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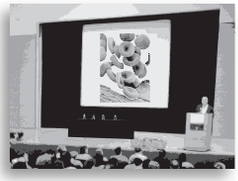

Study reports decrease in ACS patient bleeding, despite increasing use of intensive PCI

A recent study has shown that despite an increase in intensive interventional and pharmacological therapies, there has been a decrease in major bleeding for all acute coronary syndrome (ACS) patients.

The Global Registry of Acute Coronary Events was conducted between 2000 and 2007 and looked at 123 hospitals in 14 different countries. Researchers led by Keith AA Fox, of The University of Edinburgh (UK), studied changes in percutaneous coronary intervention (PCI) and adjunctive drug therapy. They then measured the frequency of major bleeding along with the impact of bleeding on myocardial infarction or death in the 50,947 ACS patients who took part.

Over the 8-year study period an increase in the use of use of intensive treatments, such as antithrombotic therapy, PCI and thienopyridine was observed.

Contrary to the researchers predictions, although the use of aggressive therapies increased, the frequency of major bleeding in patients decreased. In total, 2.3% of patients experienced a major bleed, and 44% of these presented with ST-elevation ACS.

"The hypothesis was that greater rates of interventional procedures and more aggressive antiplatelet and antithrombotic therapy might be associated with increased bleeding, but that was not what was found," explained Fox.

Major bleeding was defined as any life-threatening bleed that occurred in hospital and either required a transfusion of ≥2 U of packed red blood cells, or resulted in hemorrhagic stroke, subdural hematoma or death. Patients who experienced a major bleed had an increased risk of death in the 30-day period after the cardiac event.

The study found that patients who experienced major bleeding were more likely to have undergone cardiac catheterization or received fibrinolytic drugs than those who did not experience bleeding. Patients who did not experience bleeding were found to be more likely to have received a coronary artery bypass graft. The most significant decline was observed in ST-elevation ACS, where the percentage fell from 2.9 to 2.1%.

> *"...2.3% of patients experienced a major bleed, and 44% of these presented with ST-elevation ACS."*

Fox and colleagues found that the overall decline remained after adjusting for patient characteristics and treatments.

Individual hospital characteristics proved to be important in determining the risk of major bleeding. These characteristics included improved instrumentation for cardiac catheterization, smaller caliber catheters, physician awareness of bleeding and changing thresholds for blood transfusion.

Inappropriate dosing was also suggested as hospital practise that might influence bleeding risk. "There's been a series of studies from the USA and elsewhere showing that inappropriate dosing or overdosing of one or more agents is a key determinant of bleeding," Fox explained. "There are two issues: one is the more complex the regimen, the more likely you're going to get overdosing; second, it's the issue of body mass not being well estimated."

Source: Fox KAA, Carruthers K, Steg P et al.*: Has the frequency of bleeding changed over time for patients presenting with an acute coronary syndrome? The Global Registry of Acute Coronary Events.* Eur. Heart J. *DOI:10.1093/eurheartj/ehp499 (2009) (Epub ahead of print).*

future medicine part of fsg

New computer model examines efficiency of drug-eluting stents

Scientists from MIT (MA, USA) have devised a computer model that realistically predicts drug delivery patterns from drug-eluting stents (DES) inserted into branched arterial vessels.

Drug-eluting stents are small coronary scaffolds placed into narrowed arteries. The stents slowly release drugs to prevent artery blockages. Despite generally being considered superior to bare-metal stents – also used to widen diseased vessels – several patients fitted with DES have experienced life-threatening side effects, including increased risk of blood clotting and heart attack.

It is thought that drug distribution is determined by both the stent's position relative to arterial branches and the constant blood flow changes that are caused by arterial branching. Yet the details of drug distribution are still not fully understood. This lack of knowledge poses a challenge when evaluating the safety and efficiency of DES.

The model developed by Elazer Edelman of MIT, and colleagues simulates blood flow and drug transport in order to investigate the factors affecting drug distribution. Improving understanding of drug delivery by DES could potentially reduce the risk of life-threatening side effects.

"By observing the arterial drug distribution patterns for various settings, we understood that drug released from the stent does not reach uniformly to all regions of the vessel and this non-uniformity depends on where the stent is placed in the artery as well as the blood flow that is entering the vessel," explains Edelman.

"We now demonstrate for the first time that spatial variation in drug distribution can be significant when appreciated from a three-dimensional perspective and this viewpoint can only be gained with the use of these model systems," said Edelman.

The model suggests that a single stent in the main-branch of an arterial fork can provide drug to the side-branch. The researchers conclude that flow effects on drug deposition and subsequent uptake from endovascular DES are amplified in bifurcation lesions. The use of DES in arterial bifurcations requires a complex balance between vascular and stent geometry as well as luminal flow.

"Appreciating this phenomenon for more complex cases like branched vessels is non-intuitive, but now we have a computer model that gave us the much needed insight."

It is hoped that this modeling technique could be extended to explore several stent settings by simulating different stent designs and various arterial geometries, with and without disease.

Source: Kolachalama V, Levine E, Edelman E: Luminal flow amplifies stent-based drug deposition in arterial bifurcations. PLoS ONE *4(12), E8105 (2009).*

Hematocrit levels before and after PCI may predict mortality outcome

A recent study suggests that the presence of anemia before PCI and/or the development of anemia or bleeding after PCI are linked with increased mortality and morbidity rates.

Gabriel Maluenda and colleagues from Washington Hospital Center, Washington, DC, USA, used a multivariable Cox regression model to compare hematocrit levels measured at baseline and the overall magnitude of hematocrit decline. Up until now both of these measurements have been established as risk factors but the relationship between the two has been unclear.

The study suggests that a lower than average hematocrit level prior to PCI and a drop in hematocrit after PCI are strongly associated with long-term mortality.

The researchers evaluated 6025 consecutive patients who underwent PCI at the Washington Hospital Center between the years 2003 and 2007. The primary end point for the study was the occurrence of death or myocardial infarction at the 1-year follow-up.

The mean baseline hematocrit level was measured at 39.7% and the mean hematocrit drop was found to be 3.5%. The rate of death or myocardial infarction by the 1-year follow-up increased continuously every time hematocrit at baseline decreased and/or hematocrit dropped subsequent to PCI.

Importantly, the authors explained that transfusion "did not seem to increase the risk of late death or MI once preprocedural anemia and magnitude of hematocrit drop were accounted for."

The study concludes that both anemia before PCI and hematocrit drop after PCI should be recognized as important risk factors for adverse outcomes following PCI. Therefore, the authors recommend including the measurement of hematocrit in a risk-stratification scheme.

"The rate of death or myocardial infarction by the 1-year follow-up increased continuously every time hematocrit at baseline decreased..."

The authors express their hope that a risk model could be developed based on "the robust relationship between both baseline hematocrit and the hematocrit drop and ... long-term mortality."

Source: Maluenda G, Lemesle G, Collins S et al.*: The clinical significance of hematocrit values before and after percutaneous coronary intervention.* Am. Heart J. *158 (6) 1024–1030 (2009).*

Studies supporting FDA approval for cardiovascular devices are called into question

The first systematic examination of the evidence used by the US FDA for medical device approval has been carried out.

Rita Redberg of the University of California, San Francisco, USA, and colleagues reviewed 78 cardiovascular devices that received premarket approval of the FDA between January 2000 and December 2007.

The researchers evaluated the reliability of the 123 safety and effectiveness studies that were used to support FDA decisions during this timeframe. The findings of the study suggest that premarket approval of cardiovascular devices is often granted based on studies lacking in strength and which may be prone to bias.

The major discrepancy noted was that in many of the studies more patients were enrolled than were analyzed.

Of the 78 implantable or invasive cardiovascular devices recently accepted, 65% received approval based on data from a single study.

Out of all the studies, only 27% were randomized and 14% were blinded. Only 52% of the studies compared primary end points with controls and 31% of these used controls retrospectively.

"The findings of the study suggest that premarket approval of cardiovascular devices is often granted based on studies lacking in strength..."

Follow-up periods varied between studies. The longest median follow-up time for intracardiac devices and endovascular grafts was 365 days, whilst the shortest follow-up time was just 1 day for hemostasis devices.

Other discrepancies were found in relation to age, sex and race. These discrepancies may lead to bias, which could cause safety concerns to be overlooked.

"The importance of the 'seal of FDA approval' cannot be overstated. Many manufacturers immediately encourage widespread use of their devices based on FDA approval through direct-to-consumer advertising, detailing to physicians, and continuing medical education venues," the authors write in their article that was published in *JAMA* at the end of last year.

"To uphold the FDA's mission of ensuring 'safe and effective' medical devices, it is essential that high-quality studies and data are available," researchers conclude.

Source: Dhruva SS, Bero LA, Redberg RF: Strength of study evidence examined by the FDA in premarket approval of cardiovascular devices. JAMA *302, 2679–2685 (2009).*

Arterial Remodeling Technologies reports success of its bioresorbable stent

Arterial Remodeling Technologies (ART) has released impressive *in vivo* and *in vitro* data related to its bioresorbable stent.

Arterial Remodeling Technologies is a company that develops bioresorbable coronary stents that promote the natural remodeling of damaged arteries following angioplasty. In the development of the new bioresorbable stent, the company aimed to balance biomechanics, biocompatibility and bioresorption.

The data were published in a special supplement of EuroIntervention in a paper written by Antoine Lafont, a cofounder of ART from Georges Pompidou Hospital, Paris, France.

"The ART bioresorbable stent showed a remarkable ability to be deployed without recoil or breakage. At 1 month, endothelialization was 100% completed. Additionally important, inflammation, smooth muscle cell proliferation and collagen accumulation were equivalent to what typically occurs after balloon angioplasty," explained Lafont.

"The data published show that the ART stent provides sufficient support over the first 3 months and then successfully dismantles over time owing to the polylactic acid material that it is made from."

The innovative polylactic acid stent completely integrated into the artery wall within 6 months. There was very little inflammation reported in patients fitted with the ART stent, despite this being a common problem with other bioresorbable stents.

In recently years the industry has mainly focused on making mechanically stable stents. The data published show that the ART stent provides sufficient support over the first 3 months and then successfully dismantles over time owing to the polylactic acid material that it is made from.

The technology used by ART is based on the intellectual property of three respected institutions: the Cleveland Clinic; the French national research institute, CNRS (Centre National de Recherche Scientifique), Montpellier, France; and, Descartes University, Paris.

Source: ART (Arterial Remodeling Technologies) reports its bioresorbable stent platform restores the remodeling capacity of arterial walls www.pcronline.com/fo/exchange/news/press_releases.php?news_id=3146