Background Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by impaired clearance of apoptotic cells. Milk fat globule epidermal growth factor 8 (MFG-E8) is a protein that connects with v3 integrin of phagocytic macrophage and phosphatidyserine of apoptotic cell surface. In this study, we determine whether genetic variation of MFG-E8 gene and serum protein concentration are associated with SLE.

Methods Single nucleotide polymorphisms (SNPs) were genotyped by three steps. At first, we used polymerase chain reaction in 20 patients with SLE and 20 normal controls (NC) for sequencing of a whole MFG-E8 gene in Korean population. Then we screened 12 selected SNPs in 55 SLE and 30 NC. Finally, we used Taq-man probe assay in 225 SLE and 230 NC for genotyping of targeted 5 SNPs. Furthermore, serum MFG-E8 concentrations were analysed in SLE.

Results SLE patient's mean age was 35.7±7.8 years and 92% were women, which is not different form NC. rs2271715's C allele and rs3743388's G allele were shown higher frequency in SLE than NC (p=0.036, p=0.005, respectively). As the linkage disequilibrium test, rs1878326 and rs1878327 were shown high linkage (r^2=0.879). Three haplotypes were found by four SNPs (rs4945, rs1878327, rs2271715, and rs3743388); AACC, CGCG, and CGTC. The CGCG haplotype was significantly higher in patients with SLE compared with NC (p=0.001, odds ratio=2.31). rs4945 was associated with erythrocyte sedimentation rate and rs1878327 was associated with alopecia, C-reactive protein, complement 3, and anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibody, and systemic lupus erythematosus disease activity score. rs2271715 and rs3743388 were associated with renal disease, cumulated steroid dose, cyclophosphamide and mycophenolate mofetil usage and rs3743388 also was associated with anti-dsDNA antibody. Serum MFG-E8 concentration was shown significantly higher in SLE than NC (2.030.3±1.292.3 pg/mL vs 1.433.0±1.946.3 pg/mL, p=0.017).

Conclusions Our data suggest possibility that MFG-E8 rs2271715 and rs3743388 SNP can be involved in susceptibility of SLE. Also, these SNPs are associated with renal disease and disease activity in SLE. Furthermore, rs4945 and rs1878327 polymorphisms may be a marker of disease activity. 

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Background

Chinese SLE treatment and Research Group (CSTAR) started a multi-center prospective cohort study recruiting SLE patients with pulmonary arterial hypertension (PAH) since 2006. This study aimed to investigate the validity of a multidimensional risk assessment and the prognostic value of it in SLE-associated PAH.

Methods

All SLE patients were fulfilled the 1997 revised ACR criteria. PAH was diagnosed based on ESC/ERS guidelines by right heart catheterization. The outcome was all-cause mortality. Two different methods of risk categorization were applied according to baseline data, including low-risk criteria number of none to four and mean score of 1 (low-risk), 2 (intermediate-risk) or 3 (high-risk). According to first follow-up, patients were further divided into increased risk, remained risk and decreased risk group. A prediction model was used to distinguish SLE-PAH from vasculitic and vasculopathic subtype, based on the time interval between the diagnosis of SLE and PAH and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Kaplan-Meier survival curves and Cox proportional hazards analysis were conducted.

Results

282 patients were enrolled. The 5 year survival of patients with none, one, two, three and four low risk criteria were 42.7%, 64.8%, 86.1%, 90.2% and 91.7%, respectively (HR=0.59, 95% CI 0.44–0.78, p<0.001). The 5 year survival of patients in low-risk, intermediate-risk and high-risk group were 92.3%, 60.4% and 50.0%, respectively (Log-rank, p=0.001). Notably, in low-risk group, patients with vasculitic subtype had better survival than those with vasculopathic subtype (Log-rank, p=0.044). The 5 year survival of patients with remained, decreased and increased risk were 65.4%, 88.1% and 23.8%, respectively (log-rank, p<0.001).

Conclusions

Our study, for the first time, validated the prognostic value of risk stratification strategy at baseline and follow-up visit in patients with SLE-associated PAH. Patients are recommended to have a comprehensive evaluation on PAH and SLE at baseline and every follow-up visit. The SLE disease activity and systemic manifestations predict the phenotype of SLE-associated PAH, which also effect the long-term survival and need to be involved into risk assessment of SLE-associated PAH. Improving to low-risk group can be a future treatment target for SLE-associated PAH patients in clinical practice.

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EVALUATION OF ADVERSE EVENTS AND RELAPSE RISK OF SYSTEMIC LUPUS ERYTHEMATOSUS DURING TREATMENT WITH HYDROXYCHLOROQUINE

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Background

The antimalarial drug hydroxychloroquine (HCQ) has been widely used in the world to control the disease activity of systemic lupus erythematosus (SLE). In Japan, it has not been approved until September 2015 due to the problem of retinopathy induced by chloroquine. For these reasons, there is insufficient evidence for its effects and adverse events.