Commentary

Antiplatelet agents in out of hospital cardiac arrest survivors—does an impaired biological response increase stent thrombosis risk?

Antoinette Neylon, Philippe Garot

Institut Cardiovasculaire Paris Sud, Massy, Paris, France

Correspondence to: Philippe Garot, MD. Institut Cardiovasculaire Paris-Sud, ICPS, Ramsay-Générale de Santé, Jacques Cartier Hospital, 6 avenue Noyer Lambert, 91300 Massy, France. Email: pgarot@angio-icps.com.

Submitted Aug 02, 2016. Accepted for publication Aug 08, 2016.
doi: 10.21037/jtd.2016.08.31
View this article at: http://dx.doi.org/10.21037/jtd.2016.08.31

Llitjos *et al*. present an interesting and thought provoking paper on impaired response to aspirin in the setting of induced hypothermia after out of hospital cardiac arrest (OHCA). In this study of resuscitated cardiac arrest patients with a requirement for antiplatelet therapy, impaired responses to both intravenous and oral aspirin were observed. Interestingly, this effect was more marked in those receiving aspirin via the oral route (1). This study therefore raises important clinical questions as to the efficacy of antiplatelet agents in this setting, the optimal route of administration and potential clinical sequelae in a unique and complex cohort.

Significant coronary artery disease is present in more than 70% of patients with resuscitated OHCA (2). More favourable survival outcomes have been shown with early angiography and angioplasty (3,4). While the procedure can be executed with good immediate results there have been conflicting data concerning the incidence of stent thrombosis in this population.

Stent thrombosis (ST) is a multifactorial phenomenon and its occurrence in the setting of OHCA has been shown to further increase mortality (5). Stents are foreign bodies in the vessel wall that may induce platelet adhesion and activation of the coagulation cascade. In general the aetiology can be broadly classified into patient, procedure and device related factors (6).

Angioplasty in the setting of acute myocardial infarction (AMI) has been shown to increase the risk of stent thrombosis (7). In addition, patient-specific factors such as reduced left ventricular function and impaired response to antiplatelet therapy confer important increased risk. In comatose OHCA patients undergoing therapeutic hypothermia there are multiple patient related factors that may contribute to impaired biological response to antiplatelet therapy including accelerated platelet turnover, inflammation, high levels of shear stress, use of vasopressive support, altered gastric motility and increased coagulation.

Premature discontinuation of antiplatelet therapy in the initial 30 days after stenting is arguably the most important predictor of ST (8) underlining the importance of effective antiplatelet therapy. Many studies have shown an association between high platelet reactivity (HPR) in platelet function testing and subsequent ST (9,10). In a large prospective study of over 8,000 patients undergoing coronary stenting HPR to clopidogrel was shown to be associated with an increased risk of ST [adjusted HR =2.49 (95% CI: 1.43–4.31), P=0.001] however HPR to aspirin was not [adjusted HR =1.46 (0.58–3.64), P=0.42] (9).

There are conflicting data as to the risk of stent thrombosis in OHCA survivors undergoing therapeutic hypothermia. Penela *et al*. reported ST in 5 out of 11 cases (45%) of OHCA patients undergoing induced hypothermia after stenting (11). Joffre *et al*. reported a rate of 10.9%—five times that of a comparable group of patients with ACS but without cardiac arrest (12). In contrast to this, Patel *et al*. in a study of 180 patients with OHCA and coronary stenting undergoing induced hypothermia observed ST in 2 (1.1%) (4) while Rosillo *et al*. reported an incidence of 2.7% among 77 patients (13). In a Danish study of primary angioplasty in OHCA the rate was 1.5% (n=68) and this figure compared very favourably with the 0.9% rate of ST observed in ST-

elevation AMI patients without OHCA (14).

Patients undergoing induced hypothermia in the intensive care unit represent a complex and heterogeneous cohort. There are multiple factors that may predispose to thrombotic events. There are no randomised control trials in this setting to guide optimal antiplatelet therapy. Additionally, these patients are at the same time often at high risk of bleeding due to resuscitation manoeuvres. A consensus document form the European Association for Percutaneous Cardiovascular Interventions suggest unfractionated heparin for periprocedural anticoagulation and in keeping with the findings of Llitjos *et al*., intravenous aspirin (2). As P2Y12 inhibitors (clopidogrel, prasugrel, ticagrelor) are only available in tablet form, administration of a crushed suspension via a naso-gastric tube is the only option. There are no randomised data to suggest superiority of one agent over another.

In conclusion, mild therapeutic hypothermia is considered standard care in the treatment of patients resuscitated from cardiac arrest. While impaired biological response to asprin and P2Y12 inhibitors can be demonstrated using platelet function testing it is not known if this translates into increased clinical events. Therapeutic hypothermia has not been show to negatively affect the acute angiographic result.

Acknowledgements

None.

Footnote

Provenance: This is an invited Commentary commissioned by the Section Editor Lei Huang (Cardiac center of Tianjin Third-Central Hospital, Tianjin, China).
Conflicts of Interest: The authors have no conflicts of interest to declare.

Comment on: Llitjos JF, Sideris G, Voicu S, *et al*. Impaired biological response to aspirin in therapeutic hypothermia comatose patients resuscitated from out-of-hospital cardiac arrest. Resuscitation 2016;105:16-21.

References

1. Llitjos JF, Sideris G, Voicu S, et al. Impaired biological response to aspirin in therapeutic hypothermia comatose patients resuscitated from out-of-hospital cardiac arrest. Resuscitation 2016;105:16-21.
2. Noc M, Fajadet J, Lassen JF, et al. Invasive coronary treatment strategies for out-of-hospital cardiac arrest: a consensus statement from the European association for percutaneous cardiovascular interventions (EAPCI)/stent for life (SFL) groups. EuroIntervention 2014;10:31-7.
3. Dumas F, Cariou A, Manzo-Silberman S, et al. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac ArresT) registry. Circ Cardiovasc Interv 2010;3:200-7.
4. Patel N, Nair S, Mooney M, et al. Risk of stent thrombosis in cardiac arrest patients with st- elevation myocardial infarction undergoing percutaneous coronary intervention and therapeutic hypothermia: international cardiac arrest registry. J Am Coll Cardiol 2015;65.
5. Gouffran G, Rosencher J, Bougouin W, et al. Stent thrombosis after primary percutaneous coronary intervention in comatose survivors of out-of-hospital cardiac arrest: Are the new P2Y12 inhibitors really more effective than clopidogrel? Resuscitation 2016;98:73-8.
6. Byrne RA, Joner M, Kastrati A. Stent thrombosis and restenosis: what have we learned and where are we going? The Andreas Grüntzig Lecture ESC 2014. Eur Heart J 2015;36:3320-31.
7. Park DW, Park SW, Park KH, et al. Frequency of and risk factors for stent thrombosis after drug-eluting stent implantation during long-term follow-up. Am J Cardiol 2006;98:352-6.
8. Iakovou I, Schmidt T, Bonizzoni E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. JAMA 2005;293:2126-30.
9. Stone GW, Witzenbichler B, Weisz G, et al. Platelet reactivity and clinical outcomes after coronary artery implantation of drug-eluting stents (ADAPT-DES): a prospective multicentre registry study. Lancet 2013;382:614-23.
10. Cayla G, Hulot JS, O'Connor SA, et al. Clinical, angiographic, and genetic factors associated with early coronary stent thrombosis. JAMA 2011;306:1765-74.
11. Penela D, Magaldi M, Fontanals J, et al. Hypothermia in acute coronary syndrome: brain salvage versus stent thrombosis? J Am Coll Cardiol 2013;61:686-7.
12. Joffre J, Varenne O, Bougouin W, et al. Stent thrombosis: an increased adverse event after angioplasty following resuscitated cardiac arrest. Resuscitation 2014;85:769-73.
13. Rosillo SO, Lopez-de-Sa E, Iniesta AM, et al. Is

therapeutic hypothermia a risk factor for stent thrombosis? J Am Coll Cardiol 2014;63:939-40.
14. Chisholm GE, Grejs A, Thim T, et al. Safety of therapeutic hypothermia combined with primary percutaneous coronary intervention after out-of-hospital cardiac arrest. Eur Heart J Acute Cardiovasc Care 2015;4:60-3.

Cite this article as: Neylon A, Garot P. Antiplatelet agents in out of hospital cardiac arrest survivors—does an impaired biological response increase stent thrombosis risk? J Thorac Dis 2016;8(9):E1090-E1092. doi: 10.21037/jtd.2016.08.31