reactions leading to thrombin generation produce an explosion of coronary thrombus deposition when inhibition of thrombin activity has dissipated. (2) The concentrations of direct antithrombins required to produce a meaningful inhibition of clot-bound thrombin and prevent platelet activation are far in excess of those that can be administered safely clinically because of the risk of excessive bleeding. (3) Direct antithrombins bind to thrombin in a 1:1 stoichiometric fashion and it is therefore possible to ‘exhaust’ the extent of thrombin inhibition if an insufficient concentration of a direct antithrombin is present. In contrast, unfractionated heparin is a catalytic inhibitor of thrombin with a single molecule of heparin capable of dissociating from a given antithrombin III-thrombin complex and eventually inhibiting several other molecules of thrombin.

What are we to conclude about the prospects of direct antithrombins as an alternative to unfractionated heparin for acute coronary syndromes? While some investigators have suggested that direct antithrombins might be proven to be superior to heparin if one used a particular thrombolytic (e.g. streptokinase) or selected a specific profile of patients (e.g. young individuals with normal renal function), these beliefs are based either on post hoc analyses or relatively small angiographic trials without sufficient power to compare clinical outcomes. With the addition of the TRIM study results to the enlarging database on direct antithrombins, it now appears that the direct antithrombins are probably equally effective as unfractionated heparin but offer the clinical advantage of a more stable level of anticoagulation. To date this has not been deemed a sufficient market advantage by several pharmaceutical manufacturers who have decided to terminate their direct antithrombin drug development programmes.

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References
increasing pattern of beta-blocker use in secondary prevention which has also been detected in studies from countries other than Italy. Certainly, the dissemination of the results of large randomized clinical trials and the enormous numbers of physicians involved in them have been instrumental in this increasing pattern of use. But there is still much room for improvement.

In addition to beta-blockers being globally under-used, the pattern of prescription may not go in the right direction: as shown by studies including the present one, high-risk patients with a potentially greater benefit to be derived from beta-blockade, such as those with transient heart failure or electrical complications during the acute phase, tend to be denied beta-blocker treatment. Beta-blockers have also been uncritically avoided in elderly patients, whose risk is also high, although, as has been recently demonstrated, such an attitude is unfounded. This shying away from drugs with proven benefit and an acceptable safety profile is even more disquieting in view of the finding that a major determinant of non-prescription of beta-blockers is the prescription of calcium channel blockers, for which the evidence of benefit in such clinical context is, to say the least, scanty.

To get a fuller understanding of why this lack of compliance with evidence has developed, studies beyond the usual framework of clinical research, and falling within the boundaries of sociological investigation of medical behaviour, might be in order. It seems apparent, however, that marketing policies have been one of its major causes. Thus, pure clinical research studies cannot say why there is a gap between evidence and real practice, but they may give a description of its features. The study by Avanzini et al. shares with others dealing with the use of beta-blockers in practice the feature of being a retrospective survey of large clinical trials in relatively unselected populations. It has the additional appeal of being based on a set of trials (the GISSI studies) with an impressive number of patients and, more importantly, covering a large proportion of a country’s coronary care units. Nevertheless, even for descriptive purposes, to gain more precise information other types of design would be required. The patient population included in clinical trials and the institutions participating in them may not be as representative of the overall population receiving care as other studies, such as cohort studies from database research. For instance, the study by Avanzini et al. covers an impressive 75% of coronary care units over the whole of Italy. However, there is no information about patients not treated in coronary care settings. This means that the reported rates of compliance with the current guidelines might be an over-estimation.

On the other hand, a specific questionnaire addressed to the aim of the study, rather than the retrospective use of data designed for other purposes, might give a more precise view of the profile of definite or possible contraindications to beta-blockade in the study population, or provide information on an important aspect such as dose which was missed in the present study. In addition, evidence-based guidelines such as those by the ACC/AHA indicate different degrees of strength in the recommendations of therapy depending on the evaluation of risk in individual patients. To gain a deeper insight into the attitude of physicians in real practice, it would be interesting to view the rates of prescription or non-prescription of beta-blockers set against the backdrop of such an assessment. Certainly, it may be hard to collect sound information about the evaluation of risk in patients with myocardial infarction, even when this evaluation has been gained from large databases except when these are exceptionally well documented, as in the GISSI trials.

Notwithstanding these considerations, it should be kept in mind that prospective studies to clarify such issues may be suboptimally cost-effective. Therefore, approximative views such as those which are already abundant in the literature may be sufficient justification for implementing educational and other measures to counteract the well known tendency of practitioners to under-use beta-blockers. The different types and the desirable effects of such measures have recently been the subject of discussion, and some hints of them are provided in the study by Avanzini et al.

One should not, however, think that all questions about the indications of beta-blockade after myocardial infarction are closed and that implementation is the only remaining problem. Issues still remain to be settled, such as the optimal duration of therapy or the possible negative interaction with angiotensin converting enzyme inhibitors. Such interaction is a glaring example of the dilemmas that confront clinicians as evidence of the benefit of different unrelated interventions accumulates from independent studies, and illustrates the need for clarification in further investigations.

Some authors believe or hope that physicians’ reluctance in prescribing beta-blockers may be diminishing as a result of increasing evidence and better pathways of medical information or continuing education. Unfortunately, their own studies show that there is still a long way to go.

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Detecting coronary artery disease in patients with valvular heart disease

See page 1478 for the article to which this Editorial refers

Advances in non-invasive diagnostic techniques over the last decade have enabled accurate assessment of patients with valvular heart disease. Quantitation of haemodynamics, ventricular function, and detailed description of valve leaflet thickening, calcification and mobility by Doppler echocardiography has allowed appropriate selection of patients for valve repair or valve replacement without the need for pre-operative cardiac catheterization and without compromising their clinical outcome. However, detection of important coexistent, but asymptomatic coronary artery disease has remained the Achilles' heel of non-invasive methods used in the pre-operative evaluation of patients with valvular heart disease.

Pre-operative detection of coronary artery disease in patients undergoing valve surgery has been regarded as a prerequisite to avoid peri-operative coronary events that might compromise patient outcome. This has been particularly important in elderly patients in whom the prevalence of risk factors for coronary artery disease increases the likelihood of adverse cardiovascular events in the peri-operative period and has resulted in the recommendation of routine pre-operative coronary arteriography.

A number of attempts have been made to detect occult coronary artery disease non-invasively because this would obviate the need for cardiac catheterization, and at the same time reduce the cost of patient management. Patient demographics including age, hypertension, diabetes mellitus, plasma cholesterol levels, symptoms of angina and congestive heart failure have all been used to identify patients at high risk of sustaining coronary events undergoing non-cardiac surgery. Aortic plaque calcification on chest X-ray is associated with adverse cardiovascular outcome but the resolution of chest radiography is too limited to be useful as an effective screening tool in patients with valvular heart disease in whom intracardiac calcification is common. Recently, electron beam computed tomography of the chest has been shown to be a sensitive screening tool for detection of coronary calcification, which correlates closely with the severity of coronary artery disease, the degree of atheromatous plaque burden and the risk of cardiovascular events. Alternative diagnostic strategies have employed exercise stress testing with simultaneous myocardial perfusion scanning, but these techniques have only moderate sensitivity and specificity in valvular heart disease, and are not without risk in elderly patients with congestive heart failure.

In this issue Tribouilloy et al. report the novel use of multiplane transoesophageal echocardiographic examination of the thoracic aorta for atheromatous plaque as a potential method for recognizing significant coronary artery disease in their prospective study of 278 patients with valvular heart disease undergoing open heart surgery between 1993 and 1996 at a single institution. All patients underwent coronary arteriography, and multiplane transoesophageal echocardiography was performed within 2 days of cardiac catheterization. Of interest, only one