POLYMORPHISM OF THE MANNOSE-BINDING LECTIN (*MBL2*) GENE COULD BE ASSOCIATED WITH PROSTHETIC JOINT INFECTION

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Background

Prosthetic joint infection (PJI)

PJI is one of the most frequent early complications of total joint arthroplasty (TJA) that leads to revision surgery, long-term morbidity, and increased burden for any health-care system .

It is believed that despite complex antibacterial measures majority of TJA surgeries is mildly contaminated by bacteria that may adhere to prosthesis and cause PJI.

Based on the fact that majority of patients after TJA do not exhibit PJI we postulate concept of **"infection prone/resist" genotype.**

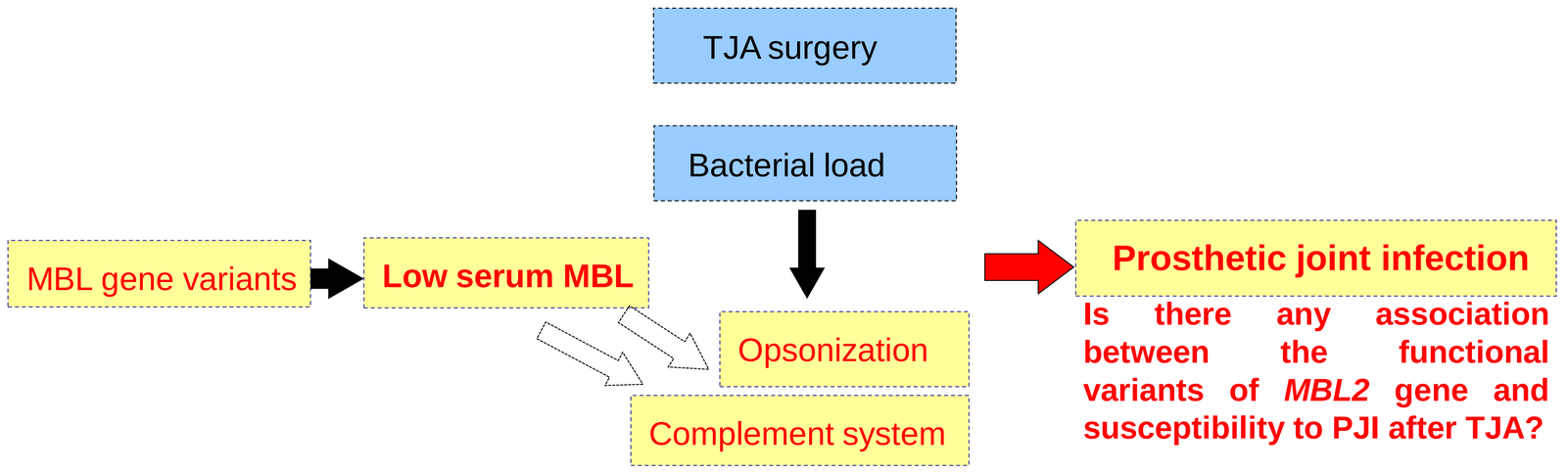
Mannose-binding lectin (MBL)

MBL is primary liver-derived serum protein that plays an important role in the innate immune system by opsonization of microbial agents, induction of complement system and phagocytosis.

Defective MBL production is common immune deficiency affecting up to 30% of Caucasians.

Several genetic **variants of MBL** gene critically affect MBL **expression / function.**

Hypothesis and Objective



Is there any association between the functional variants of *MBL2* gene and susceptibility to PJI after TJA?

Methods

1. Subjects

78 unrelated Czech patients with PJI after cementless type TJA and **two control groups:**
200 patients with non-septic TJA and 167 healthy control subjects (population controls).

***2. MBL2* SNPs genotyping**

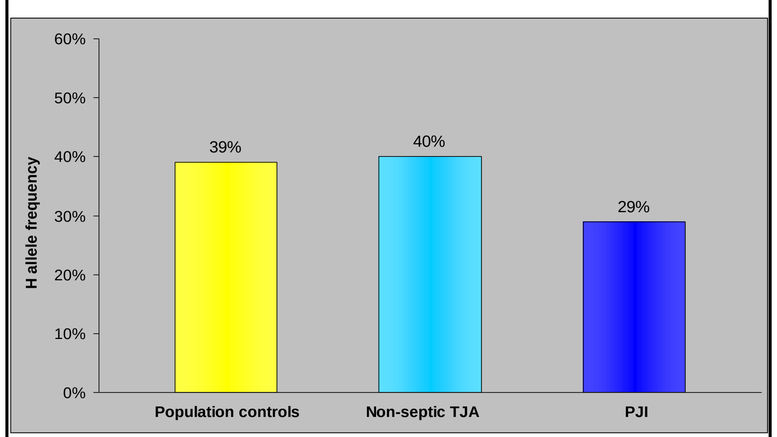
MBL2 -550 (rs11003125) genotyping: Polymerase Chain Reaction with Sequence Specific Primers (PCR-SSP)
MBL2 +54 (rs1800450) genotyping: TaqMan assay

3. Statistics

Conformity of the distribution of genotypes to the Hardy-Weinberg equilibrium: $\chi 2$ goodness-of-fit test.
Differences between allelic, genotype and phenotype („carriage rate") frequencies: $\chi 2$ test.

Results

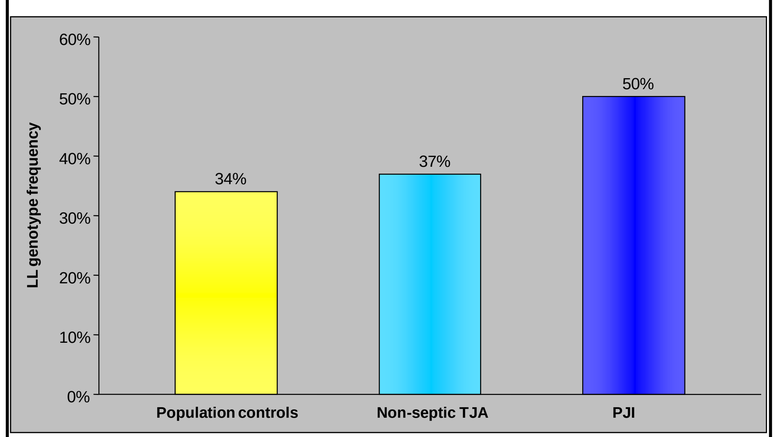
Fig 1. The frequency of *MBL2* -550 H allele in the patients with prosthetic joint infection (PJI) compared to those in the patients with non-septic total joint athroplasty (TJA) and in population controls



PJI *versus* Population controls $p = 0.04$

PJI *versus* Non-septic TJA $p = 0.02$

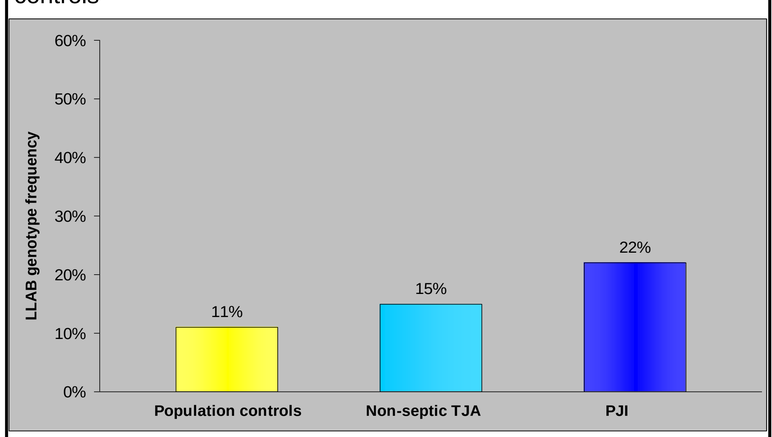
Fig 2. The frequency of *MBL2* -550 LL genotype in the patients with prosthetic joint infection (PJI) compared to those in the patients with non-septic total joint athroplasty (TJA) and in population controls



PJI *versus* Population controls $p = 0.02$

PJI *versus* Non-septic TJA $p = 0.04$

Fig 3. The frequency of *MBL2* LLAB combined genotype in the patients with prosthetic joint infection (PJI) compared to those in the patients with non-septic total joint athroplasty (TJA) and in population controls



PJI *versus* Population controls $p = 0.03$

PJI *versus* Non-septic TJA $p > 0.05$

The distribution of *MBL2* -550 and +54 genotypes complied with the Hardy-Weinberg equilibrium in the patients with PJI as well as in both control groups of the patients with non-septic TJA and population controls. Further, both control groups did not differ in the frequency *MBL2* -550 and +54 variants ($p>0.05$).

***MBL2*-550*G allele** (H variant) was less frequent in the group of patients with PJI (0.29) compared to population controls (0.39; $p=0.04$) and to non septic TJA controls (0.40; $p=0.02$, **Figure 1**). Furthermore, **CC genotype (LL) of this *MBL2* SNP was overrepresented among the patients with PJI** (0.50) compared to population controls (0.34; $p=0.02$) and to non septic TJA controls (0.37; $p=0.04$, **Figure 2**).

MBL2 +54 G/A (also called A/B) SNP alone was not related to PJI in Czech population ($p>0.05$). However, **combined *MBL2* -550CC / +54GA (LLAB)** genotype was twice more frequent in PJI (0.22) compared to population controls (0.11; $p=0.03$, **Figure 3**).

Conclusion and Discussion

In this pilot study, the *MBL2* -550 LL genotype tended to be overrepresented in patients with PJI after TJA by comparison with both control groups of the patients with non-septic TJA and population controls.

The limitation of our pilot study is its suboptimal power to clearly demonstrate an association of the *MBL2* variants with PJI. Extension of our preliminary findings in larger PJI cohorts is, therefore, warranted. Studies of other functional polymorphisms within *MBL2* gene in PJI are desirable.

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