DRUG-ELUTING STENTS FOR STENT THROMBOSIS ELEVATION ACUTE MYOCARDIAL INFARCTION: DO WE NEED RANDOMIZED TRIALS?

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Since their introduction, drug-eluting stents have rapidly altered modern medicine's approach to coronary artery disease. Before the development of drug-eluting stents, standard bare-metal stents were plagued by in-stent restenosis, requiring repeat revascularization in as many as 15-20% of patients during the first 6-12 months following implantation [1]. The currently approved drug-eluting stents have dramatically reduced this complication by using a polymer-impregnated coating that elutes either paclitaxel or sirolimus to inhibit smooth muscle proliferation. The pivotal TAXUS-IV [2] and SIRIUS [3] trials compared drug-eluting stents with standard bare-metal stents and found rates of target vessel revascularization ranging from 3 to 4.1% in stable coronary artery disease patients - far lower than that had been seen previously with conventional standard bare-metal stents. After their approval in April 2003, drug-eluting stents use in clinical practice expanded rapidly. Within 9 months of their introduction, drug-eluting stents comprised 35% of all stent implantations in the United States [4]. In the last year at our own institution, drug-eluting stents comprised over 85% of all stents implanted. Despite their extensive use, data regarding the efficacy and safety of drug-eluting stents in certain clinical scenarios are limited. To date, the only published data supporting drug-eluting stents in stent thrombosis elevation acute myocardial infarction come from the retrospective Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital registry [5] and the randomized, controlled single high-dose bolus tirofiban and sirolimus-eluting stent vs. abciximab and bare-metal stent in myocardial infarction study [6]. In this chapter, we discuss the theoretical risks and benefits of drug-eluting stents for ST elevation acute myocardial infarction, the available data regarding their use, and the areas in which future studies are needed. **(Coron. Artery Dis.2006; 17:667-671).**

NORMALIZATION OF HEMOGLOBIN LEVEL IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND ANEMIA.

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BACKGROUND: Whether correction of anemia in patients with stage 3 or 4 chronic kidney disease improves cardiovascular outcomes is not established.

METHODS: We randomly assigned 603 patients with an estimated glomerular filtration rate (GFR) of 15.0 to 35.0 ml per minute per 1.73 m2 of body-surface area and mild-to-moderate ane-

mia (hemoglobin level, 11.0 to 12.5 g per deciliter) to a target hemoglobin value in the normal range (13.0 to 15.0 g per deciliter, group 1) or the subnormal range (10.5 to 11.5 g per deciliter, group 2). Subcutaneous erythropoietin (epoetin beta) was initiated at randomization (group 1) or only after the hemoglobin level fell below 10.5 g per deciliter (group 2). The primary end point was a composite of eight cardiovascular events; secondary end points included left ventricular mass index, quality-of-life scores, and the progression of chronic kidney disease.

RESULTS: During the 3-year study, complete correction of anemia did not affect the likelihood of a first cardiovascular event (58 events in group 1 vs. 47 events in group 2; hazard ratio, 0.78; 95% confidence interval, 0.53 to 1.14; P=0.20). Left ventricular mass index remained stable in both groups. The mean estimated GFR was 24.9 ml per minute in group 1 and 24.2 ml per minute in group 2 at baseline and decreased by 3.6 and 3.1 ml per minute per year, respectively (P=0.40). Dialysis was required in more patients in group 1 than in group 2 (127 vs. 111, P=0.03). General health and physical function improved significantly (P=0.003 and P<0.001, respectively, in group 1, as compared with group 2). There was no significant difference in the combined incidence of adverse events between the two groups, but hypertensive episodes and headaches were more prevalent in group 1.

CONCLUSIONS: In patients with chronic kidney disease, early complete correction of anemia does not reduce the risk of cardiovascular events. **(N. Engl. J. Med. 2006; 355:2071-2084).**

CORRECTION OF ANEMIA WITH EPOETIN ALFA IN CHRONIC KIDNEY DISEASE.

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BACKGROUND: Anemia, a common complication of chronic kidney disease, usually develops as a consequence of erythropoietin deficiency. Recombinant human erythropoietin (epoetin alfa) is indicated for the correction of anemia associated with this condition. However, the optimal level of hemoglobin correction is not defined.

METHODS: In this open-label trial, we studied 1432 patients with chronic kidney disease, 715 of whom were randomly assigned to receive a dose of epoetin alfa targeted to achieve a hemoglobin level of 13.5 g per deciliter and 717 of whom were assigned to receive a dose targeted to achieve a level of 11.3 g per deciliter. The median study duration was 16 months. The primary end point was a composite of death, myocardial infarction, hospitalization for congestive heart failure (without renal replacement therapy), and stroke.

RESULTS: A total of 222 composite events occurred: 125 events in the high-hemoglobin group, as compared with 97 events in the low-hemoglobin group (hazard ratio, 1.34; 95%

confidence interval, 1.03 to 1.74; P=0.03). There were 65 deaths (29.3%), 101 hospitalizations for congestive heart failure (45.5%), 25 myocardial infarctions (11.3%), and 23 strokes (10.4%). Seven patients (3.2%) were hospitalized for congestive heart failure and myocardial infarction combined, and one patient (0.5%) died after having a stroke. Improvements in the quality of life were similar in the two groups. More patients in the high-hemoglobin group had at least one serious adverse event.

CONCLUSIONS: The use of a target hemoglobin level of 13.5 g per deciliter (as compared with 11.3 g per deciliter) was associated with increased risk and no incremental improvement in the quality of life. **(N. Engl. J. Med. 2006; 355:2085-2098)**.

ASSESSMENT OF THE GENETIC COMPONENT OF HYPERTENSION

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BACKGROUND: Although genetic epidemiologic studies have suggested that several genetic variants increase the risk for hypertension, the genes that underlie genetic susceptibility to this condition remain to be identified definitively. We have now performed a large-scale association study to identify gene polymorphisms for reliable assessment of the genetic component of hypertension.

METHODS: The study population comprised 4853 unrelated Japanese individuals, including 2818 subjects with hypertension (1677 men, 1141 women) and 2035 controls (1011 men, 1024 women). The genotypes for 150 polymorphisms of 128 candidate genes were determined with a method that combines the polymerase chain reaction and sequence-specific oligonucleotide probes with suspension array technology.

RESULTS: Multivariable logistic regression analysis with adjustment for age, sex, body mass index, and the prevalence of smoking revealed that four polymorphisms (1648G—>A in ITGA2, -30G—>A in GCK, A—>G in SAH, and 1117C—>A in PTGIS) were significantly ($P < .01$) associated with hypertension. A stepwise forward selection procedure demonstrated that ITGA2, GCK, and PTGIS genotypes significantly affected the prevalence of hypertension. Combined genotype analysis of these polymorphisms yielded a lowest odds ratio of 0.47 for the genotypes of AA or AG for ITGA2, GA or AA for GCK, and CC for PTGIS, which were present in 1.1% and 2.0% of hypertensive and control individuals, respectively.

CONCLUSIONS: These results suggest that the genotypes for ITGA2, GCK, and PTGIS may prove reliable for the assessment of the genetic component of hypertension. Determination of the combined genotypes for these genes may contribute to personalized prevention of this condition. **(Am. J. Hypertens. 2006; 19:1158-1165)**.

THE RELATION BETWEEN THE ERYTHROCYTE NITRIC OXIDE AND HEMORHEOLOGICAL PARAMETERS

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We stimulated human erythrocytes obtained from patients with hypercholesterolemia (HC; n = 42), renal transplantation (RT; n = 18) and hypertension (HT; n = 10) with acetylcholine (ACh 10 microM) and measured the amperometric NO production, comparing with the NO levels achieved on erythrocytes of healthy persons (n = 27). We also measured the hemoglobin, hematocrit, erythrocyte aggregation, erythrocyte deformability, plasma viscosity and fibrinogen concentration from human blood samples. The erythrocytes NO levels were of 2.5 +/- 0.7 nM (P = 0.038, HC), 2.4 +/- 1.1 nM (RT) and 2.2 +/- 0.8 nM (HT) against the 2.0 +/- 0.8 nM for the control groups. For each group and at each shear stress value, the erythrocytes deformability decreases with the increase of the NO concentration after ACh stimulation. We observed a significant increase of the control values on the erythrocyte aggregation results on each patient group. Besides the lower erythrocyte deformability obtained on HC, RT and HT blood samples, the erythrocytes produced higher NO levels after ACh stimulation than the healthy ones. The power of erythrocyte hemorheological behaviour could be compensated by the NO production at the presence of acetylcholine. We can hypothesises that cholinergic drugs could be used as co-adjuvants of specific therapeutics compounds on these studied diseases. **(Clin. Hemorheol. Microcic. 2006; 35:341-347).**