

Who's going to take the left mains?

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The left main coronary artery is a special place in the system of coronary arteries in humans and the blood supply to a huge mass of the myocardium depends on its normal functioning. Although the prevalence of left main disease is relatively low, ranging from several to a dozen or so percent of patients with coronary artery disease, the prognosis in this form of disease is grave. If left main disease manifests in the form of acute coronary syndrome, the patient's life is in danger. How then should we manage this form of coronary artery disease with such special anatomical localisation?

The American College of Cardiology and the American Heart Association guidelines recommend cardiac surgery (coronary artery bypass grafting) in patients with significant left main coronary artery stenosis. The recommendation falls within the class I recommendation and the level of evidence A and applies to patients with both stable and unstable angina and to patients with non-ST-elevation myocardial infarction [1].

The European Society of Cardiology guidelines published in 2005 placed surgically unprotected left main coronary artery angioplasty in stable angina within the class IIB recommendation and the level of evidence C with the comment that this procedure is performed in the absence of other revascularisation options [2]. Can angioplasty for left main disease be an alternative to cardiac surgery and replace the latter in the future? The answer to this question is quite complex. Early experiences with bal-

loon angioplasty in surgically unprotected left main were rather discouraging [3, 4]. In the light of unequivocally good outcomes of surgical management, the periprocedural mortality of 9% and the 3-year mortality of 64% in the case of elective procedures were unacceptable. It was not until stenting was introduced that the outcomes improved. In fact, the introduction of stenting made it possible for these procedures to be performed, minimising the risk of such unforeseeable disastrous complications as vessel dissection or acute occlusion. Unfortunately, though, even the very good immediate outcomes of left main stenting do not translate into good long-term outcomes. The reason is restenosis, the notorious and ever-present complication of angioplasty, otherwise mild and gradually developing over a period of several months, giving enough time for a planned diagnostic investigation and the initiation of appropriate treatment. In the case of the left main coronary artery, however, restenosis is typified by a different dynamics and clinical characteristics, and very often presents as sudden cardiac death [5, 6]. No wonder then that left main angioplasty has long been the no-go area for interventional cardiologists.

The uniqueness of percutaneous interventions within the left main boils down to the differences in the strategy depending on the localisation of the stenosis (ostium, distal bifurcation, middle segment) and the clinical setting in which we plan the procedure or are forced to perform it: stable coronary artery disease, co-morbidities, myocardial infarction, shock. Paradoxically, left main angioplasty usually takes place (or until recently has taken place) in the most difficult clinical situations: acute stenosis during coronary arteriography, myocardial infarction with shock. And although interventions in the left main coronary artery are among the most difficult procedures and require the highest skills and broadest experience of the team, this management option in life-threatening situations does not raise any concerns or ethical objections, even if the patient could theoretically be operated on right on

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the spot. In these situations, time, counted in minutes, is of essence and immediate action is mandatory — there is not even time for transferring the patient to the cardiac surgery ward. Interestingly, it is in this group of patients, patients with the worst prognosis (myocardial infarction complicated by shock and the left main occlusion), outcomes of emergency angioplasty are the most encouraging if we compare them with historical controls. One may question the value of anecdotal data or data from limited retrospective reports or small observational studies [7–10]. Unfortunately there have been and there probably will be no randomised prospective studies in this group of patients that would provide any evidence of superiority of surgical over interventional strategies (or *vice versa*). These patients, patients in cardiogenic shock, with left main coronary artery occlusion, should for obvious reasons receive invasive treatment: angioplasty and stenting. Such doubts never arise when patients in shock present to the more and more numerous in Poland centres without cardiac surgery facilities. Haemodynamically stable patients with myocardial infarction (with or without ST elevation) and without shock, however, are a completely different story, as surgical intervention here may be a plausible alternative. Such patients, right after coronary arteriography revealing left main stenosis, are seen by our on-call cardiac surgeon while still at the haemodynamics suite with the view to selecting the best management option. At the Silesian Centre of Heart Disease in Zabrze, Poland, in the case of patients with acute coronary syndrome in shock we follow, as a principle, the non-surgical percutaneous approach. We always strive to achieve complete revascularisation in one stage. Exceptions include patients with left main coronary artery disease and multivessel coronary artery disease with good peripheries of the vessels and, in the case of ST-elevation myocardial infarction, a short history of anginal pain (up to 4 h). In other cases we go for left main angioplasty and stenting. This approach seems reasonable and has been followed in many centres. Is it in line with the current guidelines? Let us remember that strong and unequivocal guidelines are created on the basis of randomised trials appropriately large and providing answers to precisely posed questions. Such trials are not, however, available. This interesting and difficult issue has been touched upon in this issue by our colleagues from Bydgoszcz, J. Wiśniewska-Szmyt, J. Kubica, A. Sukienik et al., in their article entitled “One-year outcomes of left main coronary artery stenting in patients with cardiogenic shock” [11]. In the study,

they evaluated the one-year outcomes of 71 patients with left main disease managed in the emergency setting. Restenosis and associated revascularisation occurred in 29% and 16% of patients with and without cardiogenic shock, respectively. While this difference was not significant, patients with cardiogenic shock had significantly lower minimum lumen diameters before the procedure. An important finding was the recognition of final minimum lumen diameter as an independent predictor of death among patients with left main stenosis and shock. We have analysed the data from the pilot stage of the PL-ACS Register covering the Silesian Province, where 23 patients with ST-elevation myocardial infarction complicated by cardiogenic shock were managed over a period of 12 months, in whom the left main coronary artery was the infarct artery. Only one patient was managed surgically (CABG) and the remaining ones underwent emergency coronary angioplasty. The in-hospital mortality in the angioplasty group was 59% and the cumulative 6-month mortality was 65%. The patient who underwent CABG survived.

And what about elective procedures? There is an increasing number of reports on good immediate and late outcomes of left main coronary artery stenting in groups of patients at various preoperative risks. In 1998 Park et al. [12] published the results of angioplasty and stenting of unprotected left main coronary artery in 42 consecutive patients with good left ventricular function. A success rate of 100% was observed, and at 6 months of follow-up restenosis had occurred in 22% of patients. Only one patient died directly after elective CABG due to restenosis. The same authors published data from a four-centre study of a similar group of 270 consecutive patients. Restenosis occurred in 21.1% of patients with a success rate of 98.9%. In 3 patients, the procedure was complicated by a Q-wave infarction. No deaths occurred in the in-hospital period. Over the follow-up of 32.3 ± 18.5 months, 20 patients died (12 of which were non-cardiac deaths) and 5 suffered from non-fatal myocardial infarction. An independent predictor of cardiac events was the left main diameter and the presence of disease in the other coronary vessels [13]. Distal stenosis of the left main coronary artery involving the bifurcation and the ostium of LAD and CX poses a special challenge to the operator. Improved techniques for bifurcation angioplasty have allowed invasive cardiologists to provide successful treatment to patients also in this location [14]. One should, however, stress out that this sort of procedures can only be performed in patients with good left ventricular

function. Patients with reduced ejection fraction below 40% and distal left main coronary artery stenosis and affected bifurcation are candidates for cardiac surgery. Although adjunctive techniques, such as directional arterectomy or rotablation, are occasionally used with good effect in selected groups of patients and types of lesions, they failed to bring a breakthrough and significant improvement of late outcomes [15, 16]. Much better stents and balloon catheters, including cutting balloons, and the selection of appropriate guiding catheters most definitely facilitate the procedure, shortening its duration and improving its safety. While bifurcation stenting methods, such as T stenting, V stenting or the Coulotte technique, the less frequently used "crush" technique and the "kissing balloon" technique, provide good immediate results, they do not always provide equally good late outcomes. Unfortunately, a good stent for bifurcation (the most common lesion where restenosis occurs) is still unavailable. According to De Lezo et al. [17], predictors of restenosis in the left main include localisation of the lesion in the bifurcation, the length of the stent and a small reference diameter of < 3.6 mm. In his analysis of 77 patients, the 9-month restenosis rate was 34%. Some authors emphasise the usefulness of intravascular ultrasound (IVUS) performed during the procedure. Although in Park's analysis [18] the use of echo did not translate into a significantly lower incidence of restenoses (18.6% vs. 19%), one cannot ignore the obvious benefits in the form of information about the left main coronary artery size, the extent and nature of the atherosclerotic plaque or even the possibility to decide the significance of a borderline stenosis. Additionally, IVUS allows to control the immediate effect and to optimise it (appropriate post-dilatation of the stent).

Drug eluting stents (DES), which inhibit restenosis, have given us greater hope for such long-desired improvement of remote outcomes of interventional procedures in the left main coronary artery, especially within the bifurcation, and in patients with elevated baseline risk of restenosis (diabetes). Some interesting data are provided by such registers as RESEARCH and T-SEARCH. Valgimili performed an analysis of the outcomes of bifurcation stenting using DES. It was also interesting to find an answer to the question if better results were seen with the stenting of both arteries branching off the left main or just one. It turned out that the stenting of two vessels (complete reconstruction of the bifurcation) is not superior to the technically easier method of stenting one vessel. The MACE

rate during the follow-up in both groups was similar: 31% vs. 28% (HR 0.96, 95% CI 0.46–1.49, $p = 0.92$) [19]. Similar results were obtained by the Korean group using complex stenting methods for the distal left main coronary artery [20]. The comparison of late effects of left main coronary artery stenting using DES and bare metal stents (BMS) was, as expected, in favour of the former, at least in terms of restenosis prevention [21–23]. Sirolimus, and paclitaxel, eluting stents demonstrate similar efficacy. In one of the comparative studies, the restenosis rate was 8% for rapamycin-eluting stents and 9% for paclitaxel-eluting stents [24]. However, DES have not completely eliminated left main coronary artery restenosis and, as expected, similarly to the conventional stents, the main predictor of restenosis was the disease of the distal left main coronary artery [25]. The recently published study by the Kraków group compared immediate and remote outcomes in patients with low preoperative risk with left main disease [26]. The selection of stents, DES or BMS, was based on the reference diameter of the vessel. Patients with left main coronary artery diameters of > 3.5 mm (36 patients) were treated with BMS and patients with the diameter of 3.5 mm or less were treated with paclitaxel, or sirolimus, eluting stents (15 and 13 patients, respectively). The in-hospital results were very good (one non-fatal myocardial infarction), and no deaths or myocardial infarctions were recorded in the long-term follow-up. Target lesion revascularisation occurred in the BMS group and the difference was significant. Interesting findings have been reported in a recent serial angiographic analysis at 3 and 9 months following implantation of sirolimus-eluting stents in a group of 50 patients (distal location in 94% of patients) [27]. Restenosis was a frequent complication (42%), although it was usually asymptomatic, did not develop in the left main proper but in the ostium of one of the branches (82%) and was focal (85%). It was more frequent in the circumflex artery. Predictors of restenosis were the minimal luminal diameter achieved following the procedure and the maximum pressure of the balloon. The data which are now being collected allow a prediction that the use of DES in left main disease will reduce the need for re-interventions due to restenosis. Will it improve the prognosis as to the patient survival? The answer is unclear, as no large randomised trials are available that would address the numerous important issues surrounding rational revascularisation management of these patients. The ongoing SYNTAX trial will be an important voice in the debate on if and to what extent cardiac surgery will

give ground to interventional cardiology in the management of left main disease and multivessel coronary artery disease [28, 29]. In this trial, patients with multivessel coronary artery disease and left main coronary artery disease are randomised to CABG or PCI using paclitaxel-eluting stents. Patients ineligible for either of the randomisation group are managed with one of the two methods and entered into a prospective registry. Results of this important trial will definitely allow us to formulate new recommendations on the management strategy in patients with left main disease. I should also mention here the Polish multicentre trial LE MANS: A Case Control Study which included 289 consecutive patients, 112 of whom were eligible for both PCI and CABG. The operative risk in most of these patients, according to the Euroscore, was low. The PCI group demonstrated better in-hospital results (fewer adverse events, such as myocardial infarction, heart failure, stroke, serious haemorrhagic complications, repeat revascularisation, infections) while the CABG group developed fewer events in the long-term follow-up. There was 1 death in the PCI group and 3 deaths in the CABG group, but the difference was not statistically significant [30].

Has the time come to use coronary angioplasty and stent implantation (mainly drug-eluting stents) in selected groups of patients, namely those at low preoperative risk with preserved left ventricular function? According to the data that are being collected, some of which have been presented in this editorial, these procedures are increasingly safe and easy to perform, and the good immediate results are encouraging to the operators. These procedures are obviously reserved for centres and teams of high expertise and, equally important, with a full range of disposables, such as stents and balloon catheters, and other adjunctive equipment (IVUS). While the outcomes of surgery are very good and the benefit is sustained for many years, the results of left main stenting, especially with the use of DES, have not been followed up for equally long time in large samples. We should also bear it in mind that drug-eluting stents do not solve all the problems encountered during invasive treatment and some disadvantages of DES may appear very late (such as thrombosis due to incomplete endothelialisation of the stent). This type of remote complications, which can occur several years after stenting, may have equally disastrous consequences, such as acute thrombosis, which is occasionally observed and managed by invasive cardiologists following recent stenting. Let us also remember that restenosis in the left main

coronary artery, despite the introduction of DES, has not disappeared, and in this specific location this complication is extremely malignant. So the answer to the question whether the time has come for widespread left main stenting is this: the time has come to conduct large randomised trials of the SYNTAX and LE MANS type, because invasive cardiologists have already learned how to safely implant stents (preferably DES) into the left main coronary artery and achieve very good immediate results even in the most anatomically complicated lesions.

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