Echocardiographic evaluation of left ventricular function in ischemic heart disease

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Chapter 1

General introduction and outline of the thesis

Nowadays, coronary artery disease is one of the leading causes of morbidity and mortality in the Western world. Data from the National Health and Nutrition Surveys (NHANES) suggest that 13.7 million persons in the United States have coronary artery disease (1). Half of these patients have a history of myocardial infarction and the other half of patients suffer from angina pectoris. The data from the NHANES study probably even underestimate the actual prevalence of coronary artery disease as the study relies on self-reported myocardial infarction and angina pectoris from health interviews. For men, the prevalence of coronary artery disease increases with age from 7% at ages 40 to 49 years to 13% at 50 to 59 years, 16% at 60 to 69 years, and 22% at 70 to 79 years. For women, these estimated prevalences are substantially lower than for men: 5%, 8%, 11%, and 14%, respectively. In The Netherlands, in 2007 every day 19 men and 14 women died due to coronary artery disease (2). Of all patients who died in 2007, 10% of men and 8% of women died as a result of coronary artery disease. Acute myocardial infarction was the major contributor to mortality among patients who died as a result of coronary artery disease, with 4566 men and 3598 women who died from acute myocardial infarction.

Recently, Yeh et al. studied population trends in the United States in the incidence and outcomes of myocardial infarction (3). The authors identified 46,086 hospitalizations for myocardial infarction from 1999 to 2008. The age- and sex-adjusted incidence of myocardial infarction increased from 274 cases per 100,000 person-years in 1999 to 287 cases per 100,000 person-years in 2000 (Figure 1). Thereafter, the incidence decreased each year, to 208 cases per 100,000 person-years in 2008, which represents a 24% relative decrease over the study period. A significant decrease in the incidence of ST-segment elevation myocardial infarction was observed throughout the study period (from 133 cases per 100,000 person-years in 1999 to 50 cases per 100,000 person-years in 2008). Thirty-day mortality was significantly lower in 2008 than in 1999 (Figure 2). It was concluded that the reductions in short-term case fatality rates for myocardial infarction mainly appear to be driven by a decrease in the incidence of ST-segment elevation myocardial

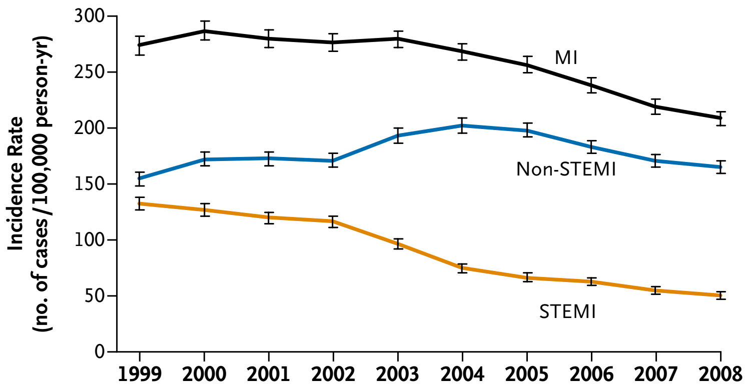

Figure 1. Age- and sex-adjusted incidence rates of acute myocardial infarction, 1999 to 2008. I bars represent 95% confidence intervals. MI: myocardial infarction; STEMI: ST-segment elevation myocardial infarction. Reprinted from Yeh et al. (3) with permission.

infarction and a lower rate of death after non-ST-segment elevation myocardial infarction. The major contributors to the improvement in 30-day mortality after STEMI are the increased use of thrombolytic therapy or primary percutaneous coronary intervention as well as the increased use of aspirin, angiotensin-converting enzyme (ACE) inhibitors, and beta blockers (4).

Despite the improved short-term outcome, survivors of a myocardial infarction still face a substantial risk of further cardiovascular events including the development of heart failure and an increase in mortality (5). At six years following a myocardial infarction, men have a two-fold increase in the age-adjusted risk of a recurrence, a four-fold increase in the risk of developing angina and a five-fold increase in the risk of heart failure. Data from the Framingham study demonstrated that heart failure developed in 21% of men and 30% of women as a result of decreased left ventricular (LV) function after myocardial infarction (6). In the SOLVD trial, it was demonstrated that patients with asymptomatic LV systolic dysfunction progress to overt heart failure over time. In the placebo arm of the SOLVD trial, patients with asymptomatic LV dysfunction who were not treated with an ACE inhibitor, progressed to symptomatic heart failure at a rate of 9.7% per year (7). In addition, the mortality rate in patients with asymptomatic LV dysfunction is increased, although to a lesser degree than in symptomatic heart failure. In the placebo arm of the SOLVD trial, the 3-year mortality rate was 16%.

The presence of a decreased LV function after myocardial infarction has demonstrated to be of considerable clinical importance. In this thesis, the role of 2-dimensional (2D) echocardiography to evaluate LV function in ischemic heart disease is investigated. Recently introduced echocardiographic parameters to describe LV function are studied and their importance for prognosis after myocardial infarction is evaluated. In addition, the role for echocardiography in the decision-making around advanced treatment options in heart failure such as cardiac resynchronization therapy (CRT) and cardiac surgery will be explored.

LEFT VENTRICULAR FUNCTION AFTER MYOCARDIAL INFARCTION

Echocardiography is useful for evaluation of LV function, risk stratification and assessment of prognosis after myocardial infarction. At present, 2D echocardiography is frequently used in the management of patients with acute myocardial infarction. It is a low-cost and safe imaging modality, which can be easily applied at bedside and is valuable for patient follow-up. Important benefit of echocardiography has been demonstrated in establishing the diagnosis, location, and extent of myocardial infarction, and in detection of mechanical complications after myocardial infarction.

In particular, echocardiography is useful for assessment of prognosis and risk stratification. For this purpose, various traditional echocardiographic parameters have been validated (Table 1), such as LV volumes (Figure 3) and LV ejection fraction (LVEF), wall motion score index, mitral regurgitation and left atrial volume (8-12). The introduction of tissue Doppler imaging and

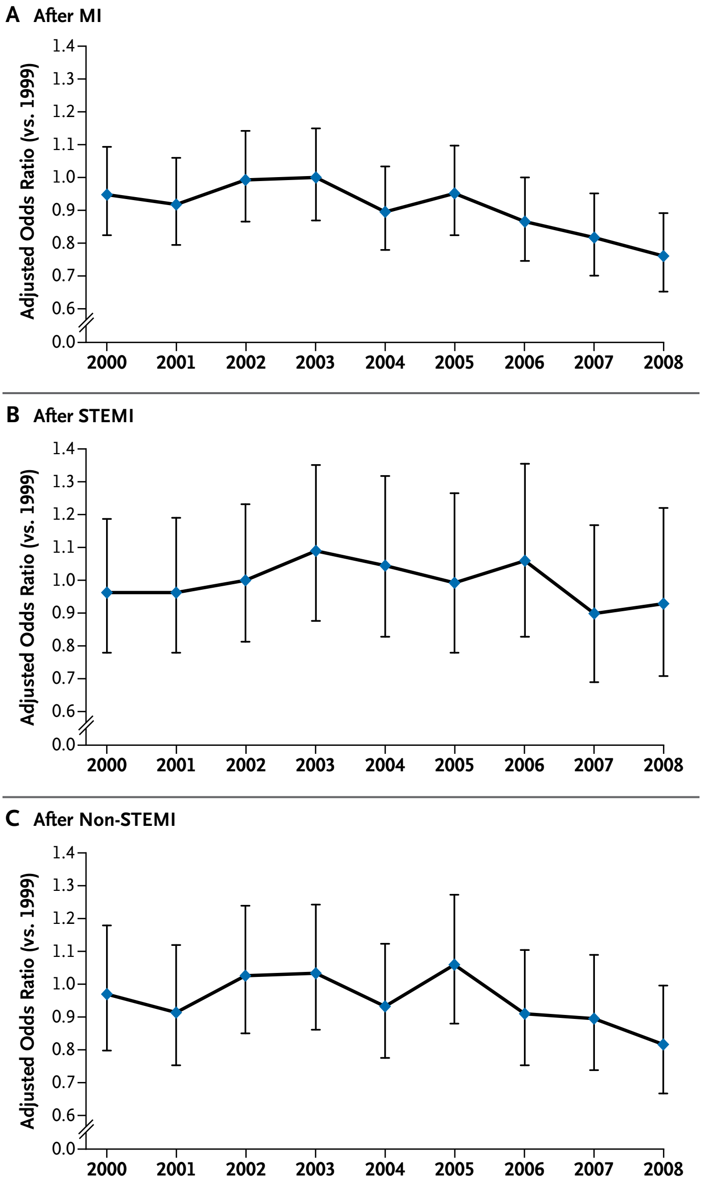

Figure 2. Adjusted odds ratio for 30-day mortality, according to year. The adjusted odds ratios after myocardial infarction (*panel A*), ST-elevation myocardial infarction (STEMI; *panel B*), and non-ST-elevation myocardial infarction (non-STEMI; *panel C*) are shown. Models were adjusted for patient demographic characteristics, previous cardiovascular disease, cardiovascular risk factors, chronic lung disease, and systemic cancer. The reference year is 1999. I bars represent 95% confidence intervals. MI: myocardial infarction; STEMI: ST-segment elevation myocardial infarction. Reprinted from Yeh et al. (3) with permission.

speckle-tracking strain imaging has provided additional promising parameters to evaluate LV function after myocardial infarction. In the first part of this thesis, the main focus is on the relation between recently introduced echocardiographic parameters to describe LV function, such as tissue Doppler imaging and speckle-tracking strain imaging, and outcome after myocardial infarction.

Table 1. Traditional echocardiographic parameters related to prognosis after myocardial infarction

· Left ventricular (LV) volumes
· LV ejection fraction (LVEF)
· Mitral regurgitation
· Wall motion score index (WMSI)
· Diastolic function
· Left atrial (LA) volume
· Right ventricular (RV) function

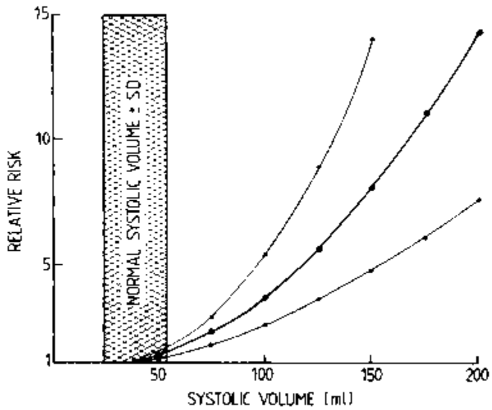

Figure 3. Estimated relationships between ESV and relative risk of cardiac death over the follow-up period. The risk is relative to that of a normal individual (with an ESV of 39 ml). The risk does not rise steeply until ESV is 3 to 4 SD above normal. Fine lines indicate 95% confidence limits of relative risk. ESV: end-systolic volume. Reprinted from White et al. (8) with permission.

LEFT VENTRICULAR FUNCTION IN HEART FAILURE

Besides its role after myocardial infarction, echocardiography plays an important role for risk stratification and assessment of prognosis in patients with heart failure. Echocardiographic assessment of LV function with quantification of LV volumes and LVEF is part of the clinical workup in patients with heart failure. Clinically evident heart failure due to systolic dysfunction is generally not apparent until the LVEF falls below 35 to 40% (13). Among patients with heart failure, prognosis varies inversely with LVEF (Figure 4). Besides LV volumes and LVEF, other traditional echocardiographic parameters, such as diastolic LV function, right ventricular function, LV mass and left atrial volume, have been associated with outcome in patients with heart failure (13-20).

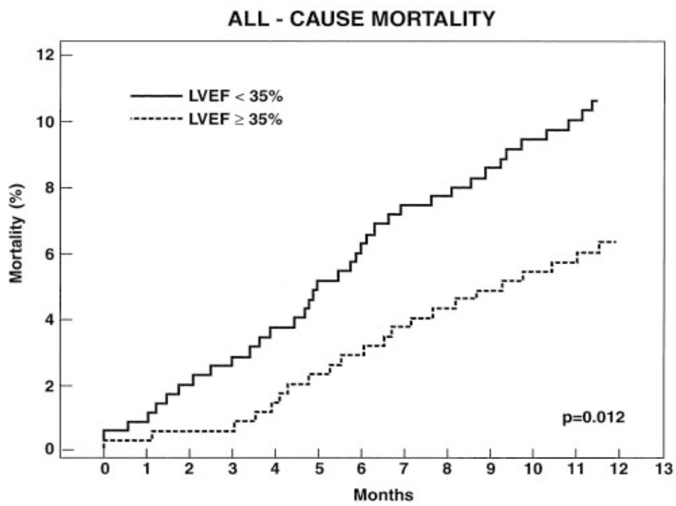

Figure 4. Kaplan-Meier unadjusted survival curves (expressed as cumulative 1-year mortality) observed in patients with LVEF at or above versus below 35%. LVEF: left ventricular ejection fraction. Reprinted from Quinones et al. (13) with permission.

The more recently introduced echocardiographic techniques of tissue Doppler imaging and speckle-tracking strain imaging have provided additional promising parameters to evaluate LV function in patients with heart failure. In particular, these parameters can be of benefit for the determination of eligibility for advanced treatment options such as CRT and cardiac surgery. In the second part of this thesis, the main focus is on the role of echocardiography in prediction of response to CRT in patients with advanced heart failure. Furthermore, the role for echocardiography in the decision making around cardiac surgery in heart failure patients is studied.

OUTLINE OF THE THESIS

The aim of this thesis is to study the role of echocardiography for the evaluation of LV function in patients with ischemic heart disease. In the first part of the thesis, the main focus is on the relation between recently introduced echocardiographic parameters to describe LV function, and outcome after myocardial infarction. In the second part of the thesis, the main focus is on the role of echocardiography in prediction of response to CRT in patients with advanced heart failure. Furthermore, the role for echocardiography in the decision making around cardiac surgery in heart failure patients is studied.

Part 1: Left ventricular function after myocardial infarction

In the first part of the thesis, the relation between recently introduced echocardiographic parameters to describe LV function, such as tissue Doppler imaging and speckle-tracking strain imaging, and outcome after myocardial infarction is evaluated. **Chapter 2** provides an extensive review on the prognostic value of echocardiography after acute myocardial infarction. In **Chapter 3** and **Chapter 4**, the value of LV dyssynchrony as assessed with tissue Doppler imaging and speckle-tracking strain imaging, respectively, for prediction of outcome after myocardial infarction is studied. In **Chapter 5**, the relation between the time to reperfusion after primary percutaneous coronary intervention for acute myocardial infarction, and LV longitudinal strain as a reflector of the extent of myocardial damage is described. Subsequently, the relation between global LV longitudinal strain assessed with novel automated function imaging and LVEF in patients with coronary artery disease is explored in **Chapter 6**. **Chapter 7** focuses on the time course of global LV strain after acute myocardial infarction. In **Chapter 8**, the ability to assess myocardial viability in chronic ischemic LV dysfunction is compared between echocardiographic speckle-tracking strain imaging and contrast-enhanced magnetic resonance imaging. The value of myocardial viability as assessed with global LV longitudinal strain for prediction of recovery of LV function after acute myocardial infarction is described in **Chapter 9**. Finally, in **Chapter 10**, the prognostic value of strain and strain rate after acute myocardial infarction is evaluated.

Part 2: Left ventricular function in heart failure

In the second part of the thesis, the role of echocardiography in prediction of response to CRT in patients with advanced heart failure is evaluated. In addition, the role for echocardiography in the decision-making around cardiac surgery in heart failure patients is studied. **Chapter 11** focuses on the value of QRS duration to predict response to CRT in patients with end-stage heart failure. In **Chapter 12**, the relation between LV resynchronization and response to CRT is analyzed in heart failure patients with echocardiographic evidence of LV dyssynchrony at baseline. In **Chapter 13**, the value of LV longitudinal strain, as a potential reflector of LV myocardial scar tissue, for prediction of response to CRT is evaluated. Finally, in **Chapter 14**, LVEF is evaluated as criterion for implantation of an implantable cardioverter-defibrillator (ICD) in heart failure patients who undergo surgical LV reconstruction.

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