

2000 and 2005 and had at least 3 years of follow-up data available.

The authors found that the risk of gastrointestinal bleeding was higher among patients who had taken a combination of antithrombotic medications in the 90 days preceding diagnosis than among those who had taken only a single medication during this period. Patients taking warfarin and acetylsalicylic acid (48 cases and 82 controls) were at the highest overall risk for bleeding (adjusted rate ratio 6.48, 95% CI 4.25–9.87). After accounting for the risks of taking the two drugs independently the rate ratio was 2.23 (95% CI 1.46–3.41)—a measure of the additional risk resulting from drug–drug interactions alone.

The combination of clopidogrel and acetylsalicylic acid also yielded a high overall risk for gastrointestinal bleeding, as did the combination of nonsteroidal anti-inflammatory drugs with either warfarin or clopidogrel. Physicians need to weigh carefully the gastrointestinal risks of these drug combinations against their cardiovascular benefits.

**Original article** Delaney JA *et al.* (2007) Drug–drug interactions between antithrombotic medications and the risk of gastrointestinal bleeding. *CMAJ* 177: 347–351

## Benefits of implantable cardioverter-defibrillators maintained in clinical setting

Patients with left ventricular systolic dysfunction are at risk of ventricular arrhythmias and sudden cardiac death. Meta-analyses of randomized controlled trials (RCTs) have demonstrated that, in these patients, implantable cardioverter-defibrillators (ICDs) reduce mortality by 26% and sudden cardiac death by 57%. Some cardiologists, however, question whether the benefits of ICDs seen in clinical trials extend to clinical practice, where physicians who perform implantation procedures might not have the same level of experience.

Ezekowitz *et al.* analyzed data from observational studies that examined the use and safety of ICDs in clinical practice and from more-recent clinical trials that assessed the risks and benefits of ICDs tested under ideal circumstances. Data were extracted from 12 RCTs that reported on mortality and ICD use and 76 observational studies that examined safety or efficacy.

Overall, in adult patients with left ventricular systolic dysfunction, ICDs reduced mortality by 20% in RCTs and by 46% in observational studies, countering the concern that ICDs might be less beneficial in clinical practice than in the trial setting. The authors recommend that future studies develop risk-stratification tools to aid the identification of those patients who are most and least likely to benefit from an ICD. It is particularly important, they note, that patients unsuitable for the procedure are not exposed unnecessarily to the risks associated with implantation.

**Original article** Ezekowitz JA *et al.* (2007) Systematic review: implantable cardioverter defibrillators for adults with left ventricular systolic dysfunction. *Ann Intern Med* 147: 251–262

## Heart failure with preserved left ventricular systolic function: is it being overlooked?

Clinical trials of therapies for heart failure (HF) are usually performed in patients with left ventricular systolic dysfunction (LVSD) and reduced left ventricular ejection fraction (LVEF). The substantial proportion of HF patients who have preserved systolic function (PSF) and an LVEF of 40–50% or more are rarely included in HF trials, and as such there are very limited data on their characteristics or outcomes.

Fonarow *et al.* used data from OPTIMIZE-HF, a large national registry of patients hospitalized for HF, to compare the characteristics, hospital courses, and outcomes after hospital discharge of patients with LVSD at the time of hospitalization for HF with those of patients with PSF at hospital admission.

The study compared 20,118 patients who had HF and LVSD with 21,149 patients who had HF and PSF (LVEF  $\geq$ 40%). Patients with HF and PSF were more likely to be older, female and white and to have HF with a nonischemic cause than were patients with LVSD. The length of hospital stay, postdischarge mortality risk and rehospitalization rates over 60–90 days were similar in the two groups, but in-hospital mortality was slightly lower in the group of patients with PSF. Treatment of patients with HF and PSF using  $\beta$ -blockers, angiotensin-converting-enzyme inhibitors or angiotensin-receptor blockers had no beneficial effect on rehospitalization rate and mortality.