Potential predictors of atrial fibrillation in embolic stroke of undetermined source (ESUS)

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Background

Among patients affected by ischaemic stroke, in 25% of all cases it is not possible to determine the most likely etiology despite extensive investigation: however, evidence in medical literature suggests that a large number of these cases the event might present an underlying embolic pattern.

Thus, a new definition of "**Embolic Stroke of Undetermined Source**" (**ESUS**) has been recently proposed[1]. In the latest years, numerous efforts have been invested in order to discover possible early markers suggestive of cardioembolism in these patients, which would then allow the prescription of an adequate anticoagulation therapy, potentially more effective in preventing further cerebrovascular accidents[2-4].

Aim of the study / Materials and methods

This study is aimed at **discovering a series of factors** (demographic, instrumental, biohumoral) **potentially predictive of development of atrial fibrillation (AF)** in patients otherwise classified as ESUS.
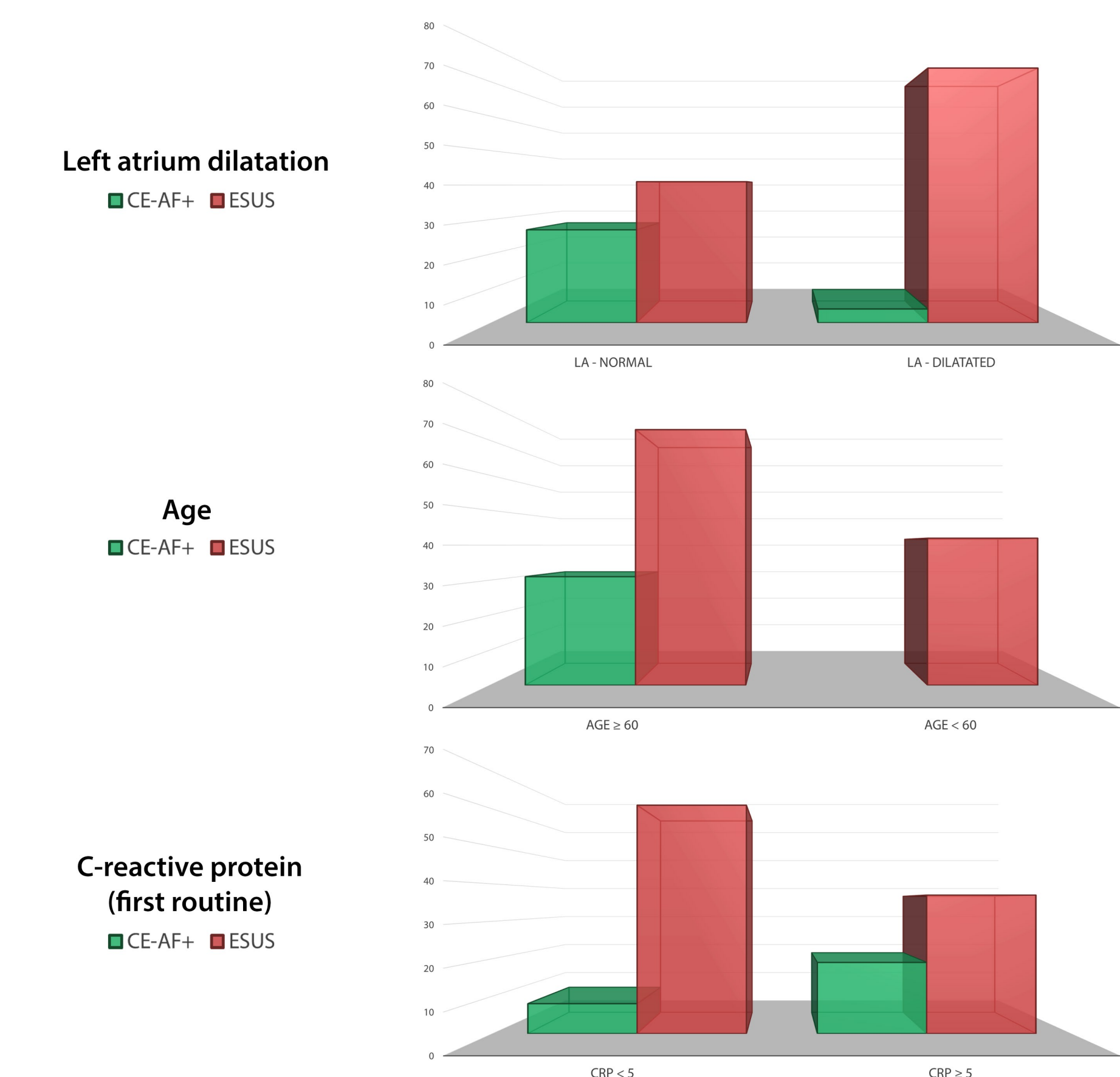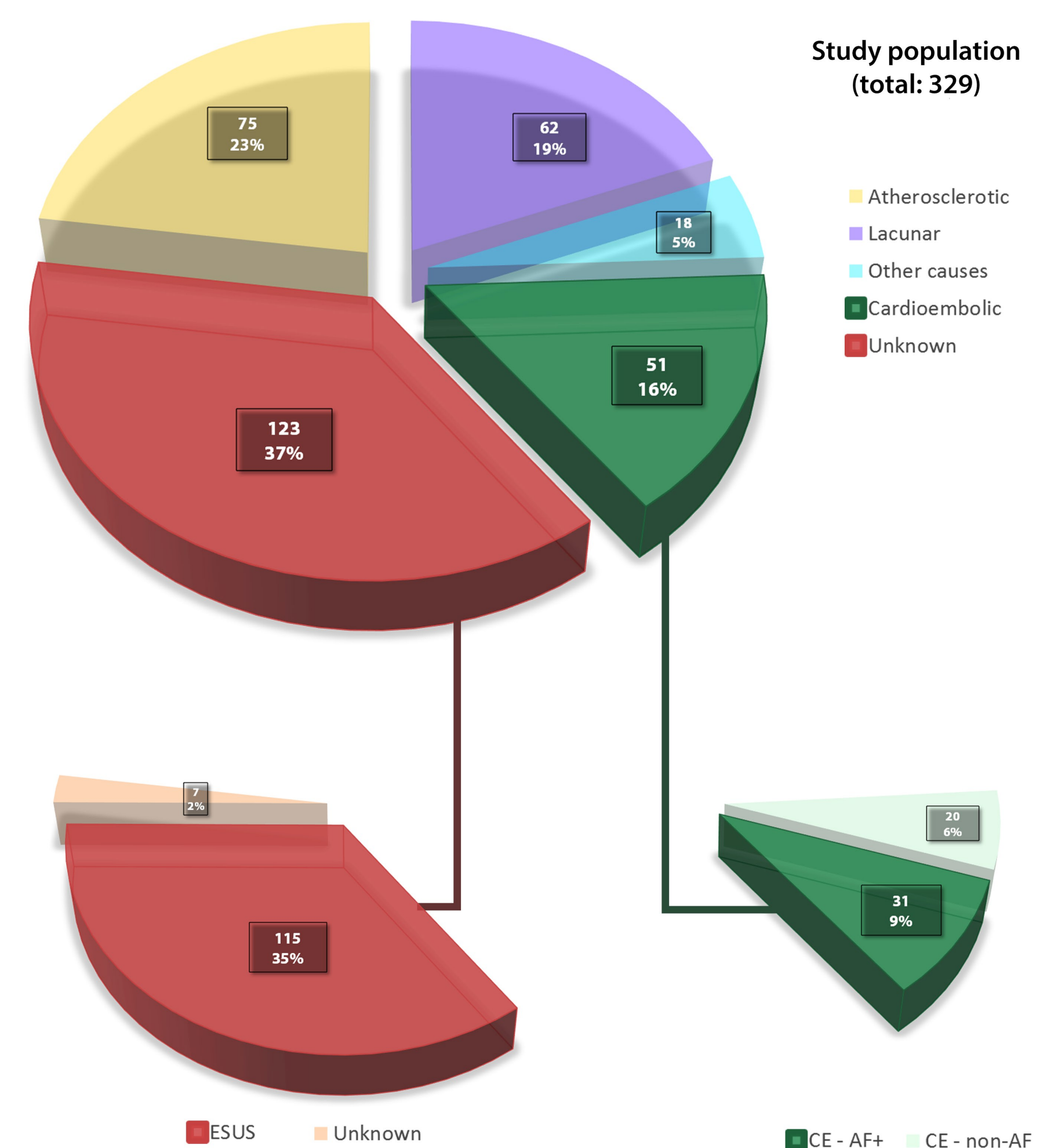
We examined and analysed the clinical records of all the patients admitted in our Stroke Unit Department from 2006 to 2015, classified with the TOAST criteria. Patients with reasonable evidence of cardioembolism (i.e. known history of AF – chronic or paroxysmal) before hospital admittance have been excluded. Also, only patients who underwent an adequate cardiological examinations (at least one echocardiogram and 2 Holter ECG registrations between hospitalization and one-month follow-up) were taken into account.

329 patients were considered, divided among a possible atherosclerotic (75), lacunar (62), cardioembolic (51) or unknown (123) origin, as well as patients for which an other determined origin had been identified (18). From the **cardioembolic** group, **31** were thus classified due to the discovery of a **new-onset atrial fibrillation** ("CE-AF+"), while the others (20) had morphological cardiac anomalies likely responsible for cardioembolism as pointed out in the TOAST definition. Among those classified as of "unknown" origin, following the TOAST guidelines, 7 were defined as such because multiple possible (and equally plausible) causes had been identified; the remaining **115** showed **no clear aetiopathogenetic mechanism**, and met the criteria for the ESUS definition ("**ESUS**").

We **analysed** the **distribution, similarities and differences** of several demographic, instrumental and biohumoral markers **between the "CE-AF+" and "ESUS" groups**.
For the echocardiographic examination, the left atrium (LA) was considered significantly enlarged for a anteo-posterior diameter higher than 39 mm in women and 41 mm in men[5]. Statistical analyses were executed using the IBM SPSS Statistics® 20 software (IBM Corporation, Armonk, USA).

Study population (total: 329)

- Atherosclerotic — 75 / 23%
- Lacunar — 62 / 19%
- Other causes — 18 / 5%
- Cardioembolic — 51 / 16%
- Unknown — 123 / 37%

115 / 35% ESUS — Unknown
31 / 9% CE - AF+ — CE - non-AF 20 / 6%

Results

When considering both groups, most of the numeric variables resulted to be **normally distributed** according to the Shapiro-Wilk test, and in particular:
- **age** ($p = 0,014$)
- **cardiac frequency in ER** ($p < 0,005$)
- **glycaemia in ER** ($p < 0,005$)
- **C-reactive protein at the first blood routine examination** ($p < 0,005$)

Among these, age, cardiac frequency, and C-reactive protein presented homogeneity of variances according to the Levene's test; thus, a **t-test for independent variables** was performed between the two groups, which produced the following output:
- **age** ($p < 0,005$)
- **cardiac frequency in ER** ($p = 0,003$)
- **C-reactive protein at the first blood routine examination** ($p = 0,003$)

Finally, for categorical variables, we performed a **Pearson's χ^2 test**.
These findings (charts on the left) emerged to be significantly different between the two groups in exam:
- **sex-adjusted diameter of the left atrium - dilatation versus normal**[5] ($p < 0,005$)
- **age less than 60 years** ($p < 0,005$)
- **C-reactive protein > 5 mg/l at the first blood routine examination** ($p = 0,01$)

Left atrium dilatation — CE-AF+ ESUS (LA - NORMAL, LA - DILATATED)

Age — CE-AF+ ESUS (AGE ≥ 60, AGE < 60)

C-reactive protein (first routine) — CE-AF+ ESUS (CRP < 5, CRP ≥ 5)

Conclusions

Due to their statistically different distribution between the "CE-AF+" and "ESUS" groups, the results above might possibly **help identify patients initially classified as ESUS** but instead having a **higher likelihood of concealing** an **underlying paroxysmal atrial fibrillation**.

Thus, patients meeting the ESUS criteria and showing a combination of the findings above **might benefit from a prolonged cardiological monitoring** and, in case of successful recognition of AF, from an **adequate anticoagulation therapy**.

References:
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