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Original article

Very Long-term Outcomes Following Drug-eluting Stent Implantation for Unprotected Left Main Coronary Artery Stenosis: A Single Center Experience

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ABSTRACT

Introduction and objectives: Encouraging results at long-term follow-up have been reported from non-randomized registries and randomized trials following percutaneous coronary intervention with drug-eluting stent implantation for unprotected left main stenosis. However, information on very long-term (>5-year) outcomes is limited. The aim of this study was to assess the very long-term outcomes (6-years) following drug-eluting stent implantation for left main disease.

Methods: All consecutive patients with unprotected left main stenosis electively treated with drug-eluting stent implantation, between March 2002 and May 2005, were analyzed according to the location of the left main lesion (distal bifurcation vs ostial/body).

Results: The study included 149 patients: 113 with distal bifurcation and 36 with ostial/body lesion. Triple-vessel disease was significantly higher in the distal than in the ostial/body group (52.2% vs 33.2%, *P*=.05). At 6-years of follow-up, the cumulative major adverse cardiovascular event rate was 41.6% (45.1% distal vs 30.6% ostial/body, *P*=0.1), including 18.8% any death (22.1% distal vs 8.3% ostial/body, *P*=.08), 3.4% myocardial infarction (3.5% distal vs 2.8% ostial/body, *P*=1), and 15.4% target lesion revascularization (18.6% distal vs 5.6% ostial/body, *P*=.06). The composite of cardiac death and myocardial infarction was 10.7% (13.3% distal vs 2.8% ostial/body, *P*=.1) while the definite/probable stent thrombosis rate was 1.4% (all in the distal group).

Conclusions: At 6-year clinical follow-up, percutaneous coronary intervention with drug-eluting stent implantation for unprotected left main disease was associated with acceptable rates of cardiac death, myocardial infarction and stent thrombosis. Favorable long-term outcomes in ostial/body lesions compared to distal bifurcation lesions were confirmed at long-term clinical follow-up.

Resultados a muy largo plazo tras la implantación de *stents* liberadores de fármacos en la estenosis de arteria coronaria principal izquierda no protegida: experiencia de un centro

Palabras clave:
Enfermedad coronaria
Angioplastia coronaria
Stent

RESUMEN

Introducción y objetivos: Se han descrito resultados alentadores en el seguimiento a largo plazo de registros no aleatorizados y de ensayos aleatorizados tras la intervención coronaria percutánea con implantación de *stents* liberadores de fármacos para el tratamiento de la estenosis de la coronaria principal izquierda no protegida. Sin embargo, la información sobre los resultados a muy largo plazo (> 5 años) es limitada. El objetivo de este estudio es determinar los resultados a muy largo plazo (6 años) tras la implantación de *stents* liberadores de fármacos en la enfermedad coronaria de la principal izquierda.

Métodos: Se analizaron los resultados de todos los pacientes consecutivos con estenosis de la coronaria principal izquierda no protegida que se trató de manera electiva con la implantación de *stents* liberadores de fármacos entre marzo de 2002 y mayo de 2005, según la localización de la lesión de la coronaria principal izquierda (bifurcación distal frente a *ostium*/cuerpo).

Resultados: Se incluyó en el estudio a 149 pacientes: 113 con una lesión de la bifurcación distal y 36 con una lesión en *ostium*/cuerpo. La presencia de enfermedad de tres vasos fue significativamente mayor en el grupo de lesión distal que en el grupo de lesión en *ostium*/cuerpo (el 52,2 frente al 33,2%; p = 0,05). A los 6 años de seguimiento, la tasa acumulada de eventos cardiacos adversos mayores fue del 41,6% (el 45,1 distal frente al 30,6% en *ostium*/cuerpo; p = 0,1), incluidos el 18,8% de muerte de cualquier tipo (el 22,1 distal frente al 8,3% en *ostium*/cuerpo; p = 0,08), el 3,4% de infarto de miocardio (el 3,5 distal

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frente al 2,8% en *ostium*/cuerpo; p = 1) y el 15,4% de revascularización de lesión diana (el 18,6 distal frente al 5,6% en *ostium*/cuerpo; p = 0,06). La variable combinada de muerte cardiaca e infarto de miocardio se produjo en el 10,7% de los casos (el 13,3 distal frente al 2,8% en *ostium*/cuerpo; p = 0,1), mientras que la tasa de trombosis definitiva/probable del *stent* fue del 1,4% (todos en el grupo distal).

Conclusiones: En un seguimiento clínico de 6 años, la intervención coronaria percutánea con implantación de *stents* liberadores de fármacos para lesiones de la coronaria principal izquierda no protegida se asoció a unas tasas aceptables de muerte cardiaca, infarto de miocardio y trombosis de *stent*. Se confirmaron los resultados a largo plazo favorables en las lesiones de *ostium*/cuerpo en comparación con las lesiones de la bifurcación distal en el seguimiento clínico a largo plazo.

Abbreviations

CABG: coronary artery bypass grafting
DES: drug-eluting stent
PCI: percutaneous coronary intervention
PES: paclitaxel-eluting stent
SES: sirolimus-eluting stent
ULMCA: unprotected left main coronary artery

INTRODUCTION

Coronary artery bypass grafting (CABG) is the standard of care for patients with critical unprotected left main coronary artery (ULMCA) stenosis[1] since it was found to improve late survival vs medical therapy.[2] Recent advances in technology (such as drug-eluting stent [DES] introduction and intravascular ultrasound [IVUS] use), operator experience, and antiplatelet therapy have led to a wide expansion of the role of percutaneous coronary intervention (PCI) in selected patients with ULMCA lesions and low-to-moderate SYNTAX (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) scores.[3] According to current guidelines, the treatment of ULMCA disease with PCI has a class IIb indication.[1] Registry data on PCI with DES implantation in ULMCA lesions have demonstrated that this approach is safe and effective at medium-term clinical follow-up.[4–8] Although recent reports showed favorable outcomes at medium- and long-term clinical follow-up,[9,10] few studies have evaluated the very long term clinical outcomes (>5 years) of this treatment strategy.[11,12] The aim of the present study was to report the 6-year clinical outcomes following treatment of ULMCA stenoses with PCI and DES implantation.

METHODS

A retrospective cohort analysis was performed of all consecutive patients with ULMCA stenosis treated with either a sirolimus-eluting (SES) (Cypher, Cordis, Johnson and Johnson, Miami Lake, Florida, United States) or paclitaxel-eluting stent (PES) (Boston Scientific, Natick, Massachussets, United States) between March 2002 and May 2005 in a tertiary referral center. The decision to perform PCI rather than CABG was taken in the presence of suitable anatomy and lesion characteristics for stenting, in patients without contraindications to at least 6 months of dual antiplatelet therapy, and 1 of the following conditions: *a)* high surgical risk defined as EuroSCORE (European System for Cardiac Operative Risk Evaluation)≥6; *b)* patient refusal to undergo CABG, and *c)* referring physician preference. All patients were carefully informed about the alternative treatment options and PCI-related risks before being asked to give written informed consent to undergo the procedure.

Intra-aortic balloon pump (IABP) and IVUS-guidance left main PCI were decided at the operator's discretion.

In particular, preprocedural factors that were considered to merit prophylactic use of IABP for elective ULMCA PCI included: *a)* systolic blood pressure≤100 mmHg; *b)* severe left ventricular dysfunction (i.e. ejection fraction [EF]≤35%); *c)* recent presentation for decompensated heart failure; *d)* dominant left circumflex or occluded dominant right coronary artery, and *e)* performance of atherectomy. Clinical follow-up was performed by telephone contact or an office visit at 1, 6, and 12 months and annually after the first year. Patients were analyzed according to the location of the ULMCA lesion: ostial/body vs distal bifurcation.

Angiographic follow-up was scheduled between 4 and 9 months or earlier if non-invasive evaluation or clinical presentation suggested the presence of ischemia. All adverse events were verified by reviewing the medical records of the patients followed at our institution or by contacting the patients' physicians and reviewing the hospital records of patients followed elsewhere.

All patients were pre-treated with acetylsalicylic acid (100 mg/day) and a thienopyridine (ticlopidine 250 mg twice daily or clopidogrel 75 mg/day) was started at least 5 days before the procedure. At discharge all patients were prescribed life-long acetylsalicylic acid and a thienopyridine for at least 6-12 months irrespective of PES or SES implantation. Dual antiplatelet therapy was prolonged indefinitely in case of ULMCA plus multivessel DES implantation. Detailed information on adherence as well as the reasons for and date of dual antiplatelet therapy discontinuation was obtained in all patients.

Definitions

The following major adverse cardiovascular events (MACE) were analyzed cumulatively at the 6-year clinical follow-up: any death, myocardial infarction (MI) and any revascularization. Deaths were classified as either cardiac or non-cardiac. Clinical end-points (death, cardiac death, target lesion revascularization [TLR], target vessel revascularization, peri-procedural MI and stent thrombosis [ST]) were defined on the basis of the Academic Research Consortium definitions.[13]

The EuroSCORE, which is based on patient-, cardiac- and operation-related factors, was used to stratify the risk of death at 30 days. According to the scoring system, patients were stratified as high risk in the presence of a EuroSCORE≥6. The SYNTAX score was also calculated from pre-intervention angiograms to reflect an anatomical assessment with higher scores indicating more