International Opinion on Priorities in Research for Small Abdominal Aortic Aneurysms and the Potential Path for Research to Impact Clinical Management

Regent Lee, Amy Jones, Ismail Cassimjee, Ashok Handa

On behalf of the Oxford Abdominal Aortic Aneurysm Study

Nuffield Department of Surgical Sciences,

University of Oxford, UK

Corresponding Author:

Regent Lee

regent.lee@nds.ox.ac.uk

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Introduction

Landmark trials of surgery for small abdominal aortic aneurysms (AAA), which included patients with AAA sizes between 40-55mm, did not demonstrate medium term survival benefits of early surgery in these patients[1]. However, these trials also showed the variation in AAA growth rates between individuals, and that the majority of patients with small AAAs would eventually progress to the threshold of 55mm within 5 years.

In the ensuing decades since these trials, we have witnessed changes in the epidemiology of AAA. Patients are being diagnosed with AAAs at an increasingly older age[2]. The operative risk for AAA surgery has also improved internationally according the data from large registries[3, 4]. It is therefore a logical hypothesis that those patients with expected fast future growth of AAA may benefit from early surgery before they reach the 55mm threshold. Although several putative markers of AAA progression have been reported, none has yet been validated for use in clinical practice[5, 6]. More research will be required to advance knowledge in this specific arena.

Given the finite research resources available, it is imperative for researchers to demonstrate the need for specific research, and a clear path to translate their findings to impact clinical practice. Initiatives such as the James Lind Alliance utilise consultation with clinicians and their patients to determine disease conditions that are considered priorities for research[7]. However, there is no existing literature to highlight priorities for research in the subject of AAA. To address this, we conducted an online survey to vascular surgery colleagues internationally to obtain a global opinion on the priorities for research for AAA.

Method

This online survey was constructed using Google Forms, and was delivered in two phases. The first phase was during the European Society of Vascular and Endovascular Surgery Annual Conference 2016 (Copenhagen), where we distributed 1,500 copies of invitation flyers at the conference. The second

phase was conducted during November 2016 and April 2017 as an online campaign. During this period, the lead Author utilised LinkedIn to randomly connect with ~2,000 vascular surgery colleagues internationally and invited each person via an email. The active link for the online survey is: http://tinyurl.com/OxAAASurveyInternational ("e-supplemental material"). Further details of the survey workflow can be found in the accompanying Data in Brief article.

In this survey, colleagues were asked to provide basic demographic details. We first asked them to choose what they view as the top priority for AAA research out of a list of 10 broad research areas (Figure 2). A brief outline then highlighted the current epidemiologic data of patients with AAAs, including the increased chance of developing other cardiovascular co-morbidities while under surveillance as compared to those without AAAs[8, 9]. We quoted contemporary surgical outcome data [<2% mortality for routine open surgical repair (OSR), <0.5% mortality for endovascular repair (EVAR)][3, 4], routine recovery time and long term follow up plans for surgery. We then presented them with a hypothetical scenario where *they* had just been diagnosed with a small AAA (40mm). In addition, a hypothetical biomarker predicted their AAA will be faster growing, and would likely to reach existing surgical threshold within the next 3-5 years. The participants were told they were fit to undergo either OSR or EVAR. Using this scenario, we ascertained their preferences regarding several aspects for the clinical management.

Results

By the end of April 2017, we received 277 online responses from vascular / endovascular surgery colleagues who have direct roles in the management of AAA patients. The median age group was 41-45 years, with a majority being male (n=245). There were participants from every continent: Africa 3%, Asia 2%, Australasia 5%, Europe 54%, Middle East 3%, North America 14%, and South America 21% (Figure 1). In terms of their professional profiles, 78% were consultant specialists, 18% were specialist trainees, and 4% were junior doctors. Sixty eight percent worked predominantly in the public sector.

Amongst the 10 topics of research for AAA, "*discovering new tests to predict an AAA will be fast growing*" and "*discovering new medications that will stop an AAA from growing further*" were identified as top priorities for research (64 and 63 votes, respectively), followed closely by "*discovering new medications to shrink an AAA back to normal size*" (54 votes) (Figure 2).

In the scenario where a biomarker predicts the AAA will be fast growing, the majority (56%) of colleagues would prefer to have surgery early rather than surveillance. When the age groups were divided by median split, there was no difference in the preferences between the younger (below 40 years, 60% preferred early surgery) and older age group (over 40 years, 54% preferred early surgery) (Fischer exact test p=0.4). Further, there was no difference in the preferences between those who predominantly worked in the public or private sector (64% and 53% preferring early surgery, respectively. Fisher exact test p=0.1) or between male or female participants (58% and 47% preferring early surgery, respectively. Fisher exact test p=0.3).

Of those who preferred to have surgery early, the preferences for OSR or EVAR were 32% vs 68%, respectively. There was no difference between the preference of the younger (≤ 40 years old, 32% preferred OSR) as compared to the older (>40 years old, 34% preferred OSR) surgical colleagues (Fisher's exact test p=0.86). To examine if there is regional difference in the preference, we compared the responses between the 3 major continents with the most number of responses (Europe, North America, South America). There was indeed no difference between their response in terms of the type of surgery preferred when undertaking early surgery (Europe: 33% prefer OSR; North America: 35% prefer OSR; South America: 36% prefer OSR).

Sixty-four percent of them would be willing to take part in a trial to see if early surgery in this scenario will be beneficial. Only 3% said they definitely would not take part. In terms of the most important outcome of this trial for them, the choices were split between "*making me live longer*", "*improve my quality of life*", and "*reduce my anxiety about the AAA*" (46%, 27%, and 29%, respectively).

Discussion

The management of abdominal aortic aneurysm is well defined in literature, with a recognised threshold for surgery at 55mm. Trials on small AAAs showed no benefit of early surgery compared to a surveillance strategy up to the intermediate term, as early surgery confers the immediate operative risk not incurred by the surveillance strategy.[1] As such current NHS, AHA, and ESC guidelines do not recommend surgery until an AAA reaches 55mm.[10-12]

Despite these guidelines, there is clear discrepancy in the threshold for offering surgery between different countries. In the United states, up to 40% of patients receive AAA surgery below 55mm, while this number is much lower for the UK or Iceland.[13-15] One of the key differences between these health care systems is the financial remuneration system (ie. private vs public hospital systems). We therefore compared the responses between vascular surgeons that worked predominantly in the public versus the private sector to see if the health care system influence their personal decision making.

There is increasing emphasis on patient views regarding disease treatment and clinical research both for health care delivery and resource allocations[16]. Notwithstanding the differences in the financial remuneration between the different health care systems, patient preferences must have clear influence in the decision making process. We took the approach of asking our vascular surgery colleagues to assume the role as a “patient” in the survey. With their direct insight in the disease are and in the clinical journey of AAA management, the opinions of international vascular colleagues should be additionally recognised to guide the future direction of AAA research.

It is important to note that these responses are received from international colleagues randomly approached from within LinkedIn and does not represent a pre-selected cohort. Our data show that their opinions are fairly consistent, irrespective of the demographic background (age, gender, region and type of practice). The study could have benefited from a larger number responses. However, this would require significant additional resources to send the invitation to more vascular surgeons

internationally. Other methods to gain a broader reach to vascular surgeons include using marketing agencies that have contact details of a registry of vascular surgeons, or through individual vascular societies (such as the Vascular Society in the UK, or Society of Vascular Surgery in the USA). However, to obtain their official approval for sending out surveys to individual members require significant administrative costs.

We were fortunate to have the support of the European Society of Vascular Surgery to distribute the invitation flyers for free during the ESVS annual conference in Copenhagen 2016. We further utilised the social media platform (LinkedIn) for the second phase of the survey, which was an economical way of getting in contact with minimal cost. In order to avoid bias related to pre-selection of vascular surgeons, the lead author attempted to connect with all the vascular surgeons that were feasibly allowed in LinkedIn.

Interestingly, as the online survey was conducted using Google Forms which allows visualisation of the summary data in real time, we noticed that the overall trend in every questions category remained steady beyond the initial hundred or so responses. From the outset, “discovering new tests to predict an AAA will be fast growing” has been consistently chosen as the top priority for research by vascular surgery colleagues. Although the number of responses presented in this study is modest, our experience and data suggests the observations are indeed representative of the international opinion.

Conclusion

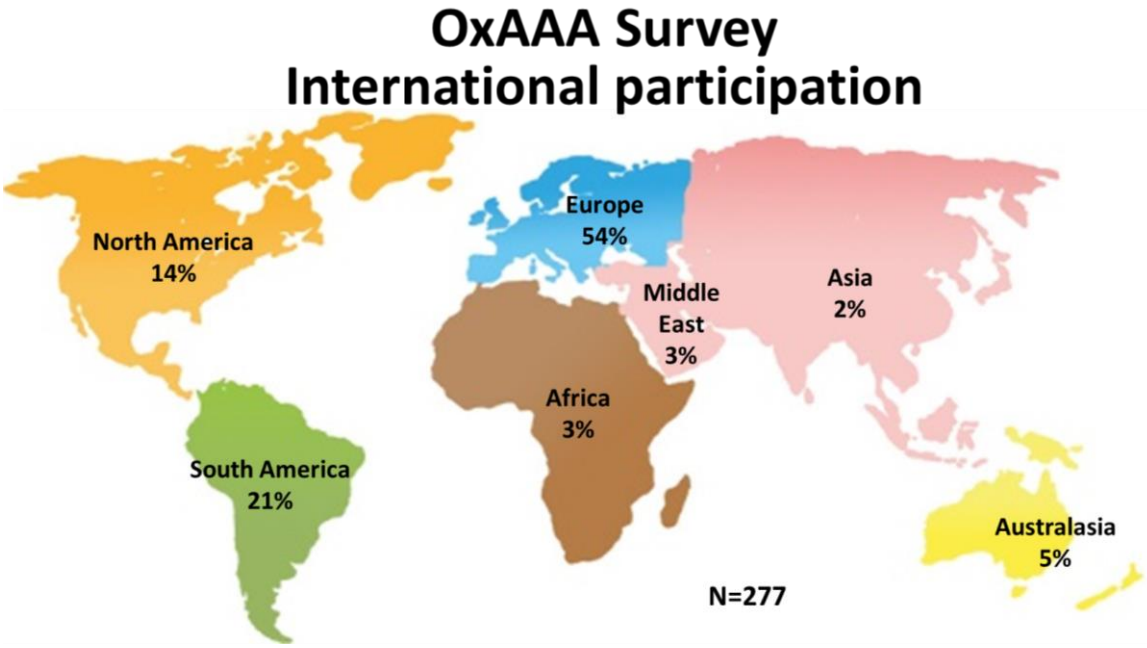
Our data provides a snapshot of international opinion from vascular colleagues regarding what they consider as top priorities for AAA research. It also provides an example of direct path to impact for biomarkers of AAA progression. Specifically, such biomarkers can disrupt the traditional strategy of management for small AAAs by affecting the patients’ preference on the timing for surgery.

Figure Legend

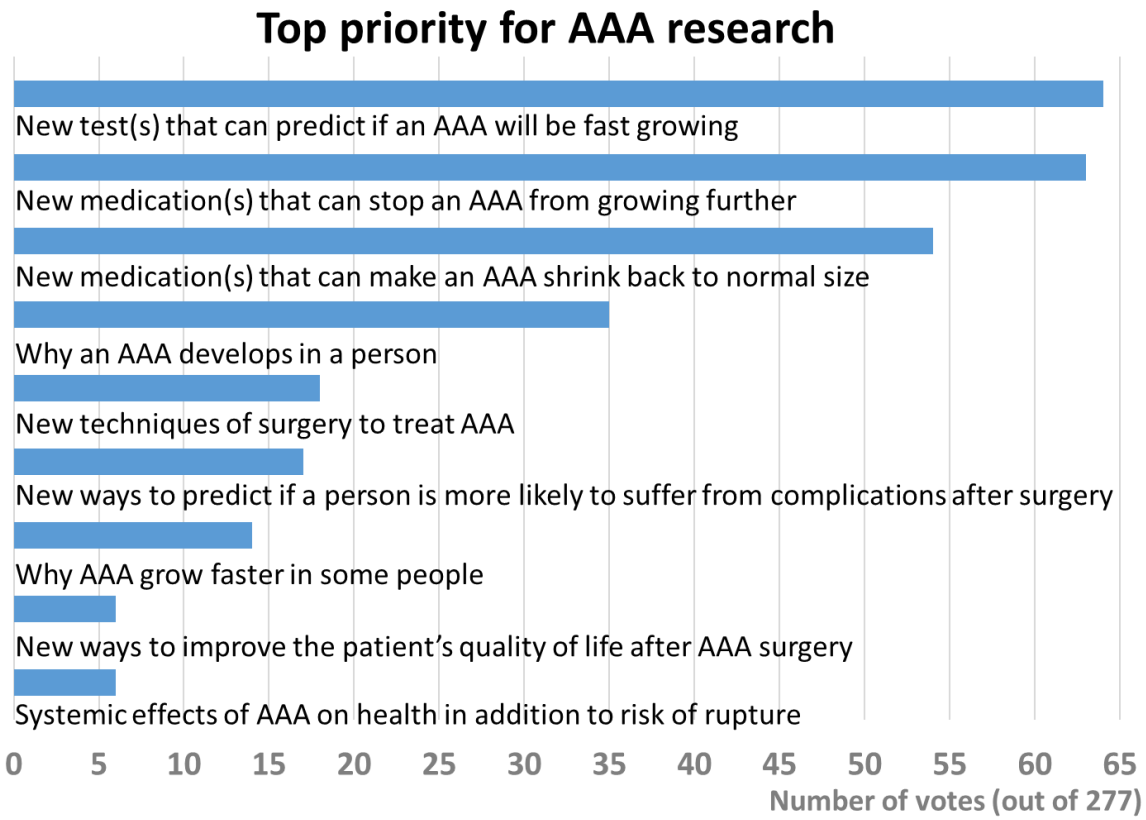
Figure 1: The OxAAA survey received responses from international vascular surgery colleagues. There were participants from every continent: Africa 3%, Asia 2%, Australasia 5%, Europe 54%, Middle East 3%, North America 14%, and South America 21%.

Figure 2: Top priority of research for abdominal aortic aneurysms (AAA). In this survey, colleagues were asked to choose what they view as the top priority for AAA research out of a list of 10 broad research areas. The total number of votes is displayed.

Figure 1


OxAAA Survey
International participation
North America
14%
Europe
54%
Middle
East
3%
Asia
2%
Africa
3%
South America
21%
Australasia
5%
N=277

158 **Figure 2**



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References

[1] Filardo G, Powell JT, Martinez MA, Ballard DJ. Surgery for small asymptomatic abdominal aortic aneurysms. Cochrane Database Syst Rev. 2015:Cd001835.

[2] Choke E, Vijaynagar B, Thompson J, Nasim A, Bown MJ, Sayers RD. Changing epidemiology of abdominal aortic aneurysms in England and Wales: older and more benign? Circulation. 2012;125:1617-25.

[3] Wanhainen A, Hultgren R, Linné A, Holst J, Gottsäter A, Langenskiöld M, et al. Outcome of the Swedish Nationwide Abdominal Aortic Aneurysm Screening ProgramClinical Perspective. 2016.

[4] Jacomelli J, Summers L, Stevenson A, Lees T, Earnshaw JJ. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. Br J Surg. 2016;103:1125-31.

[5] Wanhainen A, Mani K, Golledge J. Surrogate Markers of Abdominal Aortic Aneurysms Progression. 2015.

[6] Lee R, Bellamkonda K, Jones A, Killough N, Woodgate F, Williams M, et al. Flow Mediated Dilatation and Progression of Abdominal Aortic Aneurysms. Eur J Vasc Endovasc Surg. 2017.

[7] Chalmers I, Atkinson P, Fenton M, Firkins L, Crowe S, Cowan K. Tackling treatment uncertainties together: the evolution of the James Lind Initiative, 2003-2013. J R Soc Med. 2013;106:482-91.

[8] Norman P, Le M, Pearce C, Jamrozik K. Infrarenal aortic diameter predicts all-cause mortality. Arterioscler Thromb Vasc Biol. 2004;24:1278-82.

[9] Duncan JL, Harrild KA, Iversen L, Lee AJ, Godden DJ. Long term outcomes in men screened for abdominal aortic aneurysm: prospective cohort study. Bmj. 2012;344:e2958.

[10] NHS. Abdominal aortic aneurysm - Treatment - NHS Choices. Department of Health; 2016.

[11] Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Curtis LH, et al. Management of patients with peripheral artery disease (compilation of 2005 and 2011 ACCF/AHA guideline recommendations): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127:1425-43.

[12] Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, et al. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2014;35:2873-926.

[13] Beck AW, Sedrakyan A, Mao J, Venermo M, Faizer R, Debus S, et al. Variations in Abdominal Aortic Aneurysm Care: A Report from the International Consortium of Vascular Registries. 2016.

[14] Karthikesalingam A, Vidal-Diez A, Holt PJ, Loftus IM, Schermerhorn ML, Soden PA, et al. Thresholds for Abdominal Aortic Aneurysm Repair in England and the United States. http://dxdoiorg/101056/NEJMoa1600931. 2016.

[15] Benarroch-Gampel J. SCVS - Does Aneurysm Size Matter?: Lack of Adherence to Diameter Threshold Criteria for Repair of Abdominal Aortic Aneurysms. 2016.

[16] Petit-Zeman S, Locock L. Health care: Bring on the evidence. Nature News. 2013;501:160.