

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Cardiac diagnostic workup for atrial fibrillation after transient ischaemic attacks in England and Wales – Results from a cross-sectional survey
<b>AUTHORS</b>	Geraghty, Olivia; Korompoki, Eleni; Filippidis, Filippos; Rudd, Anthony; Veltkamp, Roland

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Luciano Sposato London Health Sciences Centre, Western University, London, Ontario, Canada.  Speaker honoraria - Boehringer Ingelheim
<b>REVIEW RETURNED</b>	14-Jun-2016

<b>GENERAL COMMENTS</b>	<p>This study was designed to estimate the overall use of ECG monitoring strategies to screen for atrial fibrillation and echocardiography in patients with TIA in England and Wales. This study shows that 24-hour Holter monitoring, a very basic and short monitoring method, is underused or used too late in the majority of TIA services. Echocardiography and MRI are also underused.</p> <p>Major comments</p> <p>1) Prolonged monitoring may not be warranted for all TIA patients. This is based on differing levels of AF suspicion related to clinical, neuroimaging and echocardiographic factors. As such, the results of question #26 in the survey are of major importance. The authors express in the discussion that “detection of AF largely depends on history” (line 23, page 8) but I was not able to see this results in the manuscript. It is stated in the abstract that “Diagnosis of AF largely depends on medical history and 12-channel ECG (94.1%)” but I am not totally sure about what this means and this number is not shown in the results section. It would be interesting to see these results presented in more detail. The discussion may need to emphasize in the discussion that, based on the clinical presentation of the TIA, not all patients may require prolonged monitoring. It would be interesting see if there is any correlation between the use of prolonged monitoring and the use of clinical/neuroimaging data to stratify the odds of detecting AF after a TIA.</p> <p>2) Regarding question #26, given the fact that this study is based on TIA patients, it would have been interesting to assess whether cortical symptoms (aphasia, neglect, etc.) influence the decision to pursue a more thorough investigation of AF. The low number of MRIs done in the study make the question about multiple or large infarcts less relevant.</p>
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	<p>3) Although correctly addressed under limitations, the low proportion of responders could have resulted in selection bias.</p> <p>Minor comments</p> <p>1) The authors may want to clarify in the methods section that for the purpose of this study</p> <p>2) In page 3, under “strengths”, The first survey among all TIA service leads in England to determine the current diagnostic and therapeutic practice in the UK”, please add “and Wales” after England.</p> <p>3) A brief description (two sentences) of how TIA services work in England and Wales would be useful for international readers.</p> <p>4) Results about neuroimaging studies are reported but this seems to be beyond the scope of the study.</p>
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<b>REVIEWER</b>	Louisa M Christensen Herlev Hospital, dept of Neurology Denmark
<b>REVIEW RETURNED</b>	22-Jun-2016

<b>GENERAL COMMENTS</b>	<p>Thank you for a nice manuscript, the aim and method are clearly stated and there are a sufficient amount of questions to be answered.</p> <p>The study uses a webbased survey questionnaire to obtain information regarding the amount of cardiac workup provided for TIA patients in NHS clinics/centers in the UK. The results showed that the majority of TIA patients recieve CT as primary modality and only a few recieve Echocardiografy. The monitoring services are also few and brief. although opinionbased on the 40 % responding leads I find it interesting and should create more focus on cardiac workup and workup in general on TIA patients.</p> <p>I have a few questions I would like to be added or maybe reflected upon.</p> <p>1. Table 1 is in my opinion not an easy read - it is unclear to me wether the row or coll. are representing the amount of services/centers. I think your figures are MUCH better ;)</p> <p>2. why is the respondents rate so low ? 40 %</p> <p>3. And probably more important; are there any differences in the responding centers vs the non responding ?</p> <p>You suggest that the "better" centers are the responders, and centers without a clearly defined TIA practice might be less willing to respond,</p> <p>The describtion of the responding centers states that the majority (75%) offers hyperacute services, yet I miss a comparison between responders and non responders.</p>
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	<p>Are your results reflecting specific acute centers or a certain geographical / soc.economic areas ?</p> <p>other than that I think it is a nice paper, eventhough as a foreign reader it does not directly relate to our standards but definetly makes one consider the level own practice for these patients.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Luciano Sposato

Institution and Country: London Health Sciences Centre, Western University, London, Ontario, Canada.

Competing Interests: Speaker honoraria - Boehringer Ingelheim

This study was designed to estimate the overall use of ECG monitoring strategies to screen for atrial fibrillation and echocardiography in patients with TIA in England and Wales. This study shows that 24-hour Holter monitoring, a very basic and short monitoring method, is underused or used too late in the majority of TIA services. Echocardiography and MRI are also underused.

#### Major comments

1) Prolonged monitoring may not be warranted for all TIA patients. This is based on differing levels of AF suspicion related to clinical, neuroimaging and echocardiographic factors. As such, the results of question #26 in the survey are of major importance. The authors express in the discussion that “detection of AF largely depends on history” (line 23, page 8) but I was not able to see this results in the manuscript. It is stated in the abstract that “Diagnosis of AF largely depends on medical history and 12-channel ECG (94.1%)” but I am not totally sure about what this means and this number is not shown in the results section. It would be interesting to see these results presented in more detail. The discussion may need to emphasize in the discussion that, based on the clinical presentation of the TIA, not all patients may require prolonged monitoring. It would be interesting see if there is any correlation between the use of prolonged monitoring and the use of clinical/neuroimaging data to stratify the odds of detecting AF after a TIA.

We agree with the reviewer that prolonged ECG monitoring beyond 24 hours may not be necessary in all TIA patients. Instead, selecting patients based on clinical, neuroimaging and echocardiographic characteristics may be a more effective approach. Thus, we asked the TIA leads to provide the reasons that prompt them to search further selected TIA patients with more prolonged ECG monitoring techniques. Interestingly, neuroimaging characteristics, i.e. multiple territory embolic looking infarcts was the most prevalent reason for more prolonged monitoring followed by cryptogenic stroke and younger age.

These results are presented in Table 2: Reasons in rank order (1: least important, 7: most important) that prompt physicians to do more prolonged ECG monitoring for occult paroxysmal AF detection in the event of a normal 24-hour ECG. (page 7)

Following the reviewer’s comment this information has been added to the manuscript: page 6 lines 22-27, page 7 (table 2) and also in discussion (page 9 lines 17-21) Unfortunately, the nature of this study does not allow us to stratify the odds of detecting AF after TIA.

With regards to the second comment, in our study 94.1% of the responders replied that the vast majority of TIA patients (>75%) receive a 12-lead ECG. This is mentioned in results (page 6, line 10), in the abstract (page 2, line 14) and in also in table 1. In light of the reviewer’s comment we have made this information more clear in the abstract (page 2, line 14-15) “Diagnosis of AF largely depends on medical history and 12-channel ECG which is performed in the vast majority of TIA patients

(>75%) in 94.1% of the TIA services.”

Regarding the third comment we have added in the discussion:

“However, we have to acknowledge that prolonged monitoring may not be required in all TIA patients but only in selected patients with specific clinical and neuroimaging characteristics. Interestingly in our study multiple embolic infarcts in neuroimaging, cryptogenic stroke and younger age were the most prevalent reasons for prolonged ECG monitoring beyond 24-hours.” (page 9, lines 17-21).

2) Regarding question #26, given the fact that this study is based on TIA patients, it would have been interesting to assess whether cortical symptoms (aphasia, neglect, etc.) influence the decision to pursue a more thorough investigation of AF. The low number of MRIs done in the study make the question about multiple or large infarcts less relevant.

Thank you very much for this very good suggestion. Unfortunately, we did not ask the TIA leads whether particular clinical symptoms upon presentation including presumed cortical syndromes serve as a guidance for decision making regarding prolonged monitoring for AF detection. In the revised manuscript, we added this limitation in the discussion on page 11, lines 15-19.

3) Although correctly addressed under limitations, the low proportion of responders could have resulted in selection bias.

We acknowledge the relatively low response rate of responses despite our efforts to maximize the rate by sending 3 reminder emails. This has been highlighted in the limitations of the study (page 3) and also in the discussion (page 10, line 30).

#### Minor comments

1) The authors may want to clarify in the methods section that for the purpose of this study

The purpose of the survey has been clarified in methods as suggested by the reviewer (Page 5 lines 7-8)

2) In page 3, under “strengths”, The first survey among all TIA service leads in England to determine the current diagnostic and therapeutic practice in the UK”, please add “and Wales” after England.

The missing words (“and Wales”) have been added.

4) A brief description (two sentences) of how TIA services work in England and Wales would be useful for international readers.

We have added this information in the introduction (page 4, line 29, page 5, lines 1-5)

“National Clinical Guidelines for TIA management in England require all high risk patients (ABCD2 score of 4 and above) to be assessed and management started within 24 hours of onset of symptoms and all other patients within 1 week. The median number of neurovascular clinics provided by each hospital per month is 20 and most are set up to provide specialist assessment and brain and carotid imaging as an out-patient on the day the patient is seen.”

1. Intercollegiate Stroke Working Party. National Clinical Guidelines for Stroke 4th edition. London 2012 <https://www.rcplondon.ac.uk/file/1299/download?token=mcyQFjEq>

2. Sentinel Stroke National Audit Programme. Acute Organisational Audit 2014 <https://www.strokeaudit.org/results/Organisational.aspx>

4) Results about neuroimaging studies are reported but this seems to be beyond the scope of the

study.

The aim of the present survey was to investigate possible variations in the cardiac work up for AF detection in TIA patients in the UK. As mentioned before (major comment 1), specific neuroimaging characteristics such as embolic infarcts, may guide medical decision for a more extensive work up for AF detection according to the TIA leads. Considering that about 1/3 of TIA patients have positive MRI findings it is important to know which modality was preferred as first choice. In 43% of the trusts less than 25% of TIA patients receive MRI as first line imaging. Therefore, we do not think that results regarding brain imaging are irrelevant to this study.

Reviewer: 2

Reviewer Name: Louisa M Christensen

Institution and Country: Herlev Hospital, dept of Neurology, Denmark

Competing Interests: none declared

Thank you for a nice manuscript, the aim and method are clearly stated and there are a sufficient amount of questions to be answered. The study uses a webbased survey questionnaire to obtain information regarding the amount of cardiac workup provided for TIA patients in NHS clinics/centers in the UK. The results showed that the majority of TIA patients receive CT as primary modality and only a few receive Echocardiography. The monitoring services are also few and brief. although opinion-based on the 40 % responding leads I find it interesting and should create more focus on cardiac workup and workup in general on TIA patients.

I have a few questions I would like to be added or maybe reflected upon.

1. Table 1 is in my opinion not an easy read - it is unclear to me whether the row or coll. are representing the amount of services/centers. I think your figures are MUCH better.

Thank you very much for your comment. Table 1 has been modified accordingly.

2. Why is the respondents rate so low ? 40 %

We acknowledge the relatively low response rate of responses despite our efforts to maximize the rate by sending 3 reminders (methods, page 5, line 27). This limitation has been highlighted in the limitations of the study (page 3) and also in the discussion (page 10, line 30). Unfortunately, this is a limitation of many surveys. For example, a recently published global survey on the diagnostic evaluation and management of cryptogenic ischemic stroke the response rate was only just above 30%. (Giruparajah, M., et al., Global survey of the diagnostic evaluation and management of cryptogenic ischemic stroke. *Int J Stroke*, 2015. 10(7): p. 1031-6.).

3. And probably more important; are there any differences in the responding centers vs the non responding ?

We agree with the reviewer that it is desirable to compare the characteristics of responders and non-responders and to perform a formal comparison in terms of baseline characteristics, geographical areas and socioeconomic status. However, our methodology consisting of an online anonymous questionnaire sent via survey monkey does not allow us to address this comment directly because characteristics of the non-responding trusts are not available. Instead we collected and analyzed as much information as possible about the responding centres (Results, page 6, lines 9-14):

“Of the clinicians who participated, 44 (74.5%) were stroke physicians, 5 (8.5%) were neurologists and 10 (17%) belonged to other specialities. A hyperacute stroke unit exists in 75% of responding

trusts providing a TIA service. A seven day TIA service is provided in 32 (54.5%) of responding trusts. The estimated number of suspected TIA patients seen per year is >500 in 50% of trusts. The majority of trusts (75%) admit less than 10% of TIA patients to inpatient services.”

In practice, our results reflect what is known about typical neurovascular services in England. Thus we added in the discussion (page 11, lines 15-20)

“The characteristics of the services provided by the responding sites reflect what is known about typical neurovascular services in England. The majority are delivered by stroke physicians with a smaller proportion by neurologists. Most run clinics at least 5 days a week and most are set up to establish the likely diagnosis and initiate appropriate secondary prevention on the day that the patient is seen.”

You suggest that the "better" centers are the responders, and centers without a clearly defined TIA practice might be less willing to respond,

We agree with the reviewer that the word “better” may be misleading in this context and have modified the text. As mentioned in the response to the previous comment we are unable to compare responding and non-responding centres directly. In light of reviewer’s comment we have modified the relevant sentence accordingly (discussion, page 11, lines 7-10). ):

“Because of our methods (use of anonymous online questionnaire sent via survey monkey) a comparison between responding and non-responding centres that could indicate whether our sample was representative cannot be made.”

The description of the responding centers states that the majority (75%) offers hyperacute services, yet I miss a comparison between responders and non responders.

Please refer to our previous responses (comments 3a, 3b).

Are your results reflecting specific acute centers or a certain geographical / soc.economic areas ?

Please refer to our previous responses (comments 3a, 3b).

other than that I think it is a nice paper, even though as a foreign reader it does not directly relate to our standards but definitely makes one consider the level own practice for these patients.

We would like to thank the reviewer for the positive feedback.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Luciano A. Sposato Western University. Department of Clinical Neurological Sciences
<b>REVIEW RETURNED</b>	20-Aug-2016

<b>GENERAL COMMENTS</b>	My comments have been addressed satisfactorily. Thank you.
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<b>REVIEWER</b>	Louisa M Christensen Dept of Neurology, Herlev Hospital Copenhagen Denmark
<b>REVIEW RETURNED</b>	22-Aug-2016

<b>GENERAL COMMENTS</b>	<p>My suggestions have been incorporated nicely. I think the manuscript is ready for publication.</p> <p>Figures and tables added helps to understand the results, thank you !</p> <p>Table 2 is a bit busy, but is very interesting and useful.</p>
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