Association of Bleeding and In-Hospital Mortality in Black and White Patients With ST-Segment–Elevation Myocardial Infarction Receiving Reperfusion

We evaluated data on blacks and whites with acute ST-segment–elevation myocardial infarction treated with either fibrinolysis or primary percutaneous coronary intervention from the National Registry of Myocardial Infarction (NRMI)-4 and -5 participating centers between July 2000 and December 2006 to determine race-related differences in bleeding and outcomes. We found that among patients with ST-segment–elevation myocardial infarction receiving fibrinolysis, the bleeding rates were higher for blacks (n=2283) than whites (n=42 243; 10.9% versus 10.3%; adjusted odds ratio, 1.21; 95% confidence interval, 1.02–1.43). Similarly, in patients receiving primary percutaneous coronary intervention, the bleeding rates were higher in blacks (n=2826) than whites (n=46 332; 10.3% versus 7.8%; adjusted odds ratio, 1.33; 95% confidence interval, 1.13–1.56). Bleeding was associated with a higher risk of death in both ethnic groups. However, there was no overall racial difference in in-hospital mortality among those with bleeding or without bleeding treated with either fibrinolysis or primary percutaneous coronary intervention. We concluded that race-related differences existed in bleeding risk among patients with ST-segment–elevation myocardial infarction receiving reperfusion therapy that portend poor prognosis. Thus, the efficacy and safety of many new drugs or treatment strategies for any disease observed in clinical trials that enroll predominantly white patients may not be similar in other ethnic groups that are underrepresented in these trials. See p 1727.

Sweetened Beverage Consumption, Incident Coronary Heart Disease, and Biomarkers of Risk in Men

Consuming sugar-sweetened beverages such as cola puts individuals at an increased risk for weight gain and type 2 diabetes mellitus, both of which are risk factors for coronary heart disease (CHD). However, few studies have assessed the relationship between sugar-sweetened beverage consumption and CHD events. In our analysis of the Health Professionals Follow-Up Study, a prospective cohort study that includes a well-characterized population of >40 000 men, we found that sugar-sweetened beverage consumption was associated with a higher risk of CHD independently of body mass index, type 2 diabetes mellitus, and other established cardiovascular risk factors. For each additional serving per day, sugar-sweetened beverages were associated with a 19% increased risk of CHD. We also found that sugar-sweetened beverage consumption was associated with adverse changes in blood lipids, higher circulating inflammatory factors, and lower leptin. These biomarker changes may help to explain why sugar-sweetened beverage consumption is a risk factor for CHD and, in the case of leptin, obesity. Conversely, consumption of artificially sweetened beverages such as diet soda was not associated with CHD risk or biomarkers in our study but was associated with baseline comorbidities, higher body mass index, pre-enrollment weight change, and dieting, which could lead to confounding. See p 1735.

Increased Risks of Coronary Heart Disease and Stroke Among Spousal Caregivers of Cancer Patients

It is known that spousal caregivers of cancer patients experience psychological and physical burdens; however, whether these care-
with diet-induced metabolic syndrome is not known. We fed mice an
“American” diet high in fat and sugar with or without concomitant
treatment with S17834 or resveratrol for up to 8 months. High-fat/
high-sugar diet–fed mice developed left ventricular hypertrophy and
diastolic dysfunction. Treatment with the polyphenols prevented the
cardiac structural and functional consequences of high-fat/high-sugar
feeding. We conclude that the high-fat/high-sugar diet–fed mouse
provides a valuable model of diet-induced myocardial hypertrophy and
diastolic dysfunction that should prove useful in elucidating the
pathobiology and treatment of metabolic heart disease. The polypheno-

cols exerted multiple effects that may have contributed to ameliora-
tion of metabolic heart disease, including decreases in myocardial
oxidative stress and oxidant-mediated protein modifications, im-
proved insulin sensitivity, and an increase in plasma adiponectin.
These findings suggest that the polyphenols could be of value in the
treatment of metabolic heart disease in humans. See p 1757.

**Regulation of Cardiac MicroRNAs by Bone Marrow
Mononuclear Cell Therapy in Myocardial Infarction**

Cell-based therapy is a promising option to treat cardiovascular
diseases. Multiple mechanisms have been proposed to mediate the
therapeutic benefits of bone marrow–derived mononuclear cell
therapy, including cell transdifferentiation, cell fusion, and the
release of paracrine growth factors and cytokines. In fact, various
cytokines and growth factors from transplanted progenitor cells have
been shown to elicit positive effects by influencing cardiomyocyte
survival, angiogenesis, and the recruitment of endogenous stem cells.
MicroRNAs are small noncoding RNAs that negatively modulate
gene expression by inhibiting protein translation or inducing degra-
dation of the targeted mRNA. MicroRNAs play an important role in
biological processes during development, tissue homeostasis, and
disease. Several microRNAs are regulated after the induction of
myocardial infarction and control neovascularization and fibrosis.
Here, we demonstrate that the paracrine regulation of cardiac
microRNAs by transplanted bone marrow–derived mononuclear
cells contributes to the protective effects of cell therapy. In particu-
lar, bone marrow–derived mononuclear cell release insulin-like
growth factor-1, which inhibits the processing of miR-34a, thereby
blocking cardiomyocyte apoptosis. Insulin-like growth factor-1-
mediated inhibition of miR-34a may contribute to several of the
known cardioprotective functions of insulin-like growth factor-1.
See p 1765.

**Role for Substance P–Based Nociceptive Signaling in
Progenitor Cell Activation and Angiogenesis During
Ischemia in Mice and in Human Subjects**

Pain and inflammation are generally thought of as medical problems.
Treatments of these defense responses is routine in patients with
myocardial and peripheral ischemia. However, blocking a defense
can be harmful. It has been shown that taking nonsteroidal anti-
flammatory drugs can increase a person’s risk of having a heart
attack or stroke. Furthermore, morphine has been associated with
higher mortality in patients with acute coronary syndrome. The
present study provides novel insight into the role of the pain mediator
substance P in vascular regeneration by bone marrow–derived stem
cells. After ischemic injury, substance P is released from central
terminals projecting to distinct brain stem centers, thus contributing
to pain perception and pain-induced reactions, as well as from
sensory fibers innervating the myocardium, leading to local neuro-
genic inflammation. In the present study, we show that substance P
also contributes to mobilize stem cells from the bone marrow and to
recruit them to the infarcted heart. Bone marrow cells attracted by
substance P are able to promote neovascularization, thereby accel-
 erating the healing of ischemic tissues. Conversely, genetic abroga-
tion of substance P signaling or pharmacological inhibition of
substance P release by morphine results in attenuation of both stem
cell mobilization and reparative vascularization in models of ischec-
mia. These new findings may have important clinical implications
for tailoring new regenerative treatments based on stem cell recruit-
ment by pain mediators. Nonetheless, the nociceptive signaling is also
used in other biological contexts in which pain is not operant. Therefore,
additional work is warranted to refine new therapeutic strategies
compatible with pain relief and cardiovascular repair. See p 1774.

**Impact of Changes in Resuscitation Practice on Survival
and Neurological Outcome After Out-of-Hospital Cardiac
Arrest Resulting From Nonshockable Arrhythmias**

Although the overall incidence of out-of-hospital cardiac arrest has
not changed in recent years, reports indicate that the proportion of
arrests caused by shockable rhythms is diminishing. The vast
majority of out-of-hospital cardiac arrests are now attributable to
nonshockable arrhythmias—asystole and pulseless electrical activity—
from which survival is especially poor and for which a treatment
strategy that improves outcome has yet to be identified. In a number
of communities, adoption of recent changes in cardiopulmonary
resuscitation guidelines that prioritized the time devoted to chest
compressions during resuscitation was associated with improved
survival among patients with out-of-hospital cardiac arrest resulting
from shockable rhythms. In this cohort investigation, we found that
implementation of these guidelines was also associated with a
significant improvement in short- and long-term survival and with
favorable neurological outcome, specifically among patients with
nonshockable out-of-hospital cardiac arrest. After multivariable
adjustment, the odds ratio of 1-year survival from nonshockable
out-of-hospital cardiac arrest on implementation of these guideline
changes compared with beforehand was 1.85 (95% confidence
interval, 1.29–2.66). Comparably significant improvements were
observed in return of spontaneous circulation, hospital admission
rates, survival to hospital discharge, favorable neurological status at
hospital discharge, and 1-month survival. These improvements could
not be merely attributed to temporal trends within the study periods
but appeared to coincide with the change in the cardiopulmonary
resuscitation protocol itself. Our findings suggest that increasing the
basic provision of cardiopulmonary resuscitation has the potential to
improve outcomes for all victims of cardiac arrest and are of
particular relevance and importance because of the changing epide-
miology of the condition. See p 1787.
The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/125/14/1713