

*Circulation: Arrhythmia and Electrophysiology*

# Safety of Sports for Young Patients With Implantable Cardioverter-Defibrillators

## Long-Term Results of the Multinational ICD Sports Registry

The potential dangers of young patients with implantable cardioverter-defibrillators (ICDs) participating in sports are unknown. This post hoc analysis assessed 129 athletes aged  $\leq 21$  years from the ICD Sports Registry, a prospective, multinational registry designed to determine the incidence of serious adverse events because of sports, with ICDs involved in competitive sports. Shocks and lead malfunction related to competition and practice occur in college and high school athletes with ICDs; however, there were no serious adverse sequelae and the rates are similar to an unselected pediatric ICD population.

**BACKGROUND:** Despite safety concerns, many young patients with implantable cardioverter-defibrillators (ICDs) participate in sports. We undertook a prospective, multinational registry to determine the incidence of serious adverse events because of sports participation. The primary end points were death or resuscitated arrest during sports or injury during sports because of arrhythmia or shock. Secondary end points included system malfunction and incidence of ventricular arrhythmias requiring multiple shocks for termination.

**METHODS:** Athletes with ICDs aged  $\leq 21$  years were included in this post hoc subanalysis of the ICD Sports Registry. Data on sports and clinical outcomes were obtained by phone interview and medical records review. ICD shocks and clinical details of lead malfunction were classified by 2 electrophysiologists.

**RESULTS:** A total of 129 young athletes participating in competitive ( $n=117$ ) or dangerous ( $n=12$ ) sports were enrolled. The mean age was 16 years (range, 10–21; 40% female; 92% white). The most common diagnoses were long QT syndrome ( $n=49$ ), hypertrophic cardiomyopathy ( $n=30$ ), and congenital heart disease ( $n=16$ ). The most common sports were basketball and soccer, including 79 varsity/junior varsity high school and college athletes. During a median follow-up of 42 months, 35 athletes (27%) received 38 shocks. There were no occurrences of death, arrest, or injury related to arrhythmia, during sports. There was 1 ventricular tachycardia/ventricular fibrillation storm during competition. Freedom from lead malfunction was 92.3% at 5 years and 79.6% at 10 years.

**CONCLUSIONS:** Although shocks related to competition/practice are not uncommon, there were no serious adverse sequelae. Lead malfunction rates were similar to previously reported in unselected pediatric ICD populations.

**CLINICAL TRIAL REGISTRATION:** URL: <https://www.clinicaltrials.gov>. Unique identifier: NCT00637754.

*Circ Arrhythm Electrophysiol.* 2018;11:e006305. doi: 10.1161/CIRCEP.118.006305

Elizabeth Vickers Saarel, MD  
Ian Law, MD  
Charles I. Berul, MD  
Michael J. Ackerman, MD, PhD  
Ronald J. Kanter, MD  
Shubhayan Sanatani, MD  
Mitchell I. Cohen, MD  
Stuart Berger, MD  
Peter S. Fischbach, MD  
David A. Burton, MD  
James Dziura, PhD  
Cynthia Brandt, MD  
Laura Simone, BA  
Fangyong Li, MS, MPH  
Brian Olshansky, MD  
David S. Cannom, MD  
Rachel J. Lampert, MD

**Correspondence to:** Elizabeth Vickers Saarel, MD, Pediatric Cardiology, Cleveland Clinic Children's, 9500 Euclid Ave M41, Cleveland, OH 44195. Email [saarele@ccf.org](mailto:saarele@ccf.org)

© 2018 American Heart Association, Inc.

<https://www.ahajournals.org/journal/circ>

*Circulation: Genomic and Precision Medicine*

# Genomic Risk Stratification Predicts All-Cause Mortality After Cardiac Catheterization

This study assessed a genome-wide polygenic risk score (PRS) for coronary artery disease (CAD) in individuals who underwent coronary angiography. The PRS was associated with all-cause mortality after accounting for traditional cardiovascular risk factors and angiographic CAD. Even individuals with high PRS, but without angiographic CAD, were at an elevated risk of mortality.

**BACKGROUND:** Coronary artery disease (CAD) is influenced by genetic variation and traditional risk factors. Polygenic risk scores (PRS), which can be ascertained before the development of traditional risk factors, have been shown to identify individuals at elevated risk of CAD. Here, we demonstrate that a genome-wide PRS for CAD predicts all-cause mortality after accounting for not only traditional cardiovascular risk factors but also angiographic CAD itself.

**METHODS:** Individuals who underwent coronary angiography and were enrolled in an institutional biobank were included; those with prior myocardial infarction or heart transplant were excluded. Using a pruning-and-thresholding approach, a genome-wide PRS comprised of 139 239 variants was calculated for 1503 participants who underwent coronary angiography and genotyping. Individuals were categorized into high PRS (hiPRS) and low-PRS control groups using the maximally selected rank statistic. Stratified analysis based on angiographic findings was also performed. The primary outcome was all-cause mortality following the index coronary angiogram.

**RESULTS:** Individuals with hiPRS were younger than controls (66 years versus 69 years;  $P=2.1 \times 10^{-5}$ ) but did not differ by sex, body mass index, or traditional risk-factor profiles. Individuals with hiPRS were at significantly increased risk of all-cause mortality after cardiac catheterization, adjusting for traditional risk factors and angiographic extent of CAD (hazard ratio, 1.6; 95% CI, 1.2–2.2;  $P=0.004$ ). The strongest increase in risk of all-cause mortality conferred by hiPRS was seen among individuals without angiographic CAD (hazard ratio, 2.4; 95% CI, 1.1–5.5;  $P=0.04$ ). In the overall cohort, adding hiPRS to traditional risk assessment improved prediction of 5-year all-cause mortality (area under the receiver-operating curve 0.70; 95% CI, 0.66–0.75 versus 0.66; 95% CI, 0.61–0.70;  $P=0.001$ ).

**CONCLUSIONS:** A genome-wide PRS improves risk stratification when added to traditional risk factors and coronary angiography. Individuals without angiographic CAD but with hiPRS remain at significantly elevated risk of mortality.

*Circ Genom Precis Med.* 2018;11:e002352. doi: 10.1161/CIRCGEN.118.002352

Michael G. Levin, MD  
Rachel L. Kember, PhD  
Renae Judy, MS  
David Birtwell, MSE  
Heather Williams, MSE  
Zolt Arany, MD, PhD  
Jay Giri, MD  
Marie Guerraty, MD, PhD  
Tom Cappola, MD, ScD  
Regeneron Genetics  
Center  
Jinbo Chen, PhD  
Daniel J. Rader, MD  
Scott M. Damrauer, MD

**Correspondence to:** Scott M. Damrauer, MD, Department of Surgery, Hospital of the University of Pennsylvania, 3400 Spruce St, Silverstein 4, Philadelphia, PA 19104. Email Scott.Damrauer@uphs.upenn.edu

*Circulation: Cardiovascular Imaging*

# Molecular Imaging of VWF (von Willebrand Factor) and Platelet Adhesion in Postischemic Impaired Microvascular Reflow

Impaired microvascular reperfusion remains an unsolved clinical problem contributing to expansion of infarct size after intervention. This study evaluates the contribution of microvascular endothelial-associated von Willebrand Factor (VWF) and platelet adhesion to microvascular no-reflow with myocardial contrast echocardiography perfusion imaging and molecular imaging. The investigators used perfusion and molecular imaging to establish that excess endothelial-associated VWF and secondary platelet adhesion in the affected microcirculation are modifiable contributors to impaired microvascular reflow.

**BACKGROUND:** Complete mechanistic understanding of impaired microvascular reflow after myocardial infarction will likely lead to new therapies for reducing infarct size. Myocardial contrast echocardiography perfusion imaging and molecular imaging were used to evaluate the contribution of microvascular endothelial-associated VWF (von Willebrand factor) and platelet adhesion to microvascular no-reflow.

**METHODS AND RESULTS:** Myocardial infarction was produced by transient LAD ligation in WT (wild type) mice, WT mice treated with the VWF proteolytic enzyme ADAMTS13 (a disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13), and ADAMTS13-deficient (ADAMTS13<sup>-/-</sup>) mice. Myocardial contrast echocardiography perfusion imaging and molecular imaging of VWF and platelet GP (glycoprotein) Iba were performed 30 minutes after ischemia-reperfusion. Infarct size was measured at 3 days. Mortality during ischemia-reperfusion incrementally increased in WT+ADAMTS13, WT, and ADAMTS13<sup>-/-</sup> mice (14%, 43%, and 63%, respectively;  $P < 0.05$ ). For WT mice, molecular imaging signal for platelets and VWF in the postischemic risk area was 4- to 5-fold higher ( $P < 0.05$ ) compared with both the remote nonischemic regions or to sham-treated mice. Signal enhancement in the risk area was completely abolished by ADAMTS13 treatment for both platelets ( $12.8 \pm 3.3$  versus  $-1.0 \pm 4.4$  IU;  $P < 0.05$ ) and VWF ( $13.9 \pm 4.0$  versus  $-1.0 \pm 3.0$  IU;  $P < 0.05$ ). ADAMTS13<sup>-/-</sup> compared with WT mice had 2- to 3-fold higher risk area signal for platelets ( $33.1 \pm 8.5$  IU) and VWF ( $30.9 \pm 1.9$  IU). Microvascular reflow in the risk area incrementally decreased for WT+ADAMTS13, WT, and ADAMTS13<sup>-/-</sup> mice ( $P < 0.05$ ), whereas infarct size incrementally increased ( $P < 0.05$ ).

**CONCLUSIONS:** Mechanistic information on microvascular no-reflow is possible by combining perfusion and molecular imaging. In reperfused myocardial infarction, excess endothelial-associated VWF and secondary platelet adhesion in the risk area microcirculation contribute to impaired reflow and are modifiable.

*Circ Cardiovasc Imaging*. 2018;11:e007913. doi: 10.1161/CIRCIMAGING.118.007913

Koya Ozawa, MD, PhD  
William Packwood, BS  
Oleg Varlamov, PhD  
Yue Qi, MD  
Aris Xie, MS  
Melinda D. Wu, MD  
Zaverio Ruggeri, PhD  
Jose A. López, MD  
Jonathan R. Lindner, MD

**Correspondence to:** Jonathan R. Lindner, MD, Cardiovascular Division, Oregon Health and Science University, 3181 SW Sam Jackson Park Rd, Portland, OR 97239. Email lindnerj@ohsu.edu

*Circulation: Cardiovascular Interventions*

# Drug-Eluting Stents Versus Bare-Metal Stents in Saphenous Vein Graft Intervention

## An Updated Meta-Analysis of Randomized Controlled Trials

The use of drug-eluting stents during percutaneous coronary intervention in saphenous vein grafts has increased, although the evidence for benefit from randomized controlled trials is conflicting. The investigators performed a meta-analysis of all eligible studies comparing drug-eluting stents (DES) versus bare-metal stents (BMS) in patients with saphenous vein graft stenosis. The results showed no significant difference between DES and BMS for mortality, major adverse cardiovascular events, target vessel revascularization, myocardial infarction, or stent thrombosis.

**BACKGROUND:** Percutaneous coronary intervention with drug-eluting stents (DES) has been increasingly used for revascularization of saphenous vein graft stenosis without strong clinical evidence favoring their use. Randomized controlled trials comparing DES versus bare-metal stents (BMS) in saphenous vein graft–percutaneous coronary intervention have been inconclusive.

**METHODS AND RESULTS:** We performed a comprehensive literature search through May 15, 2018, for all eligible studies comparing DES versus BMS in patients with saphenous vein graft stenosis in PubMed, EMBASE, SCOPUS, Google Scholar, and ClinicalTrials.gov. Clinical outcomes included all-cause mortality, cardiovascular mortality, major adverse cardiovascular events, myocardial infarction, stent thrombosis, and target vessel revascularization. Six randomized controlled trials were eligible and included 1582 patients, of whom 797 received DES and 785 received BMS. The follow-up period ranged from 18 months to 60 months. There was no statistically significant difference between DES and BMS for all-cause mortality (risk ratio [RR], 1.11; 95% CI, 0.077–1.62;  $P=0.57$ ), cardiovascular mortality (RR, 1.00; 95% CI, 0.64–1.57;  $P=0.99$ ), major adverse cardiovascular events (RR, 0.83; 95% CI, 0.63–1.10;  $P=0.20$ ), target vessel revascularization (RR, 0.73; 95% CI, 0.48–1.11;  $P=0.14$ ), myocardial infarction (RR, 0.74; 95% CI, 0.48–1.16;  $P=0.19$ ), or stent thrombosis (RR, 1.06; 95% CI, 0.42–2.65;  $P=0.90$ ).

**CONCLUSIONS:** In patients undergoing percutaneous coronary intervention for saphenous vein graft lesions, our results showed that there was no significant difference between DES and BMS for mortality, major adverse cardiovascular events, target vessel revascularization, myocardial infarction, or stent thrombosis.

Nileshkumar J. Patel, MD  
Chirag Bavishi, MD  
Varunsiri Atti, MD  
Avnish Tripathi, MD, PhD,  
MPH  
Nikhil Nalluri, MD  
Mauricio G. Cohen, MD  
Annapoorna S. Kini, MD  
Samin K. Sharma, MD  
George Dangas, MD  
Deepak L. Bhatt, MD,  
MPH

**Correspondence to:** Deepak L. Bhatt, MD, MPH, Brigham and Women's Hospital Heart and Vascular Center, Harvard Medical School, 75 Francis St, Boston, MA 02115. Email [dlbhattmd@post.harvard.edu](mailto:dlbhattmd@post.harvard.edu)

*Circ Cardiovasc Interv.* 2018;11:e007045. doi: 10.1161/CIRCINTERVENTIONS.118.007045

*Circulation: Cardiovascular Quality and Outcomes*

# Physician-Specific Practice Patterns About Discharge Readiness and Heart Failure Utilization Outcomes

Although decompensated heart failure (HF) is one of the most common inpatient medical conditions managed by both hospitalists and cardiologists, physician-level inpatient management is inconsistent and there are few evidence-based recommendations available. This study evaluates physician-specific self-reported HF practice patterns with length of stay and 30-day readmission. The results report physician-level data about inpatient discharge strategies and suggest that physician-reported practice patterns associated with less resource utilization, such as shorter length of stay, are not associated with higher 30-day readmission rates.

**BACKGROUND:** Although hospitalization for acute decompensated heart failure (HF) is common and associated with poor outcomes and high costs, few evidence-based recommendations are available to guide patient management. Thus, management of inpatient HF remains heterogeneous. We evaluated if physician-specific self-reported HF practice patterns were associated with 2 important contributors to resource utilization: length of stay (LOS) and 30-day readmission.

**METHODS AND RESULTS:** A 5-point Likert scale survey was created to assess physician-specific HF discharge strategies and administered to all cardiologists and hospitalists at a single large academic teaching hospital. Practice patterns potentially impacting LOS and discharge decisions were queried, including use of physical examination findings, approaches to diuretic use and influence of kidney function. Likert scale responses are reported as means with any value above 3.00 considered more influential and any value below 3.00 considered less influential. Physician-specific LOS and 30-day readmission rates from July 1, 2015, to June 30, 2016, were extracted from the electronic record. We received survey responses and HF utilization metrics from 58 of 69 surveyed physicians (32 hospitalists and 26 cardiologists), encompassing 753 HF discharges over a 1-year period. Median LOS was 4.5 days (interquartile range, 4.0–5.8) and total 30-day readmission rate was 17.0% (128 unique readmissions). Physicians with below-median LOS placed less importance on observing a patient on oral diuretics for 24 hours before discharge (Likert 2.54 versus 3.30,  $P=0.01$ ), reaching documented dry weight (Likert 2.93 versus 3.60,  $P=0.02$ ), and complete resolution of dyspnea on exertion (Likert 3.64 versus 4.10,  $P=0.03$ ) when compared with those above-median LOS. In contrast, no surveyed discharge practices were associated with physician-specific 30-day readmission.

**CONCLUSIONS:** We identified specific inpatient HF discharge practice patterns that associated with shorter LOS but not with readmission rates. These may be targets for future interventions aimed at cost reduction; additional larger studies are needed for further exploration.

Anish B. Bhatt, MD  
Daniel D. Cheeran, MD  
Kamal Shemisa, MD  
Lonnie Roy, PhD  
Boryana N. Manz, PhD  
Rebecca Vigen, MD, MSCS  
James A. de Lemos, MD  
Sandeep R. Das, MD, MPH

**Correspondence to:** Sandeep Das, MD, MPH, Department of Medicine, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, MC 8830, Dallas, TX 75390-8830. Email sandeep.Das@UTsouthwestern.edu

*Circ Cardiovasc Qual Outcomes.* 2018;11:e004365. doi: 10.1161/CIRCOUTCOMES.117.004365

*Circulation: Heart Failure*

# Association Between Regional Adipose Tissue Distribution and Risk of Heart Failure Among Blacks

## The Jackson Heart Study

Although obesity is prevalent and associated with a greater risk of heart failure (HF) in blacks, the differential contribution of regional adipose tissue depots toward HF risk is not well established. This study analyzed 2602 participants from the Jackson Heart Study without prevalent HF who underwent computed tomography quantification of visceral and subcutaneous adipose tissue. Higher amounts of overall and visceral adiposity are associated with higher risk of HF. Contributions of visceral adiposity toward HF risk in blacks were found to be largely related to differences in traditional risk factor burden.

**BACKGROUND:** Obesity is highly prevalent among blacks and is associated with a greater risk of heart failure (HF). However, the contribution of regional adiposity depots such as visceral adipose tissue (VAT) and abdominal subcutaneous adipose tissue toward risk of HF in blacks is unknown.

**METHODS AND RESULTS:** We included 2602 participants (mean age: 59 years, 35% men) from the Jackson Heart Study without prevalent HF who underwent computed tomography quantification of VAT and subcutaneous adipose tissue during the second visit (2005–2009). The associations between different adiposity measures and HF were evaluated using adjusted Cox models. There were 122 incident HF events over a median follow-up of 7.1 years. Higher amounts of VAT were associated with greater risk of HF in age- and sex-adjusted analyses (hazard ratio [95% CI] per 1-SD higher VAT: 1.29 [1.09–1.52]). This association was attenuated and not significant after additional adjustment for traditional HF risk factors and body mass index. Overall obesity, represented by body mass index, was associated with higher risk of HF independent of risk factors and VAT (hazard ratio [95% CI] per 1-kg/m<sup>2</sup> higher body mass index: 1.06 [1.02–1.11]). Subcutaneous adipose tissue was not associated with risk of HF in adjusted analyses.

**CONCLUSIONS:** In a community-dwelling black population, higher amounts of overall and visceral adiposity are associated with higher risk of HF. The association between VAT and HF risk in blacks may reflect differences in traditional HF risk factor burden. Future studies are needed to confirm this observation and clarify the independent role of different measures of adiposity on HF outcomes.

*Circ Heart Fail.* 2018;11:e005629. doi: 10.1161/CIRCHEARTFAILURE.118.005629

**Ambarish Pandey, MD,  
MSCS**

**Nitin Kondamudi, MD**

**Kershaw V. Patel, MD**

**Colby Ayers, MS**

**Shawn Simek, MD**

**Michael E. Hall, MD**

**Solomon K. Musani, PhD**

**Chad Blackshear, PhD**

**Robert J. Mentz, MD**

**Hassan Khan, MD, PhD**

**James G. Terry, MS**

**Adolfo Correa, MD**

**Javed Butler, MD**

**Ian J. Neeland, MD**

**Jarett D. Berry, MD, MS**

**Correspondence to:** Jarett D. Berry, MD, MS, Division of Cardiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd; Dallas, TX 75390-9047. Email jarett.berry@utsouthwestern.edu