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INTRODUCTION

Knowledge of risk and comparative outcome is the cornerstone on which quality assessment structures can be built. Risk stratified data are the essential building blocks on which analysis of quality, meaningful comparison of outcomes, and finally, improvements can be based [1].

Our current risk stratification scoring systems are surprisingly accurate at predicting mortality but we are only just beginning to identify risk factors for other adverse outcomes including bleeding, graft thrombosis, sepsis, arrhythmias and renal or cognitive dysfunction.

Evidence is accumulating as we begin to translate the genomic code into a form which clinicians can understand that small variations in an individuals genome called polymorphisms can significantly effect their outcome from cardiac surgery and their response to certain drugs [2].

GRAFT OCCLUSION AND MYOCARDIAL INFARCT

Recently the risks of suffering a deep vein thrombosis and subsequent pulmonary embolus have been highlighted in association with air travel especially on long flights. About 10% of the populations studied have a polymorphism of the coagulation Factor V called Factor V Leiden. The risk of myocardial infarction for carriers of this polymorphism alone is increased by 40% but if combined with other known risk factors such as smoking hypertension, diabetes or obesity the risk is from 3 to 6 times the risk for non-carriers [3].

In a prospective study in CABG surgery with routine angiography 3 months post-surgery 23% of the vein grafts were thrombosed. In carriers of Factor V Leiden 45% had graft occlusion compared to only 20% of non-carriers [4].

Platelets play a pivotal role in both arterial and venous graft occlusion. The glycoprotein IIb-IIIa receptor on platelets controls aggregation and adhesion.

In a prospective study of platelet receptor polymorphism in CABG surgery and outcome at 1 year post-surgery, those patients with HPA-Ib variant had a 60% chance of graft occlusion, MI or death compared to a 24% chance in those without [5].

Protection from graft occlusion depends on the fine balance of the fibrinolytic mechanism. It has been shown that an increase in plasminogen activator inhibitor (PAI) activity is associated with graft occlusion in patients post-CABG surgery due to inhibition of fibrinolysis [6]. It is also known that a polymorphism of the PAI gene is associated with a high PAI level and a progression to acute coronary syndrome [7].

ORGAN DYSFUNCTION

Variant forms of apolipoprotein E (APOE) gene that encodes the protein responsible for neuronal repair following injury have given us new insights into cognitive dysfunction following cardiac operations. One form ε4 has been shown to be associated with brain dysfunction following CABG [8].

Curiously the same APOE genotype has the opposite effect on renal injury and is associated with a decreased rise in creatinine post cardiac surgery [9].

DRUG METABOLISM

Due to the high incidence of atrial fibrillation post-cardiac surgery and the use of mechanical valves, warfarin is a widely used and valuable therapy. The risk of serious haemorrhage during warfarin therapy ranges from 1.3 to 4.2 per 100 patient years of exposure.

Widespread interindividual variation in response to a given dose of warfarin makes prediction of an accurate maintenance dose difficult with an effective dose ranging from 0.5 mg to 60 mg. Variants within the cytochrome P450 genome have been shown to impair warfarin metabolism making patients much more difficult to set up on therapy and over 3 times more likely to have a major bleed [10].

SEPSIS AND TRANSPLANT REJECTION

Tumour necrosis factor (TNF) has been recognised as a central mediator of sepsis and multiple organ dysfunction in patients with systemic inflammatory responses following cardiopulmonary bypass, infection, haemorrhage or transplantation.

Many studies have shown that polymorphism within the gene encoding TNF α not only alters the likelihood of developing septic shock but also the risk of dying from it.

In an outcome study from all causes of septic shock in 89 patients in ICU compared with healthy controls a variant TNF2 was found in 39% of septic patients compared to 18% in controls. Among the septic shock patients TNF2 polymorphism frequency was significantly greater among those who died, 52% compared to 24% in the survivors [11].

Chronic graft rejection in heart and lung transplants remains the major cause of long term graft failure. As we understand more of how genetic polymorphism influences our inflammatory response we can predict those patients of high risk of rejection. In a recent study from our unit, there was a 20 fold increased risk of progression to chronic rejection associated with the combination of the Interleukin1 β C allele and the Interleukin1RN 1 allele [12].

CONCLUSION

As we gather new and important associations between our individual genomic polymorphism and outcome in response to cardiac surgery, it is hoped that we will be able to predict morbidity and mortality with more confidence with benefit for the patients and the health care providers.

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