Editorial

Surgery after drug-eluting stent implantation: it's not all doom and gloom!

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Comment on: Egholm G, Kristensen SD, Thim T, *et al*. Risk Associated With Surgery Within 12 Months After Coronary Drug-Eluting Stent Implantation. J Am Coll Cardiol 2016;68:2622-32.

Abstract: Up to 15–23% of the patients with percutaneous coronary intervention (PCI) and drug-eluting stent (DES) implantation need a surgical procedure <12 months from PCI. Perioperative risk stratification in these patients is challenging and should take into account many individual clinical and anatomic variables, along with the intrinsic surgical risk for ischemic and bleeding events. The presence of DES has always been considered as a harbinger of doom. In fact, DES are associated with delayed vascular healing and require longer dual antiplatelet treatment. Perioperative pharmacologic management in those patients is intricate because of the tradeoff between the increased thrombotic risk associated with premature DAPT discontinuation and the increased risk of bleeding in the presence of antithrombotics. Whilst most of the studies agree upon the inverse relationship between time from stenting to surgery and cardiac risk, more recent data challenge the previous belief that surgery should be deferred at least 12 months after DES implantation and this safety window could be shortened to <6 months or even less with new-generation DES. The aim of this brief commentary is to critically review available data about cardiac risk associated with surgery in patients with coronary drug-eluting stents.

Keywords: Surgery; drug-eluting stent; antiplatelet therapy; safety

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Risk stratification before surgical procedures in patients with coronary artery disease is always challenging (1). The intrinsic risk of the procedure must be weighted along with the individual risk of the patient which, in turns, depends on several variables including: comorbidity, symptoms, presence and amount of ischemia, atherosclerotic burden, previous revascularization procedures, left ventricular function, valvular heart disease, ongoing medications. In this context, a history of previous percutaneous coronary intervention (PCI) with stent implantation has commonly been regarded as a potential source of catastrophic complications, especially when surgery is needed early after PCI (2). The advent of drug-eluting stents (DES) has further reinforced this aura of danger, because of the longer time needed for re-endothelialization and vascular healing, extending the window of stent thrombotic risk well beyond the first month after stent implantation. Accordingly, previous guidelines provided a general recommendation that elective surgery be delayed until 30 to 45 days after bare metal stent (BMS) implantation and 1 year after DES (3,4). Recently, new evidence has accrued suggesting that the safety window for surgery after implant of new-generation DES could be safely shortened to <6 months (5,6). The aim of this brief commentary is to critically review available data about cardiac risk associated with surgery in patients with coronary drug-eluting stents.

Magnitude of the clinical problem

The incidence of non cardiac surgery within 1 year after PCI was commonly reported to be around 5% (4,7-9), and 25% at 5 years. Recent data including more comprehensive identification of surgical procedures, however, changed these figures to around 15–23% within the first year (5,6,10), and up to 40% within 5 years (6). Considering that DES should be preferred over BMS to accomplish coronary revascularization (4), in clinical practice risk stratification must take into account that most of those patients do have a DES in the coronary tree (5).

Why is surgery dangerous in patients with coronary stents

After stenting, a course of dual antiplatelet therapy (DAPT) is required to prevent stent thrombosis (ST) while vascular healing and stent strut endothelialization are ongoing. In general, with bare-metal stents (BMS) re-endothelialization occurs within 4 weeks after PCI. Drug-eluting stents have been developed to reduce the risk of in-stent restenosis, through the pharmacologic interference with the cell cycle and the consequent mitigation of the proliferative signal to the smooth muscle cells of the media. Implicit in this mechanism of action there is, as side-effect, the reduction of vascular repair and re-endothelialization. Because of delayed vessel healing, first-generation DES were hampered by an increased risk of ST, especially late (>30 days) and very late (>12 months), and required prolonged DAPT.

Surgical procedures are associated with a hypercoagulable state, blood loss and need for transfusions, fluid shifts, haemodynamic derangements, inflammation and a stress response that can all contribute to increase thrombotic risk. On the other hand, hemorrhagic risk associated with the operation often requires premature discontinuation of antiplatelet agents, a strong predictor of stent thrombosis and ischemic events (11,12), thus creating a dangerous interplay of risk factors.

New-generation DES and DAPT duration

With first-generation DES the minimally required DAPT duration was at least 12 months, irrespective of clinical presentation. Newer-generation DES have been designed to overcome most of the limitations of first-generation DES. Overall, new-DES have been shown to be safer than first-generation DES, with a lower risk of ST both in the early-phase and in the long-term (13,14). Convincing evidence has led to a change in both the ESC and the ACC/AHA guidelines, and the period of mandatory DAPT duration after second generation DES has been shortened to 6 months for patients with stable CAD (4,15). Remarkably, based on post-hoc analyses of randomized trials, some stents received the CE (Conformité Européenne) mark labeling for a minimum of 1–3 months DAPT. More recently, a polymer-free biolimus-eluting DES was shown to be superior to bare metal stents (BMS) both in terms of safety and efficacy after a mandatory DAPT duration period of only 1 month among patients at high bleeding risk undergoing PCI, even after an ACS (16). Overall, even if existing clinical data do not support a routine strategy of DAPT shorter than 6 months, last ESC guidelines on management of NSTE-ACS allow $P2Y_{12}$ inhibitor administration for a shorter duration of 3–6 months after DES implantation in patients deemed at high bleeding risk (17).

Timing of surgery and cardiac risk after stenting

Time from index PCI to surgery is significantly associated with the risk of perioperative cardiac events (5,6,8,18,19). This risk is partially, but not entirely, related to the risk of stent thrombosis. Previous studies with first-generation DES suggested that a moderately increased risk might be extended up to 2–3 years after stenting (20). In a Mayo Clinic registry, the perioperative risk adverse cardiovascular events was largely related to the time from stent implantation to surgery, indicating substantially elevated risk in the first year after stenting [OR 2.59; 95% confidence interval (CI): 1.36 to 4.94] but not thereafter (OR 0.89; 95% CI: 0.59 to 1.36) (19). A recent analysis from the Western Denmark Heart Registry confirmed that surgery in patients treated with DES-PCI was associated with an increased 30-day risk of MI, and timing from PCI to surgery was linked to perioperative risk. However, the increased risk was only present within the first month after DES-PCI, and disappeared later on (5). A US national, retrospective cohort study found that although the time from stent placement to surgery was significantly associated with MACE, this was only true for surgery occurring <6 months after stenting (18) and stent type (DES *vs.* BMS) was not a predictor of MACE (18). Another registry study from Ontario, suggested that the earliest optimal time for elective surgery is >180 days after DES implantation, reaching a plateau afterwards (21). Data from the Italian REAL registry (6,22), showed that the interplay between stent type and time from PCI to surgery

was independently associated with perioperative cardiac death or MI. In that study, new-generation DES showed similar safety as BMS at any time interval between PCI and surgery, and were trendly safer when surgery occurred between 0 and 6 months after stenting, with all the benefit over BMS apparently gained when surgery occurred between 2 and 6 months after stenting (6).

Management of antiplatelet therapy

As previously mentioned, in patients with coronary stents undergoing surgical procedures the tradeoff between reduction of ischemic risk with antithrombotics and increased bleeding risk must be taken into account. The precautionary attitude suggested by the guidelines was, therefore, to postpone elective surgery >12 months after DES implantation and, whenever possible, to maintain single anti-platelet therapy through the perioperative phase preferably with aspirin.

New data published in the literature have recently changed this paradigm. In the PARIS (Patterns of Nonadherence to Antiplatelet Regimens in Stented Patients) registry, interruption of DAPT based on physician judgment in patients undergoing surgery at any time point after PCI was not associated with a significantly higher risk of MACE nor of stent thrombosis (23). Taking into account these data, the increased safety of new-generation DES, the reduced minimally recommended duration of DAPT after DES implantation and the most recent data about stent and surgery (5,6,18), the latest ACC/AHA guidelines reduced the recommended delay from DES implantation to surgery from >1 year into "optimally at least 6 months", suggesting that even >3 months can be considered in selected cases (15).

Management of antiplatelet therapy in patients with DES undergoing surgery remains complex and should take into account several factors, including timing from stent to surgery, type of stent, procedural complexity, ischemic risk of the patient and bleeding risk of the operation (both in terms of risk of blood loss and severity of the consequences in case of bleeding, irrespective on the amount). This has resulted in a number of consensus documents and position papers. However, all these documents lacked a clear definition of perioperative bleeding risk, advocating tailored treatment decided within a multidisciplinary team but without providing clear guidance. Recently, Rossini *et al.* proposed a multidisciplinary document, endorsed by 16 Italian national societies of cardiology, anaesthesiology and surgery, on perioperative management of antiplatelet therapy in patients undergoing surgery after coronary stent implantation (24). This document has been recently updated on the basis of new scientific data and is awaiting publication (Rossini R. *et al. submitted*).

Conclusions

Risk stratification and management of patients with DES undergoing surgery is complex and requires a strategy tailored for the patients, possibly determined within a multidisciplinary team. However, improved safety of new-DES and new data suggest that the presence of coronary DES should not necessarily be considered a cause of catastrophic complications, with the exception of urgent procedures performed in the first few weeks after stenting.

As general rules we can summarize the following:

(I) Elective surgical procedures should be postponed >6 months after DES implantation. However, this window could be safely shortened, if needed, to 3–6 months (15).

(II) Selection of a BMS over DES in patients undergoing PCI with planned surgical procedures does not seem anymore the optimal strategy. In fact:
  (i) The risk <30 days from stenting to surgery is very high irrespective of stent type;
  (ii) The increased risk of MI and cardiac death after DES in comparison with patients without ischemic heart disease seems confined only to the first month after DES-PCI (5);
  (iii) Between 2–6 months there is no evidence of increased risk with DES and some data suggest a potential advantage of new-generation DES over BMS between 2–6 months (6,18);

(III) Surgery should be performed, whenever possible, with at least 1 antiplatelet agent ongoing (preferably aspirin) and antiplatelet therapy should be entirely discontinued only if surgical hemostasis is predicted to be difficult or consequences of even minor bleeding (e.g., intracranial or endocular) are potentially very serious;

(IV) For non-deferrable, urgent surgical procedures, DAPT courses >1–3 months could be considered acceptable after implantation of new-generation DES. However, such surgical procedures should be performed in hospitals where 24/7 catheterization laboratories are available (1);

(V) A multidisciplinary approach is always appropriate to determine the best individual strategy.

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Footnote

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References

1. Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J 2014;35:2383-431.
2. Kaluza GL, Joseph J, Lee JR, et al. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. J Am Coll Cardiol 2000;35:1288-94.
3. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014;64:e77-137.
4. Windecker S, Kolh P, Alfonso F, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2014;35:2541-619.
5. Egholm G, Kristensen SD, Thim T, et al. Risk Associated With Surgery Within 12 Months After Coronary Drug-Eluting Stent Implantation. J Am Coll Cardiol 2016;68:2622-32.
6. Saia F, Belotti LM, Guastaroba P, et al. Risk of Adverse Cardiac and Bleeding Events Following Cardiac and Noncardiac Surgery in Patients With Coronary Stent: How Important Is the Interplay Between Stent Type and Time From Stenting to Surgery? Circ Cardiovasc Qual Outcomes 2016;9:39-47.
7. Berger PB, Kleiman NS, Pencina MJ, et al. Frequency of major noncardiac surgery and subsequent adverse events in the year after drug-eluting stent placement results from the EVENT (Evaluation of Drug-Eluting Stents and Ischemic Events) Registry. JACC Cardiovasc Interv 2010;3:920-7.
8. Cruden NL, Harding SA, Flapan AD, et al. Previous coronary stent implantation and cardiac events in patients undergoing noncardiac surgery. Circ Cardiovasc Interv 2010;3:236-42.
9. Vicenzi MN, Meislitzer T, Heitzinger B, et al. Coronary artery stenting and non-cardiac surgery--a prospective outcome study. Br J Anaesth 2006;96:686-93.
10. Hawn MT, Graham LA, Richman JR, et al. The incidence and timing of noncardiac surgery after cardiac stent implantation. J Am Coll Surg 2012;214:658-66; discussion 666-7.
11. Burger W, Chemnitius JM, Kneissl GD, et al. Low-dose aspirin for secondary cardiovascular prevention - cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation - review and meta-analysis. J Intern Med 2005;257:399-414.
12. Ferreira-Gonzalez I, Marsal JR, Ribera A, et al. Double antiplatelet therapy after drug-eluting stent implantation: risk associated with discontinuation within the first year. J Am Coll Cardiol 2012;60:1333-9.
13. Sarno G, Lagerqvist B, Frobert O, et al. Lower risk of stent thrombosis and restenosis with unrestricted use of 'new-generation' drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR). Eur Heart J 2012;33:606-13.
14. Stefanini GG, Windecker S. Stent thrombosis: no longer an issue with newer-generation drug-eluting stents? Circ Cardiovasc Interv 2012;5:332-5.
15. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular

Evaluation and Management of Patients Undergoing Noncardiac Surgery. Circulation 2016;134:e123-55.
16. Urban P, Meredith IT, Abizaid A, et al. Polymer-free Drug-Coated Coronary Stents in Patients at High Bleeding Risk. N Engl J Med 2015;373:2038-47.
17. Roffi M, Patrono C, Collet JP, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J 2016;37:267-315.
18. Hawn MT, Graham LA, Richman JS, et al. Risk of major adverse cardiac events following noncardiac surgery in patients with coronary stents. JAMA 2013;310:1462-72.
19. Mahmoud KD, Sanon S, Habermann EB, et al. Perioperative Cardiovascular Risk of Prior Coronary Stent Implantation Among Patients Undergoing Noncardiac Surgery. J Am Coll Cardiol 2016;67:1038-49.
20. Anwaruddin S, Askari AT, Saudye H, et al. Characterization of post-operative risk associated with prior drug-eluting stent use. JACC Cardiovasc Interv 2009;2:542-9.
21. Wijeysundera DN, Wijeysundera HC, Yun L, et al. Risk of elective major noncardiac surgery after coronary stent insertion: a population-based study. Circulation 2012;126:1355-62.
22. Saia F, Piovaccari G, Manari A, et al. Patient selection to enhance the long-term benefit of first generation drug-eluting stents for coronary revascularisation procedures. Insights from a large multicentre registry. EuroIntervention 2009;5:57-66.
23. Mehran R, Baber U, Steg PG, et al. Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. Lancet 2013;382:1714-22.
24. Rossini R, Musumeci G, Visconti LO, et al. Perioperative management of antiplatelet therapy in patients with coronary stents undergoing cardiac and non-cardiac surgery: a consensus document from Italian cardiological, surgical and anaesthesiological societies. EuroIntervention 2014;10:38-46.

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