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Abstract 113 Figure 1 Oneway ANOVA showed significant difference between the groups, F=5.26, \(p=0.002\), df (3.76). Post hoc comparison with Bonferroni test showed that BT was significantly higher in T2DM with non-obstructive CAD compared to the other three groups \(p<0.05\).

Abstract 113 Figure 2 Patients are grouped according to their diabetic and clinical data. Lesions were classified as either obstructive (plaque >75% of the luminal diameter) or non-obstructive (plaque 25%–75% of luminal diameter). We excluded those with minor plaques (<25% of the luminal diameter) and systemic inflammation (eg, sepsis). The subjects were divided: (i) T2DM and obstructive CAD (\(n=26\)), (ii) T2DM and non-obstructive CAD (\(n=14\)), (iii) non-diabetic and obstructive CAD (\(n=30\)) and (iv) non-diabetic and non-obstructive CAD (\(n=10\)). BT was measured by the ex-vivo Badimon chamber as total thrombus area compared to the other three groups.

Results All baseline cardiovascular risk factors were similar between groups \(p>0.05\). BT was higher in T2DM than in those without (22.481±12.536 vs 14.650±5074, \(p=0.024\)). When stratified according to CAD status, BT was highest in those with T2DM and non-obstructive CAD \(p=0.002\), ANOVA F=5.26) (Abstract 113 figure 1). Inflammatory cytokines TNF \(\alpha\) \(p=0.018\), ANOVA F=3.15) and interleukin 6 \(p=0.031\), ANOVA F=5.0) and platelet activation as measured by P selectin were highest in this group. \(p=0.022\), ANOVA F=3.422) (Abstract 113 figure 2). Interleukin 1, interferon \(\gamma\) and soluble CD40 ligand levels were similar between the groups.

Conclusion Patients with T2DM and non-obstructive CAD had highest BT and markers of platelet activation and inflammation. These findings suggest biochemical changes also play a significant role in evolution of NSTE-ACS in T2DM. A causal link, if confirmed by large-scale studies may offer us an opportunity to identify therapeutic targets like individualised anti thrombotic therapy and anti inflammatory therapy in this high risk population.

114 WHOLE GENOME SEQUENCING TO IDENTIFY GENETIC VARIANTS UNDERLYING CARDIOVASCULAR DISEASE AMONG INDIAN ASIANS


Introduction Indian Asians have a twofold higher risk of cardiovascular disease compared to Europeans which is not explained by conventional cardiovascular risk factors or known genetic variants. The genetic architecture of Indian Asians has not previously been described. We hypothesised that whole genome sequencing of Indian Asians may identify both common and rare variants specific to this population that contribute to their increased cardiovascular disease risk.

Methods We carried out whole genome sequencing (mean depth 28.4×) in eight men of Indian Asian origin participating in the London Life Sciences Population (LOLIPPO) study. Sequencing was carried out using paired end and mate pair libraries on an Illumina GA2 machine. Read alignment was done by BWA, and variants called using GATK and SAMtools. Sensitivity for single nucleotide polymorphism (SNP) detection was assessed by comparison to whole genome data.

Results We identified 6,602,840 autosomal variants, 436,823 of which are novel SNPs. Of these, 50,585 appear to be common (present at least twice, corresponding to minor allele frequency >10%). We found 21,659 autosomal SNPs that were expected to affect protein coding, of which 2174 are novel. Among the coding SNPs identified, 145 are in genes linked to human diseases, such as obesity (FTO, UCP1), diabetes mellitus (CDKAL1, GCRG, HNF1B), lipid metabolism (APOB), hypertension (NOS2), and renal disease (NPHF4, PKD1). We also found 65,613 novel autosomal indels of which 55,907 are present at least twelve, and 2501 novel deletions >100 bp. We show that >50% of the novel genetic variants are not in high LD \((r^2<0.8)\) with tag SNPs and hence not captured on available high-density microarrays.

Conclusions We identify more than 500,000 genetic variants not previously reported in 1000 genomes or dbSNP, and likely to be Indian Asian specific. The novel variants identified here are strong candidates for genetic factors underlying the increased risk of diabetes and cardiovascular disease among Indian Asians.

115 UNIQUE CHARACTERISTICS OF CD14++/CD16+ MONOCYTES IN PATIENTS WITH ACUTE HEART FAILURE AND IMPLICATIONS FOR CLINICAL OUTCOME

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Background Monocytes play important roles in inflammation, angiogenesis and tissue repair and may contribute to the