EDITORIAL

Long-term risk of stroke following percutaneous coronary intervention: can we predict the future and can we change it?

Phyo K. Myint[1,2], Zahra Pasdar[1], Mamas A. Mamas[3]

1 Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, United Kingdom
2 Aberdeen Cardiovascular and Diabetes Center, Institute of Medical Sciences, University of Aberdeen, Aberdeen, United Kingdom
3 Keele Cardiac Research Group, Keele University, Stoke-on-Trent, United Kingdom

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Percutaneous coronary intervention (PCI) reduces mortality and reinfarction after type 1 myocardial infarction (MI) and represents the contemporary gold-standard invasive treatment. Despite a relatively low incidence ranging from 0.22% to 1.3%,[1] PCI-related stroke is associated with high acute mortality rates and life-changing disabilities in patients who survive.[2] To date, many studies have therefore focused on periprocedural stroke following PCI, its predictors and complications.[2-4] Long-term stroke risk in this population is less well researched. Assessment of this risk is important as these patients are multimorbid, older people with a higher burden of cardiovascular risk factors and are often treated with potent antithrombotic regimes. Therefore, this population represents a completely different group of patients to those in the community that most stroke risk prediction scores serve and were developed in.

Zhao et al[5] contribute to this evidence gap in the current issue of *Polish Archives of Internal Medicine* (*Pol Arch Intern Med*). They derived and validated a prediction model to determine the 5-year risk of stroke in patients who had undergone PCI for acute MI at Fuwai Hospital, Beijing, China.[5] They retrospectively analyzed 4103 patients who had been treated with PCI for acute coronary syndrome indications; 3582 with ST-segment elevation myocardial infarction (STEMI) and 521 with non-STEMI. Among variables assessed, a history of hypertension, atrial fibrillation (AF), age group, and the presence of target lesions involving branches formed predictors in their model. Further, the authors developed a nomogram and performed an internal validation. The area under the curve of the validation cohort was 0.846 with appreciably high sensitivity (71.43%) and specificity (90.29%). Several predictors for stroke determined by Zhao et al,[5] including AF[6] and age,[7] seem fitting when evaluating evidence from the wider literature, although some are counterintuitive and lack biological plausibility.

The authors identified treatment of side branch disease as a predictor of future stroke. Whilst treatment of bifurcation lesions and side branches may increase the risk of major adverse cardiovascular and cerebrovascular events,[8] it is unclear why it should increase long-term risk of ischemic stroke. Furthermore, some findings of Zhao et al[5] appear to be at odds with a large body of literature. Paradoxically, the authors report that patients belonging to the youngest age category (≤40 years) had the greatest risk of stroke. They reasoned that older patients who are frail may be less likely to be chosen candidates for PCI, and therefore, the older population in their study is more "robust." Contemporary practice does not exclude older patients from PCI, even when the burden of comorbidities is significant, as the benefit associated with the procedure outweighs potential risks. There is no age cutoff in the contemporary guidelines for provision of PCI. Thus, this assertion is very unlikely. It is more likely that the apparent "lower-risk" observed in older people may be explained by the competing risk of death which was not considered.

Whilst the model by Zhao et al[5] has shown good discriminative performance, some significant limitations should be acknowledged. Firstly, the prediction model focuses only on ischemic stroke. The clinical utility is therefore uncertain, particularly in a population treated with potent antithrombotic regimes where longer-term risk of hemorrhagic stroke remains significant. Secondly, stroke in this group of patients is likely to represent 2 different pathophysiologic processes

Correspondence to:
Prof. Phyo K. Myint, MBBS, MD, FRCPE, FRCP, Room 4:013, Polwarth Building, School of Medicine, Medical Sciences and Nutrition, Foresterhill, Aberdeen AB25 2ZD, Scotland, United Kingdom, phone: +44 (0) 1224 437841, email: phyo.myint@abdn.ac.uk
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in 2 different patient groups. Stroke events occurring in the first few days post discharge are likely to be related to the PCI procedure, whilst stroke events in the longer-term are likely to occur in a distinct population of patients at a high risk of future stroke by virtue of their cardiometabolic risk profile. It is likely that predictors of these events in these 2 populations are different, and a prognostic tool would have greatest value in differentiating between these 2 scenarios.

Thirdly, due to the large-scale, retrospective design of the study, the authors were unable to consider changes to antithrombotic regimes over time, particularly de-escalation to less potent antiplatelets, the type of anticoagulant used in patients with AF (warfarin vs direct-acting oral anticoagulants) and whether these patients remained on anticoagulation alone or an additional antiplatelet was added in the longer-term, all of which influence the stroke risk. How traditional cardiovascular risk factors including lipids, hypertension, and glycemic control changed over time was not accounted for, which would impact the long-term future stroke risk. Future work should also consider the $P2Y_{12}$ type, particularly whether newer $P2Y_{12}$ agents are used which are known to influence major adverse cardiovascular and cerebrovascular events.[9] Fourthly, the authors did not consider a previous history of stroke, which is one of the strongest predictors of future stroke.[10] Finally, whilst the authors considered baseline AF, they did not consider incident AF during follow-up, which is likely to be a significant risk factor of stroke.

So where does this leave us? And how should the findings of the study be actioned? One major challenge in the development of any risk score is whether it can be used to change clinical practice. Limitations of predicting the future were identified by the ancient Greeks. In Greek mythology, Cassandra, one of the princesses of Troy, daughter of Priam and Hecuba, was blessed with the gift of foreseeing the future. Her curse was that no one believed her, a fact that weighed heavily on the destruction of Troy during the Trojan War. She was able to predict the future but could not change it. This remains a key consideration several centuries later and is as relevant to risk scores now as it was to prediction of future events then. Whilst identification of higher-risk patients in this population may allow for targeted secondary prevention strategies, such as ensuring patients with AF are anticoagulated and hypertension is managed optimally, it is unclear how treatment of side branches can be modified, or how the paradoxical higher risk of stroke in younger patients can be interpreted or whether it is artefactual. What this paper does tell us is that future stroke risk following PCI for acute coronary syndrome indications is significant in the longer-term, necessitating that the patient's risk factors should be aggressively managed in line with best available evidence-based guidelines. Risk scores such as these may be helpful in identifying those at highest risk, where aggressive risk factor management can be targeted. Whether the use of such risk scores reduces the risk of stroke in this population, remains to be seen.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

CONFLICT OF INTEREST None declared.

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