Clinical practice guidelines (CPGs) describe and define best clinical practice and standards of care based on the available scientific data from preclinical studies, randomized clinical trials and registries, and clinicians’ expert judgment. Adherence to CPGs has been clearly shown to improve quality of care and, ultimately, patient outcome. Clinicians dedicated to the delivery of optimal care in the field of acute coronary syndromes (ACS) are faced with two major factors that may complicate daily treatment decisions: limited resources and the rapid evolution of the knowledge database. Acute coronary syndromes may be the field in clinical cardiology that is the fastest moving target, with a myriad of clinical trials being conducted and completed each year, rendering the half-life of CPGs shorter while increasing the need of timely updates. The study by Kereiakes and Antman is important and relevant because the ACS guidelines of the American College of Cardiology/American Heart Association (ACC/AHA) on ST-segment elevation myocardial infarction (STEMI) date back to 2004 (1) and the ACC/AHA guidelines on non-STEMI and unstable angina date back to 2002 (2). In the field of non–ST-segment elevation (nSTE)-ACS, Kereiakes and Antman reiterate the importance of risk stratification for the triage of appropriate patients to an optimal treatment strategy, as the relative benefit from early invasive treatment is directly proportional to patient risk profile. However, from the practicing clinician’s perspective, it is important to determine just what level of risk defines the patient group that would benefit most from early invasive treatment. Should alternative approaches be considered, what is the optimal concomitant medical treatment, and what are the logistical and financial consequences of treatment decisions?

In the ICTUS (Invasive versus Conservative Treatment in Unstable Coronary Syndromes) trial, we could not demonstrate an early invasive strategy to be superior to a selective invasive strategy in 1,200 patients with an elevated cardiac troponin T against a background of optimized medical therapy after 1 year follow-up (3). The result was unexpected, and many questions have been raised regarding methodology, patient profiles, and external validity of the study. The contention that a non–high-risk patient population was included in the ICTUS study, which may explain the findings, is in contrast with previous publications, the 2002 AHA/ACC guidelines, and the 2003 ESC guidelines that designate nSTE-ACS patients with an elevated cardiac troponin as high risk, qualifying such patients for glycoprotein IIb/IIIa inhibitor treatment, angiography, and subsequent revascularization (4). In fact, the baseline characteristics in our study population are quite comparable to those in the FRISC-II (FRagmin and Fast Revascularisation during Instability in Coronary artery disease II) and RITA (Randomized Intervention Treatment of Angina)-3 trials, with 15% of patients with diabetes being typical for a European nSTE ACS population (5). We did not show a mortality benefit, which is in contrast with the 2-year results of the FRISC-II study (6) and the 5-year results of the RITA-3 study (7) but confirms the conclusion of the recent meta-analysis by Mehta et al. (8) of all previous randomized controlled clinical trials. Long-term follow-up in the ICTUS study will show whether the early hazard of revascularization is offset by a late benefit, as was shown in the RITA-3 5-year follow-up study (7).

We showed that an early invasive strategy with percutaneous coronary intervention (PCI) at a median of 24 h after randomization is associated with an increase in small PCI-related myocardial infarctions. This early hazard was also shown in the meta-analysis by Mehta et al. (8). Meta-analyses of strategy trials in nSTE ACS that were conducted over a 10-year time span should, however, be interpreted with caution, not only because treatment has changed substantially over time (as Kereiakes and Antman acknowledge) with the use of clopidogrel, glycoprotein IIb/IIIa inhibitors, and stents, but also because revascularization rate differs significantly among studies. The in-
hospital revascularization in the FRISC-II study in the non-invasive and invasive treatment arms was 9% and 71%, respectively; in the RITA-3 study it was 10% and 44%; and in the ICTUS study 40% and 76%. Moreover, the revascularization rate at 1 and 2 years in the invasive treatment arm of the RITA-3 study, for example, is nearly identical to the revascularization rate in the non-invasive treatment arm in the ICTUS study, yet they are categorized in separate categories in the meta-analysis. With optimized medical treatment and revascularization rate at 1 year around 55% to 60%, an early invasive treatment may not be necessary for all nSTE ACS patients with a positive cardiac troponin. Indeed, a sub-analysis of the FRISC-II study suggested that the combination of a positive troponin and ST-segment changes on the electrocardiogram identifies the patients that derived the most benefit from early invasive treatment (9). Although the data from randomized controlled clinical trials come from highly selected patient populations, as we know, data from large “real world” registries regarding invasive or non-invasive practice patterns in nSTE ACS are conflicting and not all reassuring. A consistent finding has been a hazard associated with invasive management, as shown in several large-scale registries (from the OASIS [Organization to Assess Strategies for Ischaemic Syndromes] and GRACE [Global Registry of Acute Coronary Events] investigators) that reported on clinical practice from centers around the world in which hospitals with catheterization facilities did not show better outcomes for ACS patients than did hospitals without such facilities (10,11). Moreover, a recent analysis from a large Medicare database has shown that a high “area level invasive treatment intensity” did not provide a clinical benefit over lower invasive treatment intensity when beta-blocker treatment intensity in appropriate patients was high (12).

In contrast to the field of nSTE ACS, rapid mechanical reperfusion in patients with STEMI has been clearly and consistently shown to be superior to thrombolytic therapy, provided that the procedure is performed swiftly and in high-volume centers by experienced operators (13,14). Kereiakes and Antman justly summarize the arguments for the establishment of “ACS centers of excellence” that may function as the nucleus of a hub-and-spoke regional care network dedicated to the timely triage, transfer, and treatment of STEMI patients. Such networks have been shown to be effective in Europe in reducing door-to-needle time and symptoms-to-reperfusion time and, consequently, in reducing mortality.

In summary, the greater truth might be that in view of limited resources for the care of ACS patients, practicing cardiologists should follow CPGs as much as possible, organize care in regional collaborations, and optimize the delivery of timely mechanical reperfusion for all eligible STEMI patients. The benefit from early invasive treatment in nSTE ACS patients is dependent on risk profile, and with the application of more effective medical treatment, the benefit may be modest for non-high-risk patients. Moreover, clinicians should be aware of the early risk associated with early revascularization and should verify whether the complication rate associated with revascularization in nSTE ACS patients in their own practice mirrors the complication rate in the centers in which the randomized strategy trials were conducted. In this rapidly moving field, future studies will demonstrate what level of risk beyond an elevated cardiac troponin qualifies nSTE ACS patients for early invasive treatment and what concomitant medical treatment will ensure best medical practice.

Reprint requests and correspondence: Dr. Robbert J. de Winter, Department of Cardiology, B2-137, Academic Medical Center, Meibergdreef 9, PO Box 22660, 1100 DD Amsterdam, the Netherlands. E-mail: r.j.dewinter@amc.uva.nl.

REFERENCES


