5 Tacher V, Lin M, Desgranges P, Deux JF, Grünhagen T, Becquemin JP, et al. Image guidance for endovascular repair of complex aortic aneurysms: comparison of two-dimensional and three-dimensional angiography and image fusion. *J Vasc Interv Radiol* 2013;**24**(11):1698–706.
6 Michel M, Becquemin JP, Clément MC, Marzelle J, Quelen C, Durand-Zaleski I. Thirty-day outcomes and costs of fenestrated and branched stent-grafts versus open repair for complex aortic aneurysms. *Eur J Vasc Endovasc Surg* 2015;**50**:189–96.
7 Kristmundsson T, Sonesson B, Dias N, Törnqvist P, Malina M, Resch T. Outcomes of fenestrated endovascular repair of juxtarenal aortic aneurysm. *J Vasc Surg* 2014;**59**(1):115–20.

J.P. Becquemin*, M. Raux, F. Cochennec, J. Marzelle
Henri Mondor Hospital, University Paris XII, Creteil, France

*Corresponding author. Henri Mondor Hospital, University Paris XII, Creteil, France.
Email-address: jpbecquemin@gmail.com (J.P. Becquemin)

http://dx.doi.org/10.1016/j.ejvs.2015.06.006
DOI of original article: http://dx.doi.org/10.1016/j.ejvs.2015.06.005

Response to "Re: The Awakening of Alice"

It was with great interest that I read the various comments from Jean-Pierre Becquemin and his colleagues in response to our recent editorial.[1,2] I agree with the authors that it is occasionally difficult to match results produced from high-volume expert centers in the "real world". Examples include the "Bolia subintimal angioplasty technique" or (more relevant to this debate) the results of open thoracoabdominal aortic aneurysm (TAAA) surgery. However, it is still our primary task to provide the best possible patient care, especially in pathologies that require more complex surgery.

If one wishes to embark on treating TAAAs with fenestrated and/or branched grafts, a number of prerequisites are necessary. These include (i) *dedicated* surgeons who want to *invest* in these techniques in order to acquire much-needed expertise; (ii) perfect *organization* with regard to *logistics*, including access to a *hybrid room*; and (iii) the creation of a *professional team*, including anesthesiologists and nurses. While I agree that not all of these prerequisites require a high-volume center, there should be no doubt that this type of complex pathology is best treated in large-volume centers. There is simply no place for amateur behaviour or inexperienced operators, as even minor technical errors can be costly to the patient, as we have all experienced.

Pioneers have to take new techniques forward and should report their results. In order to help others move forward, we fully agree with the authors that these reports should provide more detail regarding indications, limitations and lessons learned. Fenestrated endovascular aortic aneurysm repair (FEVAR) has become a standardized technique in our center, with low mortality and excellent midterm results. We also agree that follow-up should be enforced, and the fact that so many patients were not followed up in the Windows trial could be interpreted as a lack of organization and dedication. Our paper on 10 years of experience in TAAA branched grafting concluded that "too high-risk" patients should not be treated at all. Indeed, the highest-risk patients had a higher early mortality and lower survival.[3] We also agree that patients who are unlikely to survive for 2 years after their surgery will not (by definition) have benefitted from the repair. Our conclusion in that article was meant to help other centers. Obviously, it is difficult for surgeons to deny a patient treatment when he or she has been referred as "a last resort", but we have to learn from experience and help others not to make the same mistakes.

It was a little disappointing that the authors considered our published work to be of lower evidential quality (compared with the Windows trial). They have reported that there was no statistical difference in mortality between the two high-volume and the other five centers in the Windows trial, but (by their own criteria) this type of post-hoc analysis is also "lower-quality evidence" as the numbers are too small to enable any meaningful comparison. A non-inferiority study would require about 600 patients in each arm to prove that the lack of difference was not due to a type II error. In other words, the Windows Registry was never powered to prove this statistical difference.

Our caveat emptor editorial was intended to warn colleagues about problems associated with uncritically developing endovascular programmes for treating complex TAAAs and to motivate them to invest more in organization, logistics, and team approaches. Dedicated endovascular teams can perform standard FEVAR after thorough training, even in lower-volume centers. However, for triple and quadruple FEVAR cases, the imaging requirements are clearly higher (longer fluoroscopy times, including lateral viewing) and the operative risks inevitably increase. For cases of branched TAAA, all of the prerequisites discussed above should be met in order to address numerous potential intraoperative complications. It is, therefore, shameful that politics and/or professional organizations are not able (or unwilling) to promote the centralization of treatment for patients with complex aortic pathology. As Holt and Thompson recently stated: "if we fail to centralize complex aortic pathology, we will have failed our patients".[4]

REFERENCES

1 Verhoeven EL, Katsargyris A, Haulon S. Caveat emptor: lessons learned from the endovascular treatment of complex aortic pathologies. *Eur J Vasc Endovasc Surg* 2015;**49**:363–5.
2 Becquemin JP, Raux M, Cochennec F, Marzelle J. Re: "The awakening of Alice". *Eur J Vasc Endovasc Surg* 2015.
3 Verhoeven EL, Katsargyris A, Bekkema F, Oikonomou K, Zeebregts CJAM, Ritter W, et al. Editor's choice — ten-year experience with endovascular repair of thoracoabdominal aneurysms: results from 166 consecutive patients. *Eur J Vasc Endovasc Surg* 2015;**49**:524–31.
4 Holt P, Thompson MM. Centralisation: putting patients first. *Eur J Vasc Endovasc Surg* 2010;**40**:280–1.

E.L. Verhoeven*, A. Katsargyris
Department of Vascular and Endovascular Surgery, Paracelsus Medical University, Nürnberg, Germany

S. Haulon
Department of Vascular Surgery, Aortic Centre, CHRU Lille, France

*Corresponding author.
Email-address: eric.verhoeven@klinikum-nuernberg.de (E.L. Verhoeven)

http://dx.doi.org/10.1016/j.ejvs.2015.06.005
DOI of original article: http://dx.doi.org/10.1016/j.ejvs.2015.06.006

Re: 'Prothrombin G20210 Mutation and Lower Extremity Peripheral Arterial Disease: A Systematic Review and Meta-analysis'

Vasquez et al.[1] showed that prothrombin G20210 mutation is significantly elevated in patients with peripheral occlusive arterial disease (POAD) suffering from critical limb ischemia (CLI) but not in the others. Interestingly, this mutation has been reported to be more prevalent in patients with Buerger's disease.[2,3] Avcu et al.[2] found an increased frequency of the G20210 mutation in Buerger's disease (OR 7.98, 2.45—25.13). Buerger's disease is characterized by diffuse arterial thrombosis and a severe clinical picture, most often at the CLI stage. In a recently published case control study among patients with premature POAD the author's team found that G20210 mutation was significantly more frequent in Buerger's disease (4.2% vs. 1.7 in controls).[3] This difference was not found for atherosclerosis related POAD (2.6%). When compared with the 64 POAD patients, the 49 with Buerger's disease had CLI in 88% versus 28% in atherosclerosis related POAD. As suggested by Vasquez et al.,[1] G20210 mutation might be one among several factors favouring thrombosis and leading to CLI in POAD, and prospective cohort studies would be useful to evaluate the role of this mutation to predict progression in POAD.

REFERENCES

1 Vasquez F, Roger M, Carrier M, Le Gal G, Reny JL, Sofi F, et al. Prothrombin G20210 mutation and lower extremity peripheral arterial disease: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2015;**50**(2):232—40.
2 Avcu F, Akar E, Demirkiliç U. The role of prothrombotic mutations in patients with Buerger's disease. *Thromb Res* 2000;**100**:143—7.
3 Berard A, Bedel A, Le Trequesser R, Freyburger G, Nurden A, Colomer S, et al. Novel risk factors for premature arterial occlusive disease in non diabetic patients: a case-control study. *PloS One* 2013;**8**:e37882.

C. Boulon*
Service de Medecine vasculaire, Hôpital Saint André, Bordeaux, France

A. Berard
Laboratoire de biochimie, Hôpital du Haut-Lévêque, Pessac, France

G. Freyburger
Laboratoire d'hématologie, Hôpital Pellegrin, Bordeaux, France

J. Constans
Service de Medecine vasculaire, Hôpital Saint André, Bordeaux, France

*Corresponding author. Service de Medecine vasculaire, Hôpital Saint André, 1 rue Jean Burguet, 33075 Bordeaux, France.
Email-addresses: carine.ferjoux@wanadoo.fr, carine.boulon@chu-bordeaux.fr (C. Boulon)

http://dx.doi.org/10.1016/j.ejvs.2015.07.043
DOI of original article: http://dx.doi.org/10.1016/j.ejvs.2015.08.009

Response to 'Re: Prothrombin G20210A Mutation and Lower Extremity Peripheral Arterial Disease. A Systematic Review and Meta-analysis'

We read with interest the letter by Boulon et al.[1] The proposed association between prothrombin G20210A and thromboangiitis obliterans is very interesting. Prior studies have suggested that prothrombin G20210A interacts with other cardiovascular risk factors (especially smoking) to increase the risk of vascular events,[2] and this interaction could further explain the association of prothrombin G20210A and thromboangiitis obliterans seen by Bérard et al. and Avcu et al.[3,4] The literature search conducted in our systematic review did not identify the study by Bérard et al.[3,5]; had the study been included there would have been no changes in the association of lower extremity peripheral arterial disease (PAD) prothrombin G20210A (pooled random effect odds ratio 1.68 [95% confidence interval 0.94—3.00]; I^2 52.1%; $p = .08$). Furthermore, the addition of the study by Bérard et al. does not modify the association between prothrombin G20210A and critical limb ischemia secondary to PAD (even in the absence of positive cases).[3] Finally, we agree that well-designed prospective cohort studies are needed to evaluate the role of prothrombin G20210A in the progression and outcome of patients with PAD.

REFERENCES

1 Boulon C, Berard A, Freyburger G, Constans J. Re: Prothrombin G20210A mutation and lower extremity peripheral arterial