

*Circulation: Arrhythmia and Electrophysiology*

# Laser Balloon or Wide-Area Circumferential Irrigated Radiofrequency Ablation for Persistent Atrial Fibrillation

## A Multicenter Prospective Randomized Study

This prospective, randomized multicenter study compares the efficacy and safety of laser balloon with wide-area circumferential pulmonary vein isolation with radiofrequency ablation. The results demonstrated that laser balloon ablation is similarly effective as radiofrequency ablation in patients with persistent atrial fibrillation.

**BACKGROUND:** Pulmonary vein isolation is the cornerstone of ablation for persistent atrial fibrillation (AF). The role of balloon catheters in this patient population remains ill defined. We sought to compare efficacy and safety of the laser balloon (LB) with wide-area circumferential pulmonary vein isolation using irrigated radiofrequency current (RF) ablation and 3-dimensional mapping.

**METHODS AND RESULTS:** In 6 European centers, patients with persistent AF were prospectively randomized. Follow-up included 3-day Holter ECG recordings and office visits at 3, 6, and 12 months. The primary efficacy end point was freedom from AF between 90 and 365 days after a single ablation. The primary safety end point was the incidence of any periprocedural complications. Of 152 enrolled patients, 134 (n=68 LB and 66 RF; 63% men; mean age, 66±10 years) with persistent AF (median AF history, 14 months; Q1–Q3, 7–36 months) underwent pulmonary vein isolation and completed the entire follow-up. Baseline parameters were similar in both groups. Procedure and fluoroscopy times were similar in both groups (135±38 and 14±9 minutes (LB) versus 128±51 and 11±9 minutes). The primary efficacy end point was met by 71.2% versus 69.3%, in the LB and RF groups, respectively ( $P=0.40$ ). In the LB group, stroke (n=1), a false aneurysm (n=1), and phrenic nerve palsy (n=1) were observed. In the RF group, 2 patients developed a false aneurysm, and 1 patient needed surgical repair.

**CONCLUSIONS:** An LB-guided strategy was associated with similar efficacy as wide-area circumferential pulmonary vein isolation using irrigated RF in patients with persistent AF.

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# Analysis of 60 706 Exomes Questions the Role of De Novo Variants Previously Implicated in Cardiac Disease

This study used the large population-representative Exome Aggregation Consortium database to evaluate the pathogenicity of de novo variants that have previously been associated with arrhythmias and structural heart disease based on a literature search. The authors found higher-than-expected prevalence of the previously described de novo variants, highlighting the need to distinguish pathogenic variants from standing variation.

**BACKGROUND:** De novo variants in the exome occur at a rate of 1 per individual per generation, and because of the low reproductive fitness for de novo variants causing severe disease, the likelihood of finding these as standing variations in the general population is low. Therefore, this study sought to evaluate the pathogenicity of de novo variants previously associated with cardiac disease based on a large population-representative exome database.

**METHODS AND RESULTS:** We performed a literature search for previous publications on de novo variants associated with severe arrhythmias and structural heart diseases and investigated whether these variants were present in the Exome Aggregation Consortium (ExAC) database (n=60 706). We identified monogenic variants in single case reports and smaller studies ( $\leq 200$  subjects) and variants considered to increase susceptibility of disease in 3 larger trio studies ( $> 1000$  subjects). Of the monogenic variants, 11% (23/211) were present in ExAC, whereas 26% (802/3050) variants believed to increase susceptibility of disease were identified in ExAC. Monogenic de novo variants in ExAC had a total allele count of 109 and with  $\approx 844$  expected cases in ExAC, these variants would account for 13% of all cases in the studied diseases if truly monogenic.

**CONCLUSIONS:** We observed numerous de novo variants associated with cardiac disease as standing variation in ExAC, thus these variants are less likely monogenetic causes or major risk contributors for cardiac disease. This highlights the importance of investigating the pathogenicity of de novo variants because they are not as exclusive and pathogenically evident as presumed previously.

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*Circulation: Cardiovascular Imaging*

# Increased Aortic Diameters on Multidetector Computed Tomographic Scan Are Independent Predictors of Incident Adverse Cardiovascular Events

## The Framingham Heart Study

This Framingham Offspring analysis sought to determine if measures of enlarged aortic diameters can improve the prediction of incident adverse cardiovascular disease. The results show that abdominal aortic diameter measurements may provide important, incremental risk information independent of traditional risk factors.

**BACKGROUND:** Adverse aortic remodeling, such as dilation, is associated with multiple cardiovascular disease (CVD) risk factors. We sought to determine whether measures of enlarged aortic diameters improve prediction of incident adverse CVD events above standard CVD risk factors in a community-dwelling cohort.

**METHODS AND RESULTS:** Participants from the Framingham Offspring and Third Generation Cohorts (n=3318; aged 48.9±10.3 years), who underwent noncontrast thoracic and abdominal multidetector computed tomography during 2002 to 2005, had complete risk factor profiles, and were free of clinical CVD, were included in this study. Diameters were measured at 4 anatomically defined locations: the ascending thoracic aorta, descending thoracic aorta, the infrarenal abdominal aorta, and lower abdominal aorta. Adverse events comprised CVD death, myocardial infarction, coronary insufficiency, index admission for heart failure, and stroke. Each aortic segment was dichotomized as enlarged (diameter ≥upper 90th percentile for age, sex, and body surface area) or not enlarged; the hazard of an adverse event for an enlarged segment was determined using multivariable-adjusted Cox proportional hazards models. Over a mean 8.8±2.0 years of follow-up, there were 177 incident adverse CVD events. In models adjusted for traditional CVD risk factors, enlarged infrarenal abdominal aorta (hazard ratio=1.57; 95% confidence interval=1.06–2.32) and lower abdominal aorta (hazard ratio=1.53; 95% confidence interval=1.00–2.34) were associated with an increased hazard of CVD events. Enlarged ascending thoracic aorta and descending thoracic aorta were not significantly associated with CVD events.

**CONCLUSIONS:** Among community-dwelling adults initially free of clinical CVD, enlarged infrarenal abdominal aorta and lower abdominal aorta, on noncontrast multidetector computed tomography scans, are independent predictors of incident adverse CVD events above traditional risk factors alone.

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# Thirty-Day Readmission Rate and Costs After Percutaneous Coronary Intervention in the United States

## A National Readmission Database Analysis

This study of percutaneous coronary intervention (PCI) cases from the Healthcare Cost and Utilization Project National Readmission Database analyzes short-term readmissions and costs after PCI. The results found a mean rate of 30-day readmission after PCI of 12%, the majority of which did not require any further interventions. Readmissions were associated with a significant increase in cumulative costs and a nonnegligible death rate of 3%. More effort is needed to recognize any possibly preventable post-PCI readmissions and complications.

**BACKGROUND:** The association of short-term readmissions after percutaneous coronary intervention (PCI) on healthcare costs has not been well studied.

**METHODS AND RESULTS:** The Healthcare Cost and Utilization Project National Readmission Database encompassing 722 US hospitals was used to identify index PCI cases in patients  $\geq 18$  years old. Hierarchical regression analyses were used to examine the factors associated with risk of 30-day readmission and higher cumulative costs. We evaluated 206 869 hospitalized patients who survived to discharge after PCI from January through November 2013 and analyzed readmissions over 30 days after discharge. A total of 24 889 patients (12%) were readmitted within 30 days, with rates ranging from 6% to 17% across hospitals. Among the readmitted patients, 13% had PCI, 2% had coronary artery bypass surgery, and 3% died during the readmission. The most common reasons for readmission included nonspecific chest pain/angina (24%) and heart failure (11%). Mean cumulative costs were higher for those with readmissions (\$39 634 versus \$22 058;  $P < 0.001$ ). The multivariable analyses showed that readmission increased the log<sub>10</sub> cumulative costs by 45% ( $\beta$ : 0.445;  $P < 0.001$ ). There was no significant difference in cumulative costs by the type of insurance.

**CONCLUSIONS:** In a national sample of inpatient PCI cases, 30-day readmissions were associated with a significant increase in cumulative costs. The majority of readmissions were because of low-risk chest pain that did not require any intervention. Ongoing effort is warranted to recognize and mitigate potentially preventable post-PCI readmissions.

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*Circulation: Cardiovascular Quality and Outcomes*

# Mortality of Myocardial Infarction by Sex, Age, and Obstructive Coronary Artery Disease Status in the ACTION Registry–GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With the Guidelines)

This analysis of the ACTION registry (Acute Coronary Treatment and Intervention Outcomes Network Registry) evaluated mortality after myocardial infarction (MI) by age, sex, and presence of obstructive or nonobstructive coronary artery disease (CAD). MI with nonobstructive coronary artery disease was more common in women and was associated with lower mortality than MI with obstructive CAD. In patients with obstructive CAD, a higher rate of post-MI death was observed among women than in men.

**BACKGROUND:** Sex differences in early mortality after myocardial infarction (MI) vary by age. MI with nonobstructive coronary arteries (MINOCA [ $<50\%$  stenosis]) is more common among younger patients and women, and MINOCA has a better prognosis than MI with obstructive coronary artery disease (MI-CAD). The relationship between age, sex, and obstructive CAD status and outcomes post-MI has not been established.

**METHODS AND RESULTS:** Adults who underwent coronary angiography for acute ST-segment–elevation and non–ST-segment–elevation MI in the National Cardiovascular Data Registry ACTION Registry–GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With the Guidelines) from 2007 to 2014 were identified. Patients with cardiac arrest, thrombolytic therapy, prior revascularization, or missing demographic or angiographic data were excluded. The primary outcome was all-cause, in-hospital mortality. Secondary outcomes included major adverse cardiovascular events. Demographics, clinical history, presentation, and in-hospital treatments were compared by sex and CAD status (MI-CAD or MINOCA). Mortality and major adverse cardiovascular outcomes were analyzed by age, sex, and CAD status. Among 322 523 patients with MI, MINOCA occurred in 18 918 (5.9%). MINOCA was more common in women than men (10.5% versus 3.4%;  $P<0.0001$ ), and women had higher mortality than men overall (3.6% versus 2.4%;  $P<0.0001$ ). In-hospital mortality was lower after MINOCA than MI-CAD (1.1% versus 2.9%;  $P<0.0001$ ). Among patients with MI-CAD, women had higher mortality than men (3.9% versus 2.4%;  $P<0.0001$ ) while no sex difference in mortality was observed with MINOCA (1.1% versus 1.0%;  $P=0.84$ ). The higher risk of post-MI death among women with MI-CAD was most pronounced at younger ages.

**CONCLUSIONS:** MINOCA was associated with lower mortality than MI-CAD. Higher risk of post-MI death among women in comparison to men was restricted to patients with MI-CAD.

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*Circulation: Heart Failure*

# Trends in the Use of Inotropes to List Adult Heart Transplant Candidates at Status 1A

This study analyzed all heart-only transplant candidate registrations from 2000 to 2015 from the Scientific Registry of Transplant Recipients data set to determine whether those listed with inotropes contribute to the rising number of status 1A candidates. The results demonstrate that the number of candidates being listed as status 1A with inotropes is increasing, whereas the doses of inotropes have declined. The risk of death or deterioration of status 1A candidates has declined. These data suggest programs have increased the use of multiple inotropes with improved waitlist outcomes and this may be contributing to an excess of status 1A candidates.

**BACKGROUND:** The number of adult heart transplant candidates waiting at the most urgent status 1A has increased over time despite the expansion of geographic sharing of hearts in 2006. We aimed to determine whether candidates listed with inotropes contribute to the excess status 1A candidates.

**METHODS AND RESULTS:** The initial registrations of all adult heart-only candidates listed from 2000 to 2015 were analyzed using the Scientific Registry of Transplant Recipients data set. Trends in listing status, justifications, and candidate factors were measured. Adjusted trends in listing status pre- and post-geographic sharing were estimated using multilevel logistic regression. Competing risks models provided trends in transplant-free waitlist survival. There were 46 853 adult heart-alone listings during 2000 to 2015. Pre-sharing, status 1A listing was unchanged over time (adjusted odds ratio, 0.98; 95% confidence interval, 0.78–1.23). Post-sharing, the adjusted odds of status 1A listing increased 117% over 9 years (adjusted odds ratio 2.17, 95% confidence interval, 1.82–2.58). The number of candidates listed as status 1A with inotropes increased by 193 a year, whereas the dobutamine, dopamine, and milrinone doses used decreased 49%, 55%, and 29% ( $P<0.001$ ). The risk of waitlist death or deterioration of status 1A inotrope candidates relative to status 2 candidates decreased 62% for 2006 to 2010 and 70% for 2011 to 2015 compared with that for 2003 to 2006.

**CONCLUSIONS:** After the wider geographic sharing of hearts in 2006, transplant programs used multiple inotropes to list candidates at status 1A more frequently with progressively lower doses. Concurrently, the status 1A inotrope candidate waitlist outcomes improved substantially. These trends suggest that overtreatment with multiple inotropes contributes to the current critical excess of status 1A candidates.

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