suggested, the likelihood of early recurrence of atrial fibrillation recedes very rapidly after the first few minutes following cardioversion as a result of the rapid early phase of reverse remodelling of atrial myocardial electrophysiology, to pace the atria rapidly during this period, such as the 300 ms intervals as in the study in this issue[3], may actually attenuate this reverse remodelling and perpetuate the profibrillatory state. This may explain the lack of incremental benefit of pacing if excessively rapid[3].

What can be concluded about pacing in early recurrence of atrial fibrillation? Is the evidence so compelling that we should consider cardioverting all patients internally in order that they can all be paced for a period after initial success? From the study in this issue, in that only 12 patients fulfilled the inclusion criteria of having repeatable early recurrence of atrial fibrillation after two successive shocks, broad generalizations for clinical practice cannot be drawn. What also cannot be established from this study is whether post cardioversion right atrial pacing in all patients would actually provoke atrial fibrillation in a proportion of patients who would not otherwise have had early recurrence of atrial fibrillation. It would not take many of the remaining 33 non-EARAF patients to have atrial fibrillation reinitiated by routine use of pacing to annihilate the benefits. The tiered strategy of atrial pacing and then intravenous sotalol for early recurrence of atrial fibrillation adopted in this study resulted in a 96% success rate of a single session of internal cardioversion. It remains to be proven whether such an impressive outcome can be achieved in larger studies.

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References

CRP: does it stand for Coronary Restenosis Prediction?

See page 1152 for the article to which this Editorial refers

CRP: does it stand for Coronary Restenosis Prediction?

Of course not! CRP stands for C-reactive protein which is one of the acute phase reactants, a nonspecific marker for inflammation. C-reactive protein activates the complement system and neutrophil adhesion. C-reactive protein also attracts complement within the coronary plaque by adhering to phosphorylcholine groups that become exposed by enzymatic degradation of tissue-deposited LDL[1]. C-reactive protein is thus thought to be involved in the development and progression of atherosclerotic lesions. Perhaps in a more consistent way than fibrinogen, serum amyloid type A or other markers of inflammation, increased plasma levels of C-reactive protein were shown to be associated with increased risk of coronary disease as well as with a worse prognosis in patients with either stable or unstable angina.

The study by Gottsauner-Wolf et al[2] was performed in a small group of stable patients undergoing elective coronary stenting. C-reactive protein levels were normal prior to the procedure but increased after stenting, irrespective of the antithrombotic/antiplatelet therapy. However, in 11 patients later shown by follow-up angiography and QCA to have developed in-stent restenosis, post-procedural C-reactive protein elevations were significantly higher and lasted longer (peak at 96 h after stenting vs at 48 h in patients without later restenosis). The authors thus concluded that a prolonged inflammatory
reaction might be causally related to the mechanisms responsible for in-stent restenosis.

This single-centre, miniature study can be criticized in many aspects, just to mention a few:

- The sample size is minute and the authors do not provide the assumptions on which it was calculated.
- Diabetes was twice as frequent in patients with restenosis and it is not known whether this risk factor was independent from the C-reactive protein levels.
- Multivariate analysis did not even identify post-procedural C-reactive protein levels as a significant predictor of restenosis, probably because of the small size of the study group (personal communication by the authors).
- The procedural technique may be seen as suboptimal by current standards (low deployment pressures, high residual diameter stenosis resulting in high restenosis rates of 28%).

Nevertheless, at a time when evidence-based medicine only relies on the results of expensive ‘Jumbo’ trials, we find it refreshing to see that important observations can still be drawn from inexpensive but careful clinical investigations. It was known that increased C-reactive protein levels pre-procedure, as commonly the case in unstable angina, are a useful marker of restenosis after angioplasty[3,4]. In the presence of elevated markers of systemic inflammation, focal injury induced by mechanical dilatation triggers hyper-responsiveness of the inflammatory system which results in increased restenosis by some unknown mechanisms. The current study emphasizes that stent implantation per se induces systemic inflammation and that restenosis is more likely when inflammation is prolonged. Prolonged inflammatory reaction may result from increased pre-existing plaque inflammation, as suggested by the higher C-reactive protein levels in patients with type C lesions. Alternatively, other potential mechanisms include metal allergy or deficiencies in anti-inflammatory cytokines such as interleukin-10[5]. A local mechanism is more likely to result in focal in-stent restenosis while a systemic mechanism is more likely to induce diffuse or proliferative in-stent restenosis[6]. Unfortunately, the authors do not provide a detailed description of the type of restenosis that they have observed. The potential clinical importance of the current observation has already been suggested by Azar et al.[7] and Gaspardone et al.[8]. Using clinical surrogates for restenosis, the event rates were shown to be higher in patients with elevated C-reactive protein levels 48 to 72 h after stent implantation.

How will this information be used for clinical decision making in the individual patient? Presumably the major advances in instrumentation and catheter technology have been achieved. Improving the results and durability of interventional procedures should now be achieved by selecting the right approach for the right person. Thus it becomes critical to be able to identify ‘a priori’ which patients/lesions are at increased risk for restenosis after stenting. To this end, the following patient-related factors have been identified:

- diabetes
- the deletion polymorphism of the ACE gene[9], and
- the systemic inflammatory status as determined from the C-reactive protein level.

When confirmed by a larger prospective study, a repeat determination of the C-reactive protein level 72 to 96 h after the procedure might be of additional value. Depending on the risk status, coronary surgery should be preferred to a percutaneous treatment in some patients. When stent implantation was nevertheless performed in patients identified as being at very high risk for restenosis, a strong antirestenosis medicine such as intracoronary radiation therapy[10] should perhaps be prescribed as a complement to the interventional approach. Another strategy would be to treat patients with persistently elevated C-reactive protein levels with steroids, as currently done in the IMPRESS trial in a randomized, placebo-controlled, double-blind design.

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Hospitalization in ICD recipients

See page 1186 for the article to which this Editorial refers

The cost of an ICD implant is still very high. Studies tackling the cost/benefit issue have so far looked at expensive devices with complicated implant techniques, such as via the abdomen[1,2]. These studies concluded that the average cost of a single life saved/year was not superior to that which could be obtained from other systems, similar to how dialysis works for renal failure. Time in hospital during follow-up is a major cost, particularly if this is a result of the device.

The published data on this topic is sparse and the paper by Korte et al.[3] in this issue on 180 consecutive patients prospectively evaluated in a relatively short (25±18 month) follow-up gives us some new and interesting data. However, before interpreting the data in this report we have to consider the following:

Population evaluated

The study by Korte et al. deals with a population whose left ventricular function is relatively good (an average EF of >40%), of a young age (57±12 years), with CAD as the main heart problem (as usual). The vast majority were implanted with a single chamber endocardial Medtronic device (139 pts), with an abdominal pocket in 41%.

This population substantially differs from the MADIT trial[4], which had a higher hospitalization rate. Those patients, however, had a lower EF, a higher mean age and in 47% an epicardial ICD system was implanted. Thus different populations, and different sites of implantation of electrodes and devices are certainly points to take into account a priori when considering follow-up costs.

Were hospitalizations strictly related to the device?

In 75% of the cases, according to the Korte paper[3] the causes of hospitalization were not related to the device per se.

Batteries lasted, on average, just over 3 years, confirming the longevity of modern devices. In 30% of cases, hospitalization was due to the type and condition of the heart disease or as a result of non-cardiac causes. Twenty-six per cent of hospitalizations were, however, secondary to appropriate shock, a primary reason for hospital referral and which frequently occurred with the first devices. We think that to-day, an appropriate shock, particularly when isolated (and not in storm) in an ambulant patient can be managed on an out of hospital basis, thus avoiding costly hospitalization.

Twenty-five per cent of hospitalizations were apparently ICD related, with 6% due to the device implants per se (infection, etc.). Such hospitalizations are now less frequent because nearly all implants are via the thorax. A thoracic implant is related to a shorter hospitalization time and is less costly because it does not need any specific surgical aid. Lead problems accounted for 8% of hospitalizations, but this number may actually be lower since leads are shorter and there are active fixed atrial leads in the most recent ICD standard implants.

Data[3] show that 12% of hospitalizations were due to atrial fibrillation or flutter with or without inappropriate shocks. While the number is remarkable, it does not exceed that of other studies[5]. This lower number may be related to the population type (younger age and better EF). Today, combination therapy devices and more sophisticated algorithms, especially those introduced with bichamber ICD devices, are trying to counteract the false detection