQR 14.9–5.1). According to this algorithm, 46 patients (54.8%) were classified as low-risk (score <10%), and 38 (45.2%) as high-risk (score ≥10%). By comparison, according to the same algorithm, the estimated risk score in an age-, sex- and ethnicity-matched healthy ideal population would be 2.3% (IQR 4.3–1.4) in median and 4.1% in mean. Median relative risk was 3 (IQR 4.4–2), and "QRISK3 healthy heart age" showed a median of 65.5 years (IQR 73–60), with a mean of 66.2 years.

In the entire cohort, 13 (10.6%) patients were considered at high-risk by QRISK3 and at low-risk by the Framingham (Fig. 3): their median age was 49 years (IQR 54–41), with several cases under 40 years. Chronic kidney disease (stage ≥3) was present in 61.5% of them, and 100% were regularly taking steroids. No significant differences were observed between those patients and the whole cohort with regard to epidemiological data, SLE clinical features and TRF.

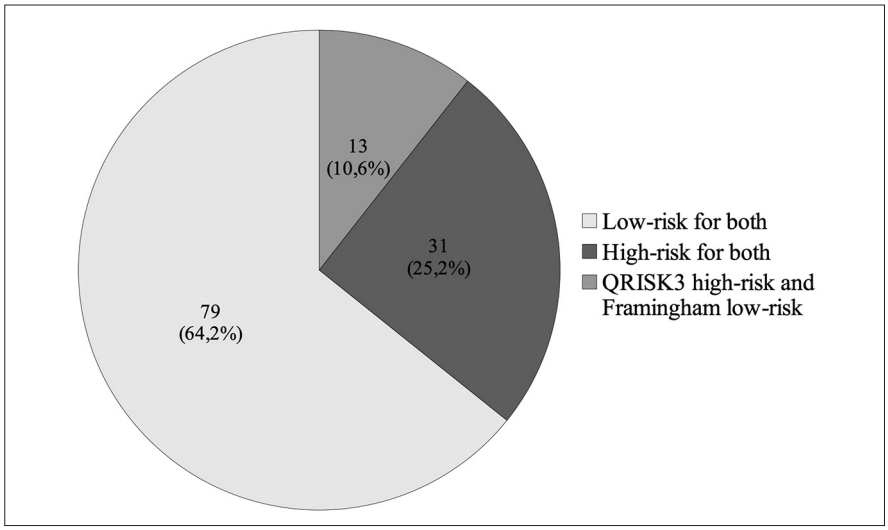


**Fig. 3.** Comparison between risk classes by Framingham and QRISK3 on 123 SLE patients.

**Table III.** Comparison between patients considered at high-risk by QRISK3 but not by Framingham and patients considered at low-risk by both algorithms.

| | Newly identified QRISK3 high-risk patients (n=13) | Framingham and QRISK3 low-risk patients (n=79) | *p*-value |
|---|---|---|---|
| Female (%) | 12 (92.3) | 74 (93.7) | ns |
| Caucasian (%) | 13 (100) | 75 (94.9) | ns |
| Age (yrs) median (IQR) | 49 (54-41) | 40 (47.5-30.5) | **0.01** |
| Disease duration (yrs) median (IQR) | 10 (18-5) | 11 (17-6) | ns |
| Joint involvement (%) | 10 (76.9) | 59 (74.7) | ns |
| Skin involvement (%) | 7 (53.8) | 44 (55.7) | ns |
| Haematological involvement (%) | 4 (30.8) | 46 (58.2) | ns |
| Kidney involvement (%) | 8 (61.5) | 29 (36.7) | ns |
| Serositic involvement (%) | 1 (7.7) | 13 (16.4) | ns |
| Neuropsychiatric involvement (%) | 1 (7.7) | 4 (5.1) | ns |
| ENA (%) | 6 (46.1) | 45 (57) | ns |
| ds-DNA (%) | 8 (61.5) | 59 (74.7) | ns |
| Antiphospholipid antibodies (%) | 9 (69.2) | 37 (46.8) | ns |
| SLICC ≥1 (%) | 4 (30.8) | 20 (25.3) | ns |
| SLICC ≥1 median (IQR) | 4 (5-3.5) | 1 (2-1) | **<0.01** |
| Corticosteroids (%) | 13 (100) | 39 (49.4) | **<0.01** |
| - Daily intake (mg) median (IQR) | 4 (4-4) | 1 (4-0) | ns |
| HCQ (%) | 11 (84.6) | 63 (79.7) | ns |
| Other immunosuppressants | 6 (46.1) | 34 (43) | ns |
| BMI (Kg/m$^2$) median (IQR) | 23.7 (24.2-21.6) | 21.2 (22.5-19.6) | **<0.01** |
| Family history of early CVD (%) | 0 (0) | 9 (11.4) | ns |
| Smoking habit (%) | 9 (69.2) | 33 (41.8) | ns |
| SAH (%) | 6 (46.1) | 5 (6.3) | **<0.01** |
| Diabetes mellitus (%) | 0 (0) | 2 (2.5) | ns |
| Hyperhomocysteinaemia (%) | 2 (15.4) | 12 (15.2) | ns |
| Hyperuricaemia (%) | 2 (15.4) | 0 (0) | **<0.01** |
| Total cholesterol high values (%) | 5 (38.5) | 18 (22.8) | **0.01** |
| HDL-cholesterol low values (%) | 3 (23.1) | 27 (34.2) | ns |
| LDL-cholesterol high values (%) | 2 (15.4) | 16 (20.2) | ns |
| Triglycerides high values (%) | 4 (30.8) | 9 (11.4) | **0.01** |

ns: not significant.

Also in the subgroup of patients over 40 years of age, 12 (14.3%) were still considered at high-risk by QRISK3 and at low-risk by the other two algorithms. Their median age was 52 years (IQR 55.2–47.7), 41.7% of them presented chronic kidney disease and 100% were regularly taking steroids. Epidemiological, SLE-specific and TRF-related characteristics are substantially similar to those found in the total of the examined patients.

A statistical comparison was then performed between patients considered to be at high-risk by QRISK3 but not by Framingham and those considered at low-risk for both indices (Table III). Regarding epidemiological and SLE-specific characteristics, the former subgroup was significantly older ($p$=0.01) and had more occurrences of at least one permanent organ damage (SLICC ≥1; $p$<0.01). On the other hand, there were no noteworthy differences regarding disease duration, specific organ involvement and serology. Patients at high-risk were more likely on chronic glucocorticoid therapy ($p$<0.01), unlike other drugs (immunosuppressants and HCQ). Among TRF, significant differences were found for the presence of SAH ($p$<0.01), higher BMI ($p$<0.01), total cholesterol ($p$=0.01), triglycerides ($p$=0.01) and uric acid ($p$<0.01).

## Discussion

Data from the literature have shown that the increased incidence of CVD and of premature atherosclerosis in SLE cannot be entirely explained by TRF (9, 20). In this study we evaluated the prevalence of traditional CV risk factors in a cohort of patients with SLE and we estimated the 10-year risk of CV events with three different algorithms. Based on the score percentage, they all make it possible to classify patients into various risk categories, thus indicating which patients will benefit the most from preventive therapy.

This study demonstrates how QRISK3, a recently validated algorithm that (in addition to TRF) also considers specific items such as the presence of SLE and the regular intake of steroids, classifies a greater number of SLE patients at high-risk of developing CVD in the next 10 years in comparison with classic algorithms such as Framingham and ACC/AHA.

Comparing baseline data collected in our cohort with those from the Toronto study by Bruce *et al*. (20), which is one of the widest studies concerning SLE-related CVD, they are substantially similar. The only exceptions are that our cohort showed a lower SLE-

DAI score, a lower kidney involvement (both in previous history and at recruitment time), a lower daily intake of corticosteroids and a higher assumption of HCQ. In addition, the TRF were similar in the two cohorts.

The results clearly point out that median risk scores are higher when evaluated with QRISK3 (6.2%) in comparison with Framingham (4.7%) and ACC/AHA (1.4%). Based on the score percentage, patients classifiable as high-risk were 29 according to Framingham and 17 for ACC/AHA, but this number rose to 44 when using QRISK3. Analysing the subgroup of patients over 40 years of age, QRISK3 still presents higher median scores in comparison with Framingham and ACC/AHA. In this subgroup, patients considered at high CV risk were 29 according to Framingham, 17 to ACC/AHA, and increased to 38 when using QRISK3. Notably, according to both Framingham and ACC/AHA, the number of high-risk patients remains the same when subjects under 40 years of age are excluded. When applying QRISK3, instead, there is a reduction in the high-risk population. This can be interpreted both that age is a parameter of primary importance for Framingham and ACC/AHA, and that QRISK3 has a higher sensitivity in the younger age group.

The aforementioned data show how QRISK3, thanks to its specific items, gives greater weight to CV risk in SLE compared to traditional algorithms, thus allowing the setting of a preventive therapy in a greater number of patients.

Analysing the characteristics of the patients considered at high-risk by QRISK3 and at low-risk by Framingham, we found that they cover a wide age range with several cases under 40 years of age. This result strengthens the hypothesis that QRISK3 could be useful in the prevention of CVD especially in younger patients, whereas Framingham and ACC/AHA give higher scores only after 50 years of age. This is also important considering that the 40–49 age group is proportionately the one with the highest CV risk in SLE-women compared to women in the general population (21). The evaluation of chronic kidney disease and chronic intake of glucocorticoids as a determinant of the CV risk estimation are other distinguishing features of the QRISK3. This is particularly important in SLE patients; indeed, almost half of our cohort at high-risk for QRISK3 but at low-risk for Framingham presented chronic kidney disease (stage ≥3) and almost all were regularly taking steroids.

Comparing patients considered at high-risk by QRISK3 but not by Framingham and those considered at low-risk by both indices, it emerges that newly identified QRISK3 high-risk patients are more likely to take chronic glucocorticoids and to have organ damage. Notably, it is quite unexpected that that newly identified QRISK3 high-risk patients have a significant higher presence of SAH, since arterial pressure is one of the major parameters for the Framingham algorithm.

Interestingly, QRISK3 allows calculating the risk score of a healthy person of the same age, sex and ethnicity, and consequently it was possible to calculate the median relative risk that suggested that our cohort has at least a 3-fold increased risk of CVD compared to the general population. Thus, the relative risk provided by QRISK3 is greater than that provided by other large studies reporting about 2-fold increased risk (1, 20). A further consideration can be made with respect to the aforementioned Toronto study, whose data were collected between 1998 and 2000 (20). Given the similar age of onset and disease duration, our patients have a disease with a more recent onset and therefore they likely benefit from better treatments than twenty years ago. Nevertheless, their CV risk was not reduced at all compared to the patients analysed in the Toronto study. This leads to the hypothesis that SLE CV risk is an intrinsic condition which is not modifiable by SLE-specific therapeutic improvements. Moreover, considering that the median age was 44 years (IQR 52–34.5), patients showed a median "QRISK3 healthy heart age" of 62 years (IQR 71–53). This should make us reflect on how SLE is a disease that can strongly impact on the health condition of the affected.

Recently, another study concerning the role of QRISK3 in SLE has been published (22). They reported a 22.4% difference between Framingham and QRISK3 in the identification of high-risk (score ≥10%) patients (4.6% *vs*. 27%, respectively), which is much greater than the 12.2% we found. Similarly to what we found in our cohort, their patients considered at high-risk by QRISK3 and at low-risk by the Framingham presented chronic kidney disease and a regular intake of steroids more frequently. This subgroup of patients, unlike ours, also had a significantly higher BMI and prevalence of diabetes mellitus.

There are some limitations in our study. First, as expected according to SLE epidemiology, the vast majority of patients are females, thus limiting the applicability of our considerations to male patients, who instead are those with the highest general CV risk. The major limitation of this study is the cross-sectional design that excludes ascertaining the link of causality between clinical variables, CV risk factors and the CV events that occurred in our cohort. With respect to traditional algorithms, QRISK3 allows the identification of a greater proportion of patients at high 10-year CV risk, but its predictive accuracy in SLE patients is unverified in a prospective cohort. Indeed, it should also be mentioned that, when applied for CV risk estimation in rheumatoid arthritis, QRISK2 did not prove to be superior to classical algorithms in longitudinal studies, but it rather overestimated CV risk in these patients (23, 24). If the accuracy of QRISK3 in SLE were prospectively proven, it would mean that the use of this algorithm as a tool in the evaluation of SLE patients could lead to the early detection in a considerable part of high-risk CVD development individuals who would have otherwise been underestimated by the application of Framingham or ACC/AHA algorithms.

**Acknowledgments**

We wish to thank all the patients who participated in the study, and the research nurses of the Lupus Clinic of the Rheumatology Unit of Pisa who actively contributed to carrying out the study: Sabrina Gori, Lucia Pedrocco, Carla Puccini, Manuela Terachi, Maria Tristano, Valentina Venturini, Catiuscia Zoina.

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