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Different benefits, different risks, equal cost

See page 1572 for the article to which this Editorial refers

An 88-year-old man who is undergoing coronary angioplasty for a type A lesion of the obtuse marginal branch should be considered a less ideal candidate for IIb/IIIa antiplatelet therapy than a 50-year-old man with unstable angina and a bifurcated lesion of the left anterior descending coronary artery and the diagonal branch. A severe haemorrhagic complication would be less likely to be justified if it occurred in the first patient rather than in the second.

The CAPTURE trial[1] is the first, if not the only, abciximab study in which an attempt has been made to investigate, according to the clinical characteristics of the patients and the morphological characteristics of the lesions, the presence of a gradient in the benefits obtained following intravenous antiplatelet therapy.

In the CAPTURE trial, death or non-fatal myocardial infarction occurred at 6 months in 7·5% of the patients treated with placebo and in 9·5% of the patients treated with abciximab when the troponin T levels were negative. In contrast these events occurred in 23·9% of the patients treated with placebo and in 9·5% of the patients treated with abciximab (relative risk = 0·32, 95% confidence interval, 0·14–0·62; P = 0·002) when the baseline troponin T levels were elevated[2]. These findings raise the issue of different benefits according to the baseline risk level, with minimal or no demonstrable benefit in the low risk group.

In the angiographic analysis of the CAPTURE trial presented in this issue, van den Brand et al. analyse the morphological characteristics of the culprit lesions before and following abciximab treatment[3]. Changes following active therapy are compared to the ones following placebo administration. More importantly, the authors look for the presence of a relationship between lesion characteristics or location and clinical benefit following active treatment.

In this study, 1233 patients with refractory unstable angina (Brawnew class III), were randomized to standard therapy (nitrates, heparin oral antiplatelets) and placebo vs standard therapy and abciximab bolus and infusion. Prior to enrolment in this trial, patients underwent diagnostic angiography and were found to have a culprit lesion suitable for percutaneous intervention. Treatment was started following the diagnostic angiogram and the intervention was scheduled 18–24 h later. The major end-points of this study were the occurrence of death, myocardial infarction or urgent revascularization by 30 days.

The first items the authors addressed in the angiographic analysis within this trial were the differences, if any, between the lesion and the flow appearance at baseline and following completion of the active treatment. The comparison of the lesion characteristics at baseline with the ones evaluated just prior to the intervention demonstrated a decrease in the angiographic presence of thrombus in the patients treated with abciximab compared to placebo. The presence of TIMI flow 0 or 1 decreased in the abciximab group from 9·6% to 6·7% and in the placebo group from 7·7% to 6·7%. Overall, there was no difference in improvement from TIMI 0 or 1 flow or in reaching TIMI 3 flow between abciximab and placebo-treated patients.

Interestingly, when the final TIMI flow in the culprit artery after angioplasty was less than 3 the incidence of death and myocardial infarction at 30 days was 11·5% in placebo and 4·1% in abciximab patients. This finding supports the role of abciximab.
in lessening the consequences of post-procedural slow flow.

When the lesion complexity was evaluated, the combination of B2 and C lesions was associated with an incidence of end-points of 19.1% for placebo vs 11.5% for abciximab \( (P=0.055) \). By multivariate analysis, only lesions located at a bifurcation, especially in a young patient, were associated with an increased risk of an end-point. When interpreting the data of this study it is worth emphasizing that stents were implanted in about 10% of the patients of each group.

The findings of this work are important and need appropriate emphasis. The demonstration of a selective benefit according to the lesion characteristics in a population with unstable angina is a novel conclusion. It is important for every interventionist to know when a drug or a device gives the higher benefit. Side effects and cost of aggressive antplatelet therapy are difficult to avoid. It is for this reason we should positively welcome this results which highlight a way to proceed in clinical practice.

These conclusions are different from the ones reported in an analysis of all patients included in the EPIC\[4\] and EPILOG\[5\] looking for a differential effect of abciximab to reduce complications according to lesion morphology\[6\]. The conclusion of this combined analysis was that the usage of abciximab was associated with a significant reduction of complications compared to placebo in a variety of lesions, with the only exception, degenerated saphenous vein grafts and chronic total occlusions. Differences in patient populations, interventional strategies, stent usage and the small number of observations in some subgroups of lesions (type II error) could explain these differences. Further studies are necessary to finalize recommendations in this particular field.

Regarding the conservative usage of stenting in the CAPTURE, EPIC and EPILOG trials, this fact could explain the low angiographic success rate (88% in the CAPTURE trial) reported in the placebo group. A more liberal stent usage should not be viewed as a tool to lower the incidence of end-points as selected in this trial. As a matter of fact, most of the complications such as non-Q wave myocardial infarction, frequently occur because of distal embolization of microparticles or small branch transient or permanent closure. A more liberal usage of stents could have lowered complications in some types of lesions but not in others, such as bifurcations or areas where a number of small branches originate. In our experience, coronary stenting in complex bifurcations has been associated with an incidence of thrombosis up to 5%\[7\]. A recent study reported a procedural related 8% incidence of non-Q wave myocardial infarction when complex stenting is applied to bifurcations\[8\]. It is for these reasons that we should not assume that liberal stent usage could compensate for a restriction in IIb/IIIa usage.

A well known large randomized study demonstrated that unrestricted stent usage with abciximab is superior to stenting in lowering the incidence of major cardiac events at 30 days\[9\]. This important finding should not be viewed as a reason not to ask ‘is the benefit worth the risk and cost?’

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References