

Predictive Factors for Symptomatic Osteonecrosis in Patients with Systemic Lupus Erythematosus

Thesis

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List of Abbreviations

Abb.	Full term
<i>ACLE</i>	<i>Acute cutaneous lupus erythematosus</i>
<i>AIHA</i>	<i>Autoimmune haemolytic anaemia</i>
<i>ANA</i>	<i>Antinuclear antibodies</i>
<i>anti-dsDNA</i>	<i>Anti-double-stranded DNA</i>
<i>APCs</i>	<i>Antigen presenting cells</i>
<i>APL</i>	<i>Antiphospholipid antibodies</i>
<i>APS</i>	<i>Antiphospholipid syndrome</i>
<i>ARCO</i>	<i>Association Research Circulation Osseous</i>
<i>AUC</i>	<i>Area under curve</i>
<i>AVN</i>	<i>Avascular necrosis</i>
<i>AZA</i>	<i>Azathioprine</i>
<i>BA</i>	<i>Biologic agents</i>
<i>BLys</i>	<i>B lymphocyte stimulator</i>
<i>BMD</i>	<i>Bone mineral density</i>
<i>Bps</i>	<i>Bisphosphonates</i>
<i>CBC</i>	<i>Complete blood count</i>
<i>CBCAPs</i>	<i>Cell bound complement activation products</i>
<i>CCLE</i>	<i>Chronic cutaneous lupus erythematosus</i>
<i>CD</i>	<i>Core decompression</i>
<i>CD40L</i>	<i>Costimulatory protein 40 ligand</i>
<i>CHF</i>	<i>Congestive heart failure</i>
<i>CHLE</i>	<i>Chilblain Lupus</i>
<i>CLE</i>	<i>Cutaneous lupus erythematosus</i>
<i>CM</i>	<i>Cardiomyopathy</i>
<i>c-Mpl</i>	<i>Cloned myeloproliferative leukemia</i>
<i>CMV</i>	<i>Cytomegalovirus</i>
<i>COX-2</i>	<i>Cyclooxygenase-2</i>
<i>CRP</i>	<i>C-reactive protein</i>
<i>CS</i>	<i>Corticosteroids</i>
<i>CsA</i>	<i>Cyclosporine A</i>
<i>CT</i>	<i>Computed tomography scan</i>
<i>CVD</i>	<i>Cardiovascular disease</i>
<i>CYC</i>	<i>Cyclophosphamide</i>

List of Abbreviations Cont...

Abb.	Full term
<i>CYP</i>	<i>Cytochrome P450</i>
<i>DAH</i>	<i>Diffuse alveolar hemorrhage</i>
<i>DCs</i>	<i>Dendritic cells</i>
<i>DHEA</i>	<i>Dehydroepiandrosterone</i>
<i>DLE</i>	<i>Discoid lupus erythematosus</i>
<i>DNMT3A</i>	<i>DNA Methyltransferase 3 Alpha</i>
<i>EBV</i>	<i>Epstein–Barr virus</i>
<i>eGFR</i>	<i>Estimated glomerular filtration rate</i>
<i>ELISA</i>	<i>Enzyme linked immunosorbant assay</i>
<i>EPO</i>	<i>Erythropoietin</i>
<i>ERK</i>	<i>Extracellular signal-regulated kinases</i>
<i>eSDI</i>	<i>Early SLICC/ACR Damage Index</i>
<i>ESR</i>	<i>Erythrocyte sedimentation rate</i>
<i>FH</i>	<i>Femoral head</i>
<i>FHCD</i>	<i>Femoral head core decompression</i>
<i>FM</i>	<i>Fibromyalgia</i>
<i>FRAX</i>	<i>Fracture Risk Assessment Tool</i>
<i>FVFG</i>	<i>Free vascularized fibular graft</i>
<i>GCs</i>	<i>Glucocorticoids</i>
<i>GI</i>	<i>Gastrointestinal</i>
<i>GN</i>	<i>Glomerulonephritis</i>
<i>GSPE</i>	<i>Grape seed proanthocyanidin extract</i>
<i>HBO</i>	<i>Hyperbaric oxygen therapy</i>
<i>IFNα</i>	<i>Interferon α</i>
<i>IgG</i>	<i>Immunoglobulin G</i>
<i>IPO</i>	<i>Intestinal pseudo-obstruction</i>
<i>IQR</i>	<i>Inter-quartile range</i>
<i>ISN/RPS</i>	<i>International Society of Nephrology/Renal Pathology Society</i>
<i>JA</i>	<i>Jaccoud’s arthropathy</i>
<i>LDL</i>	<i>Low-density lipoprotein</i>
<i>LET</i>	<i>Lupus erythematosus tumidus</i>

List of Abbreviations Cont...

Abb.	Full term
<i>LKM</i>	<i>Liver-kidney-mitochondrial</i>
<i>MMF</i>	<i>Mycophenolate mophetil</i>
<i>MRI</i>	<i>Magnetic resonance imaging</i>
<i>MSC</i>	<i>Mesenchymal stem cells</i>
<i>NO</i>	<i>Nitric oxide</i>
<i>NOFH</i>	<i>Nontraumatic osteonecrosis femoral head</i>
<i>NPSLE</i>	<i>Neuropsychiatric involvement in SLE</i>
<i>NPV</i>	<i>Negative predictive value</i>
<i>NVBG</i>	<i>Non vascularized bone graft</i>
<i>OA</i>	<i>Osteoarthritis</i>
<i>ONFH</i>	<i>Osteonecrosis of the femoral head</i>
<i>P/C ratio</i>	<i>Protein / creatinine ratio</i>
<i>PFT</i>	<i>Pulmonary function test</i>
<i>PGA</i>	<i>Physician Global Assessment</i>
<i>PPV</i>	<i>Positive predictive value</i>
<i>PRCA</i>	<i>Pure red cell aplasia</i>
<i>PVD</i>	<i>Peripheral vascular disease</i>
<i>RBCs</i>	<i>Red blood counts</i>
<i>RF</i>	<i>Risk factors</i>
<i>SC</i>	<i>Stem cell</i>
<i>SCLE</i>	<i>Subacute cutaneous lupus erythematosus</i>
<i>SLAM</i>	<i>Systemic Lupus Activity Measure</i>
<i>SLE</i>	<i>Systemic lupus erythematosus</i>
<i>SLEDAI</i>	<i>SLE Disease Activity Index</i>
<i>SLS</i>	<i>Shrinking lung syndrome</i>
<i>SPECT/CT</i>	<i>Single photon emission computed tomography/ computed tomography</i>
<i>SPSS</i>	<i>Statistical Package for Social Science</i>
<i>TAC</i>	<i>Tacrolimus</i>
<i>TdT</i>	<i>Terminal deoxynucleotidyl transferase</i>
<i>THA</i>	<i>Total hip arthroplasty</i>
<i>THR</i>	<i>Total hip replacements</i>

List of Abbreviations Cont...

Abb.	Full term
<i>TPBS</i>	<i>Three-phase bone scintigraphy</i>
<i>TTP</i>	<i>Thrombotic thrombocytopenic purpura</i>
<i>TUNEL</i>	<i>dUTP Nick-End Labeling</i>
<i>US</i>	<i>Ultrasonography</i>
<i>UV</i>	<i>Ultraviolet</i>
<i>VAS</i>	<i>Visual analogue scale</i>
<i>VBG</i>	<i>Vascularized bone graft</i>
<i>VEGF</i>	<i>Vascular endothelial growth factor</i>

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease with heterogeneous performance. It can produce a variety of autoantibodies with complement activation and immune complex deposition, leading to damage to multiple tissues and organs (*Wang et al., 2016*).

The disease most often affects women of childbearing period. Its onset and development are associated with genetic predisposition and environmental factors, such as exposure to ultraviolet light and certain drugs. Its most common manifestations are arthritis, fatigue and malar erythema; beyond these manifestations, some individuals may develop serious complications such as renal, neurological and cardiopulmonary dysfunction (*Marques et al., 2016*).

Osteonecrosis (ON) is one of the most common complications of SLE, which is reported in 3–30 % lupus patients. The key mechanism of ON is destruction of the nourishing vessels of bone, which leads to osseous ischemia, degeneration, and necrosis. The most common site of ON is femoral head, while it is less common in knee & shoulder (*Zhao et al., 2016*).

Several factors have been associated with the development of ON in SLE, although corticosteroid (CS) therapy has been the most consistent association. However, a

considerable proportion of SLE patients with ON complications have no history of CS treatment, while most SLE patients who receive CS do not develop ON during the course of the disease (*Faezi et al., 2015*). Many other risk factors such as vasculitis, antiphospholipid antibodies, Raynaud's phenomenon and hyperlipidemia have been reported for ON in patients with SLE; however, no proven association factor has yet been found (*Wang et al., 2016*).

Symptomatic hip ON is a disabling condition with a poorly understood aetiology and pathogenesis. Numerous treatment options were for hip ON were described, including non-operative management and joint preserving procedures, as well as total hip replacement. Non-operative management includes drugs such as; bisphosphonates, anticoagulants, hypolipemics, vasodilators, or other procedures such as extra-corporeal shock wave treatment, pulsed electromagnetic therapy, or hyperbaric oxygen which have all shown efficacy in the reduction of pain, and improved function during early-stages of the condition (*Issa et al., 2013*).

AIM OF THE STUDY

The aim of the study is to identify the clinical and laboratory risk factors for development of Osteonecrosis in SLE patients.