in the upper lobe, and the tendency for relapses was independent of the treatment. It is unusual that 8 of the 9 patients who had recurrences were in systemic remission as they were receiving immunosuppressive therapy, with a mean of 3 recurrences per patient. One of them had 12 relapses.

Our patient had a web-like stenosis (WLS) or "in diaphragm", that is believed to develop due to an exaggerated inflammatory response and hypertrophy of the mucosa, and formation of fibromembranous tissue that comes to progressively occlude the bronchial lumen.[7–9] Web-like stenoses have been related to infections, traumatic injury and local or systemic inflammatory processes. Three cases of WLS have been reported with GPA and one with microscopic polyangiitis,[8] and isolated cases with vasculitis, sarcoidosis, amyloidosis, Behçet's disease and ulcerative colitis.[9,10] In contrast to non-web-like BS, lung CT is normal. Thus, only pulmonary functions tests and bronchoscopy enable the establishment of the diagnosis. The prognosis is poor, requiring dilatations using a rigid bronchoscope, endobronchial laser, local steroid injections and even the placement of stents in the case of proximal stenoses. Treatment and follow-up should be discussed with bronchoscopists or thoracic surgeons. The purpose is to perform the available endobronchial technique and optimize immunosuppressive therapy.

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## A Reflection on How We Define, Determine and Interpret the Finding of Lupus Anticoagulant☆

### *Una reflexión sobre el anticoagulante lúpico: cómo lo definimos, determinamos e interpretamos*

*To the Editor,*

International criteria for the diagnosis of antiphospholipid syndrome (APS) include the detection of antiphospholipid antibodies: anticardiolipin and anti-β2-glycoprotein I (anti-β2GPI) of immunoglobulin (Ig) G and IgM isotopes and lupus anticoagulant (LA), and its detection in patients with a history of thrombosis or pregnancy complications is considered to be essential in the management of APS.[1–3]

During the 1950s, it became evident that patients with systemic lupus erythematosus (SLE) had a circulating anticoagulant factor, and the concept of LA was coined to designate a heterogenic group of coagulation inhibitors that affect prothrombin activation by the prothrombinase enzyme complex.[4] Lupus anticoagulant is currently described as an Ig like IgG/IgM that inhibits phospholipid (PL)-dependent coagulation reactions *in vitro*. However, is LA always associated with SLE? Does it inhibit coagulation? Is it an antibody? First, the majority of the patients who are positive for LA do not have SLE. In the absence of concomitant thrombocytopenia or a deficiency of coagulation factors or inhibitors of coagulation factors, with certain exceptions, LA is related to processes of hypercoagulability and arterial and venous thrombosis, but is not, *per se*, a risk factor for bleeding or hemorrhage. With the currently available scientific evidence, it can be said the LA is constituted by a group of antibodies that have yet to be characterized.[5,6]

Lupus anticoagulant is detected using functional assays that demonstrate a PL-dependent prolongation of the clotting time, due to the *in vitro* interference of antibodies with PL-dependent function, as with certain essential cofactors in the coagulation cascade (Fig. 1) that result in the prolongation of the activated partial thromboplastin time. The International Society on Thrombosis and Haemostasis (ISTH),[7] a society that has unsuccessfully attempted to change the name, established the following criteria to confirm the presence of LA:

1. Phospholipid-dependent prolonged coagulation tests.
2. Demonstration of the coagulation inhibitor utilizing mixed plasma.
3. Demonstration of the PL dependence of the inhibitor.
4. Ruling out other coagulation disorders, particularly due to deficiency of coagulation factors.

Lupus anticoagulant can be detected in patients with SLE, and with other autoimmune diseases, infections like human immunodeficiency virus, hepatitis and malaria, neoplastic disease or those taking certain drugs (procainamide and chlorpromazine).[6,8] A prevalence of 5% has been reported in the general adult population and up to 9.5% in women of reproductive age. Although the

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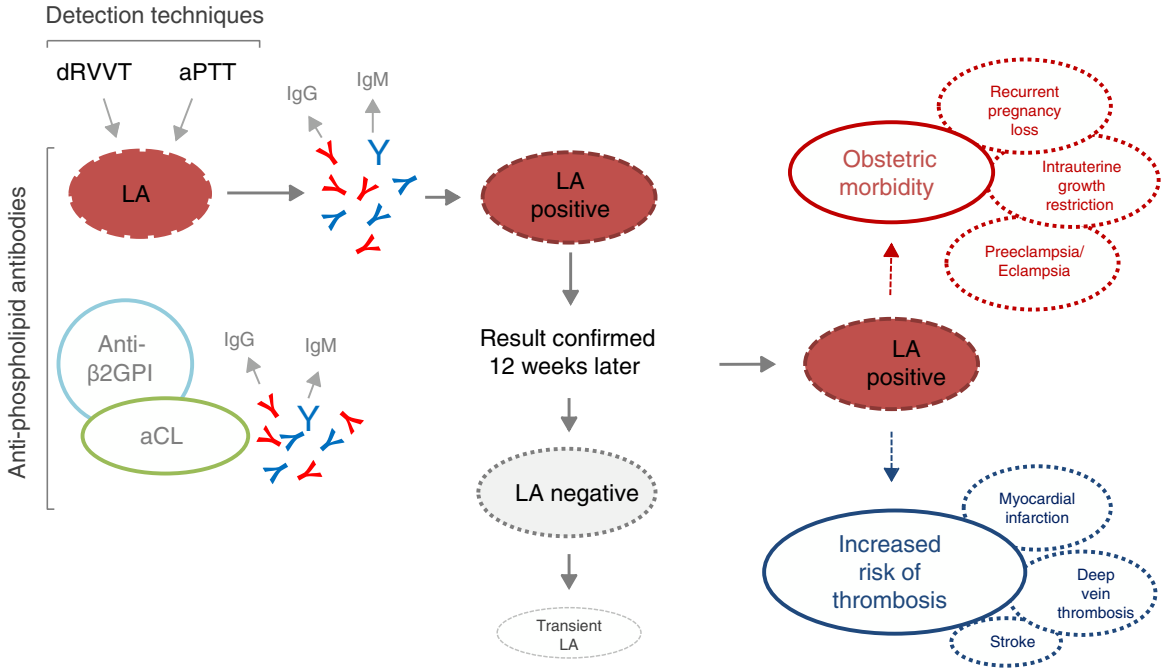


**Fig. 1.** Detection, interpretation and possible clinical consequences of a positive result in lupus anticoagulant testing. aCL, anti-cardiolipin; anti-β2GPI, anti-β2-glycoprotein I; aPTT, activated partial thromboplastin time; dRVVT, dilute Russell's viper venom time; Ig, immunoglobulin; LA, lupus anticoagulant; PL, phospholipid.

pathogenic mechanism has not been defined, the presence of LA has been related to stroke, transitory ischemic attack, acquired thrombophilia and obstetric events, like early and/or recurrent pregnancy loss.[7] Although it is certain that, in general, antiphospholipid antibodies have been associated with the clinical manifestations of APS, this association seems to be more evident with LA both in thrombosis and in the morbidity related to pregnancy.[8,9]

Studies dealing with the relationship between the processes of coagulation and inflammation would establish the clinical relevance of the detection of LA alone, as well as the emergent association of LA to C-reactive protein and mortality. The therapeutic management of asymptomatic carriers of LA could require prophylactic treatment given the presence of cardiovascular risk factors or autoimmune disease.[5,8]

In view of the potential thrombotic risk in patients who are positive for LA, it is essential to develop an accurate method for performing its assessment in terms of the diagnosis and follow-up of these patients and the decision on the anticoagulant therapy they should receive. Unfortunately, since we lack a technique to serve as a reference for the detection of LA, laboratories utilize heterogeneous and non-quantitative assays, impeding the characterization of positive results in terms of low or elevated titers.[10,11] This requires that the validation of the results be performed only by expert staff. In turn, it impedes their being standardized, the establishment of a consensus and the automation of this determination.[6,11] A study published by Devreese et al. points out the need to analyze other additional procoagulant markers, like P-selectin (a marker of platelet activation) and coagulation factor VII in patients with weak LA, in order to optimize its clinical utility.[12,13] It is evident that both overrating and underrating LA would expose our patients to long-term anticoagulation or to an increase in the risk of recurrent thrombosis, respectively.[13] Likewise, it should be possible to report LA quantitatively to enable the identification of low titers or those near the reference value. There is an unquestionable need to perform prospective studies, that examine the relevance of these laboratory tests. This, together with possible new prognostic laboratory parameters, would help in the stratification of the patients in accordance with the risk groups and in making therapeutic decisions.

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## Prevalence of Risk Factors for the Development of Avascular Hip Necrosis in a Third-level Hospital☆

### *Prevalencia de los factores de riesgo para el desarrollo de necrosis avascular de cadera en un hospital de tercer nivel*

*To the Editor,*

Avascular hip necrosis (AHN) is characterized by the death of osteocytes and of the bone marrow caused by interruption of the blood supply to the femoral head.[1–3]

It commonly affects young adults.[2,4,5] In the United States, the incidence is estimated to be between 10,000 and 30,000 cases each year, accounting for 5%–12% of the total hip arthroplasties performed to treat patients who have AHN.[2,4,6–8] Despite the identification of a number of risk factors (RF), the etiology and pathogenesis of the disease remain unclear. A number of proposals have been made, including ischemia, direct cell toxicity and changes in the differentiation of mesenchymal stem cells.[4,6]

Given the impact of this disease, which has an insidious onset and shows no clear symptoms or signs, it is necessary to be aware of those RF that promote it in order to maintain our vigilance in these patients. That will enable early diagnosis and the establishment of the necessary preventive measures and the proper treatment strategies.[1,2]

On this basis, the objective of our study was to estimate the prevalence of the different RF for AHN in patients admitted to Hospital Universitario 12 de Octubre in Madrid, Spain. We included, from January 2010 to December 2015, a total of 129 patients with a diagnosis of AHN. The mean age ± standard deviation was 58.35 ± 15.33 years; 56.6% were men. The diagnostic criteria to define the presence of AHN were mainly obtained from the results of imaging studies. The study was approved by the clinical research ethic committee of our hospital.

The most prevalent RF were tobacco use (n = 57; 44.2%) and dyslipidemia (n = 46; 35.7%), which we consider to be associated. Among the RF with the greatest etiological burden for the development of AHN, the most prevalent were corticosteroid therapy (n = 37; 28.7%), alcoholism (n = 26; 20.2%) and previous traumatic injury (n = 20; 15.5%). Of the 18 patients (13.9%) with autoimmune and/or inflammatory disease, 3 (16.7%) had systemic lupus erythematosus. The 3 were being treated with corticosteroids and 2 of the 3 were positive for antiphospholipid antibodies. In this respect, Gontero et al.[9] found no differences in the total accumulated dose, daily dose and duration of steroid therapy or the presence of antiphospholipid antibodies.

In 17 patients (13.2%), no RF was identified (Table 1). However, there were patients with several RF, with an accumulation of up to 6 in 1.6%. The most prevalent finding was 2 and 3 RF associated with 32 cases (24.8%) and with 27 cases (20.9%), respectively.

The sample was divided into 2 groups to study the differences between the younger and older patients, randomly setting 50 years as the cutoff point. We found that there was an absence of known RF in the individuals over 50 years of age, resulting in a statistically significant difference ($P = .006$).

As other authors have indicated, this disease has a gradual onset, without specific symptoms or signs, meaning that the diagnosis is established late.[2] Malizos et al.[2] mention that, given the numerous associated factors that have recently been described, it is now less common to classify osteonecrosis as idiopathic. The results of our study concur in terms of our findings in the group of patients aged 50 years or less (2.2%). The prevalence of idiopathic AHN in patients over the age of 50 years in our series (19.3%) is similar to that reported by other authors (20%–25%).[1,8,10] It is certain that, although this study is retrospective, it has its limitations. For example, missing information because these RF are not recorded in the medical records, contributing to the number of patients without

**Table 1**
Risk Factors for Avascular Hip Necrosis.

| | Total (n = 129) | ≤50 years (n = 46) | >50 years (n = 83) | *P* |
|---|---|---|---|---|
| Tobacco use | 57 (44.2%) | 24 (52.2%) | 33 (39.8%) | .198 |
| Dyslipidemia | 46 (35.7%) | 20 (43.5%) | 26 (31.3%) | .184 |
| Corticosteroid therapy/ hypercortisolism[a] | 37 (28.7%) | 17 (37%) | 20 (24.1%) | .155 |
| Alcoholism | 26 (20.2%) | 13 (28.3%) | 13 (15.7%) | .11 |
| Traumatic injury | 20 (15.5%) | 4 (8.7%) | 16 (19.3%) | .133 |
| Autoimmune/ inflammatory disease | 18 (13.9%) | 8 (17.4%) | 10 (12.1%) | .434 |
| Diabetes mellitus | 13 (10.1%) | 3 (6.5%) | 10 (12%) | .377 |
| Liver cirrhosis | 13 (10.1%) | 6 (13%) | 7 (8.4%) | .543 |
| Transplantation | 11 (8.5%) | 4 (8.7%) | 7 (8.4%) | 1.00 |
| HIV | 10 (7.8%) | 5 (10.9%) | 5 (6%) | .327 |
| Chemotherapy | 9 (7%) | 6 (13%) | 3 (3.6%) | .068 |
| Thrombophilia | 8 (6.2%) | 3 (6.5%) | 5 (6%) | 1.00 |
| Radiotherapy | 6 (4.7%) | 4 (8.7%) | 2 (2.4%) | .186 |
| Pro-embolic phenomenon | 2 (1.6%) | 0 (0%) | 2 (2.4%) | .538 |
| Myeloproliferative syndrome | 1 (0.8%) | 0 (0%) | 1 (1.2%) | 1.00 |
| Unknown | 17 (13.2%) | 1 (2.2%) | 16 (19.3%) | .006 |

[a] A case of adrenocorticotropic hormone-dependent Cushing syndrome.
HIV, human immunodeficiency virus.

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