Editorial

Drug-Eluting Stents: Where Are We Today?

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Nowadays, there continues to be great concern among cardiologists with regard to the use of drug-eluting stents (DES), to the extent that their use in angioplasty procedures ranges widely, from 90% to 10%.[1] The solution to the problem may be found in two basic unanswered questions. The first is how much more susceptible to thrombosis DES are after the first year following their implantation, compared with bare metal stents (BMS); while the second concerns how long the patient with a DES needs to be protected by a combination of antiplatelet drugs and clopidogrel. The whole matter is made even more complex by the fact that the incidence of death, myocardial infarction, and stent thrombosis does not appear to be lower in patients with BMS compared to DES, according to a meta-analysis of 22 studies, whose disadvantage, however, was a relatively short follow-up period (2.9 years).[2]

The development and introduction to clinical practice of percutaneous coronary angioplasty brought a revolution in the treatment of coronary artery disease, and mainly of acute coronary syndromes, at which the method was principally directed. However, the widely known and accepted COURAGE trial showed that patients with chronic coronary artery disease, even three-vessel disease, did not benefit especially in terms of complications, including myocardial infarction and sudden death, if at the same time as optimal medical therapy they also underwent angioplasty.[3] Restenosis was the main practical complication of angioplasty, and was initially managed partly with the introduction of BMS, and later more effectively with the emergence of DES. With the introduction of DES into clinical practice, many people maintained that the problem of coronary reperfusion had been solved for ever. Quickly, however, the general euphoria was followed, as often happens in medicine, by scepticism, as it became apparent that stent implantation was more of a modification of the disease rather than a definitive treatment. More specifically, the antimitotic drugs eluted by DES effectively prevent restenosis, but at the cost of a significant delay in endothelialisation of the stent and in consequence an extended risk of stent thrombosis. This requires the patient to take dual antiplatelet medication: aspirin and clopidogrel. And while the danger of thrombosis for BMS, and consequently the need for dual medication, lasts for a few weeks, the duration in the case of DES still remains undetermined.

Stent thrombosis is a severe and possibly fatal complication, especially when the stent has been implanted in a large vessel (e.g. proximal anterior descending branch), as it leads to an extensive myocardial infarction. The observation that there is a rise in acute coronary syndromes and deaths from stent thrombosis in DES following the early cessation of dual an-

tiplatelet treatment within the first six months after implantation, caused considerable commotion in the international scientific community and led to a "war" between fanatical supporters and fanatical opponents of DES.[4]

After the outbreak of the "stent wars", studies and meta-analyses provided evidence that DES were safe, even though there was an increased risk of death from myocardial infarction. The possible increase in the incidence of myocardial infarction could be counterbalanced by a corresponding decrease, because of the reduction in restenosis and the need for revascularisation associated with DES.[1] On the other hand, the follow-up duration in many of the above studies may not have been sufficiently long to document the safety of DES.[1] In consequence, the question whether DES are associated with an increased risk of very late (>1 year after implantation) thrombosis compared with BMS remains effectively unanswered. The matter is complicated still further by a series of other factors, such as the fact that there are probably differences between different types of DES as regards the risk of thrombosis, while the latter is also influenced by the special characteristics of each coronary lesion as well as by the general clinical context in which the implantation is performed.[1]

The second question that still remains unanswered, as mentioned above, has to do with the duration of dual antiplatelet treatment after DES implantation. The haemorrhagic tendency resulting from dual antiplatelet therapy can be a significant problem when the patient needs to undergo an emergency surgical procedure, as in the case of an accident. However, cessation of dual antiplatelet medication in advance of a scheduled procedure has led in some cases to extensive acute infarctions with subsequent development of heart failure or even death as the result of stent thrombosis. On the other hand, it is likely that the observed benefit from the prolongation of dual antiplatelet therapy may not be due to the prevention of very late DES thrombosis, but to a general reduction in the risk of thrombosis anywhere else in the circulation.[1]

The prevailing practice today is the administration of dual antiplatelet therapy with aspirin and clopidogrel for at least one year after DES implantation and from that point on it is continued "until further notice". Data published in the New England Journal of Medicine involving 2701 patients with DES showed that prolongation of the dual antiplatelet medication with aspirin and clopidogrel beyond one year from implantation was not superior to monotherapy with aspirin as regards the incidence of acute myocardial infarction and cardiac deaths at two years.[5] However, these results are from an intermediate analysis of two studies (REAL-LATE and ZEST-LATE) that did not have the expected number of events up to the point of analysis.[1]

Apart from the above study, there are other similar ones in progress that may answer the question concerning the safe time of cessation for dual antiplatelet therapy. Until then – or perhaps even for longer, until the problem in question is made moot by new technological advances in the field of coronary artery disease – a series of measures allows the minimisation of the risk that arises from percutaneous coronary angioplasty. First of all, we should avoid the excessive use of angioplasty in cases without a clear indication, and especially in chronic stable coronary artery disease and in non-culprit lesions in acute coronary syndromes. Secondly, the type of stent should be chosen carefully, based on a co-evaluation by the treating physician of the patient's overall medical history. Thus, DES should be avoided in patients who are to undergo a scheduled surgical procedure in the near future, when interruption of the dual antiplatelet therapy would be required, as well as in patients who are already taking warfarin or who are known to be unreliable in their compliance with medication. Finally, it is essential that the patient should be carefully informed and, wherever possible, should be an active participant in decisions about treatment.

As regards Greece, unfortunately there are no data concerning either the number of coronary stents or, of course, their complications; nor do we know to what extent the relevant guidelines are followed.

From the discussion above, and the rapid technological developments in the field of medicine, we can see that Hippocrates' maxim is more pertinent than ever: "... to help, or at least, to do no harm." Restraining premature enthusiasm on the introduction of a new therapeutic development, careful and critical evaluation of research and clinical data, and compliance with the indications for each procedure and the relevant guidelines are essential measures for ensuring safety in clinical practice.

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