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EDITORIAL COMMENT

Sirolimus-eluting stents: A small piece of the story of percutaneous coronary intervention

Stent revestido de sirolimo – uma pequena peça na história da ICP

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Since the first percutaneous coronary intervention (PCI) was performed by Andreas Gruntzig in 1977,[1] the procedure has evolved greatly to become the dominant revascularization technique for obstructive coronary artery disease.

The use of stents, introduced in 1986, improved the success and safety of balloon angioplasty and the addition of an antiproliferative agent to the metal struts (drug-eluting stents or DES), via a polymer coating, significantly reduced restenosis.[2] The downside of their antiproliferative effect was the increased risk of late stent thrombosis associated with impaired re-endothelization.[3]

First-generation DES using sirolimus or paclitaxel were first introduced in 2002. Sirolimus, also known as rapamycin, is an immunosuppressive agent that arrests the cell cycle in the G1/S phase and inhibits proliferation and migration of vascular smooth muscle cells (VSMCs).[3] Paclitaxel is an antineoplastic agent that inhibits microtubules and hence proliferation and migration of VSMCs. The increased risk of stent thrombosis reported in several studies for these DES, even mitigated by improvements in procedure-related factors (stent malapposition and/or underexpansion) and enhanced stent design, led to the development of second-generation DES, which were covered with less potent antiproliferative agents (everolimus, zotarolimus and biolimus) in conjunction with new platforms and polymers.[3] Newer-generation DES showed lower rates of stent thrombosis and major adverse clinical events and became the preferred type for PCI.[4]

Ricardo Seabra Gomes was the pioneer of PCI in Portugal, performing the first balloon angioplasty in May 1984,[5] the first stent implantation in June 1990 and the first DES implantation – of sirolimus-eluting stents (SES) – in April 2002.

The quest for PCI with no residual metal footprint led to the development of bioresorbable scaffolds, but clinical assessment demonstrated that they carried an unacceptable increased risk of device thrombosis.[6] On the other hand, the success of DES led to the development of drug-eluting balloons, which have become a valid option in several clinical scenarios.[7]

In this issue of the *Journal*, Vale et al. report 10-year survival of 600 patients undergoing PCI with first-generation SES compared to 594 patients with bare-metal stents (BMS) in a single tertiary center.[8] The value of this study is based on its long-term follow-up, 10 years for the entire cohort. Regulatory approval of novel devices usually depends on demonstration of efficacy and safety at one year, but longer-term follow-up is required to assess the extended risk/benefit profile.[9] Thrombosis, strut fracture, neoatherosclerosis, and even increased mortality have in fact been described long after DES implantation.[9,10] In the study by Vale et al., 10-year all-cause death was lower in patients who underwent SES implantation compared with BMS (20.1% vs. 25.4%), corresponding to a significant adjusted relative risk reduction of 26%.[8] Survival benefit associated with SES implantation was already evident at five-year follow-up and was mainly observed in patients

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with acute coronary syndromes, left ventricular systolic dysfunction and age 65 years or more. The mechanisms underlying this benefit could not be ascertained because atherothrombotic and revascularization events were not collected, nor was cardiovascular death. Notwithstanding, the study outcome of all-cause death is not associated with any definition bias and allows the assessment of unexpected non-cardiovascular effects. Furthermore, all-cause death incorporates both effectiveness and safety, acting as a net clinical benefit outcome.

Another important feature of this study is its real-world nature. The post-marketing effectiveness and safety of drugs and devices need to be evaluated in unselected patients in daily clinical practice. The study population fits the attributes of a real-world population characterized by high prevalences of older age, comorbidities and advanced coronary disease.[11] Most of these baseline characteristics were independent predictors of long-term survival.

Finally, although first-generation SES are no longer used in clinical practice, no safety concern was raised concerning these devices after 10-year implantation, unlike the safety concerns raised about another antiproliferative agent used in first-generation DES.[10]

Conflicts of interest

The author has no conflicts of interest to declare.

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