A worldwide survey on intra-operative antithrombotic strategies during non-cardiac arterial procedures

Research protocol

V2.4, dated 2023-03-30

Rationale

Optimal anticoagulation is of vital importance the achieve safe and effective non-cardiac arterial procedures (NCAP). Unfractionated heparin is being used for over 70 years in this regard to prevent thrombo-embolic complications (TEC), such as peripheral emboli, graft thrombosis, intestinal ischemia and myocardial infarction.[1,2] However, heparin also increases bleeding risk. Heparin has a non-linear dose response curve and elimination curve, which makes the effect in the individual patient unpredictable.[3,4] These disadvantages could legitimize heparin monitoring strategies during NCAP. The Activated Clotting Time (ACT) can be used to monitor the intra-operative heparin effect, an already widely accepted concept during cardiac surgery.[5,6] But in anticipation of the first randomised trial comparing heparinization strategies during NCAP, high quality evidence on heparin administration and ACT-monitoring is still lacking.[1,7-9] Few guidelines across the world give recommendations about heparin administration, heparin monitoring, and heparin reversal with protamine. However, if recommendations are made, they vary widely across guidelines and are primarily based on observational studies or on no literature at all.[1,10-15] These might lead to substantial differences in local practices worldwide.

A recently performed survey on heparinization strategies in the Netherlands (to be published) showed considerable variation in antithrombotic protocols between hospitals. The majority of hospitals (39/54; 74%) used a single dose of 5 000 IU heparin for all types of NCAP, regardless of the patient characteristics. A minority (28%) monitored the heparin effect by ACT. There was a large variation in ACT target values (180 – 250 seconds or two times the reference value). International antithrombotic strategies during vascular and interventional radiological procedures have been described and indicated that a fixed primary heparin dose of 5000 IU is administered in 90-100% during NCAP.[2,16-18] Also, a previous survey on differences between surgeons in Europe (European Society of Vascular Surgery) and the United States (Society of Vascular Surgery), described that individually calculated heparin doses were used in 39% vs. 56% respectively, instead of a fixed heparin dose. ACT monitoring was used in 43% vs. 80% respectively during CEA.[19]

Optimal antithrombotic strategies during NCAP are of vital importance to minimize TEC, without increasing bleeding risk. High quality evidence is lacking, and therefore might be the cause for a wide variation in the various international guidelines and local protocols worldwide. Previously published overviews showed substantial differences in applied heparinization strategies and heparin monitoring strategies. The current variation in protocols worldwide is however not known, since the previously published overviews are of older date. Also, these overviews describe single countries or limited amount of vascular surgical societies.

Mapping the current practice in antithrombotic strategies worldwide, gives a complete overview. We aim to identify most widely accepted antithrombotic protocols and specify possible international and intercontinental differences in antithrombotic strategies during NCAP. With this extensive overview we aim to identify possible new research targets and the potential need to harmonize protocols or create new protocols between the various hospitals and vascular surgery and interventional radiology societies worldwide.

Methods

Study design
A comprehensive online survey study. The survey will be accessible via SurveyMonkey: a web-based survey company (www.surveymonkey.com). In order to increase the survey quality and the

international scope, the European Vascular Research Collaborative (EVRC) will consulted during the survey construction phase and data collection phase.

Survey
The survey consists of questions antithrombotic strategies, focussing on unfractionated heparin use, heparin monitoring strategies by ACT and heparin reversal strategies using protamine during NCAP. Questions will specified for carotid endarterectomy, open abdominal aortic aneurysm repair, EVAR/TEVAR, FEVAR/BEVAR and peripheral arterial surgical interventions. The maximum completion time of the survey will be 15 minutes. The complete survey is added in appendix 1.

Recruiting participants
Participants in the direct network of the study team and EVRC steering committee will be contacted via E-mail. The invitational E-mail is added in appendix 2. The survey will be directly accessible via the known social platforms. Frequent reminding requests for participation and inclusion updates will be sent via social platforms. Apart from the steering committee of EVRC, representatives from Europe and beyond will be contacted to participate in spreading the survey.

Analysis
Data will be exported and analysed using the most current version of SPSS (Armonk, NY: IBM corp). Descriptive statistics will be generated. Antithrombotic strategies between different countries, different continents and different international vascular societies will be compared.

Timeframe
We target to include over 1000 participants into the ACTION-survey. The estimated inclusion period is six months. The targeted inclusion period is March 2023 – September 2023.

Ethics and privacy

General Data Protection Regulation (GDPR) of the European Union is taken into consideration. Participants will be asked to share their contact details. The answers to the survey will be processed under a pseudonym. The identity of participants only will be known to the coordinating researcher (MH) and principal investigator (VJ). The data will be used for research purposes only.

Publication policy

The results of research will be submitted for publication in a peer-reviewed scientific journal. The publication authors will be: Max Hoebink, Liliane Roosendaal, Lan Tran, Arno Wiersema, Vincent Jongkind, ACTION-1 collaborative, EVRC collaborative.

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Appendices

Appendix 1: survey questions

The ACTION Survey

Survey about heparin use, heparin monitoring and heparin reversal during non-cardiac arterial procedures (NCAP).

This is a digital survey regarding intra-operative antithrombotic strategies during Non-cardiac Arterial Procedures (NCAP).

With this survey we aim to get detailed insight into the current practice of antithrombotic strategies during NCAP worldwide.

To reach out to you for any additional questions and to analyse any possible geographic trends we ask you to state your name, country of origin, hospital and E-mail address.

Your answers will be processed under a pseudonym. Your personal data will be protected by a password and will only be saved in the database of the Amsterdam University Medical Centre. Your data will be deleted from the database 10 years after publication. The General Data Protection Regulation (GDPR) will be taken into consideration when processing your data

Taking the survey will take approximately 10 minutes.

Thank you for participating in this survey

Page 1 #Introduction

1. Do you agree with processing the data of this survey, according to the previous statement?
2. What is your profession?
    a. Vascular surgeon
    b. Interventional radiologist / angiologist / interventional cardiologist
    c. Other
3. Which country do you work?
4. Which hospital do you work?
5. What is your E-mail address?

#Questions per type of procedure (CEA, EVAR/TEVAR, FEVAR/BEVAR, open abdominal aortic repair, peripheral arterial surgical procedures)

Page 2 #Antithrombotic strategy (fill in per type of procedure)

1. What kind of antithrombotic strategy do you use?
    a. I do not perform this procedure (go to next procedure)
    b. I use the same antithrombotic strategy as during ….. (go to next procedure)
    c. I use a different antithrombotic strategy

Page 3 #Heparin dose (fill in per type of procedure)

1. What kind of IV anticoagulant do you administer during the procedure?
    a. A fixed starting dose of heparin (for example: 5000 IU)
        i. Explain how many IU …….
    b. A heparin dose based on actual bodyweight (for example: 100 IU/kg
        i. Explain how many IU/kg ……..
    c. A heparin dose based on ideal bodyweight (for example: 100 IU/kg
        i. Explain how many IU/kg ……..
    d. I use LMWH instead of unfractionated heparin (go to next procedure)
    e. I do not use heparin (go to next procedure)
    f. Other heparin starting dose, please specify …… (go to next procedure)
2. Do you consider giving additional unfractionated heparin after the starting dose?
    a. No (go to protamine)
    b. Yes, a fixed dose according to a standardized protocol (not based on ACT) (go to protamine)
    c. Yes, a dose based on bodyweight according to a standardized protocol (not based on ACT) (go to protamine)
    d. Yes, by using a continuous heparin perfusor (with or without ACT)
        i. Explain how many IU / hour or IU / kg / hour
        ii. Do you adjust continuous heparin perfusion based on ACT?
            1. Yes
            2. No, based on APTT (go to protamine)
            3. No, please specify …… (go to protamine)
    e. Yes, primarily based on ACT
    f. Yes, primarily based on APTT (go to protamine)
    g. Yes, a fixed dose primarily based on subjective coagulation status and/or length of surgery (not according to a standardized protocol, not based on ACT) (go to protamine)
    h. Yes, a dose based on bodyweight primarily based on subjective coagulation status and/or length of surgery (not according to a standardized protocol, not based on ACT) (go to protamine)
    i. Other, please specify …….. (go to protamine)

Page 4 #Activated Clotting Time (fill in per type of procedure)

1. What is your target ACT? (choose 1 of the following options)
    a. ……..seconds (minimal acceptable value)
    b. ……..times the reference value
2. How many minutes after heparin administration do you perform the first ACT measurement?
    a. ……. seconds
3. How many minutes after reaching the target ACT do you measure the ACT again?
    a. ……. seconds
4. How much additional heparin do you administer? (explain how many IU of heparin at which ACT)
    a. ……. heparin (IU of IU/kg) at ACT (sec)
    b. ……. heparin (IU of IU/kg) at ACT (sec)
    c. ……. heparin (IU of IU/kg) at ACT (sec)
5. What is the target ACT at the end of the procedure?

a. ……. seconds (fill in the maximum acceptable ACT value)

Page 5 #Protamine (fill in per type of procedure)

1. What is the primary indication to give protamine?
    a. I do not administer protamine during this type of procedure (go to next procedure)
    b. Based on subjective intra-operative coagulation status and/or length of surgery (not based on ACT) (go to next procedure)
    c. Based on the amount of heparin administered (nog based on ACT) (go to next procedure)
    d. Based on ACT at closure
    e. Other indication (explain): …….. (go to next procedure)

Page 6 #General questions

1. Would you like to improve something on your current antithrombotic protocol(s)? (multiple options possible)
    a. No
    b. I would like protocol(s) to be more tailored to the individual patient
    c. I would like to monitor the effect of heparin intra-operatively by ACT
    d. Other, explain:……
2. If you measure the ACT, what device do you use to measure the ACT during NCAP?
    a. I do not monitor the effect of heparin by ACT
    b. Haemostasis Management System plus (HMS plus, Medtronic®)
    c. ACT Plus (Medtronic®)
    d. Hemochron® Signature Elite
    e. Hemochron® Response
    f. i-STAT (Abbot®)
    g. other, please specify:……..

Page 7 #Additional comments

1. Do you have any additional comments regarding your antithrombotic strategies during NCAP?
    a. ……..

Page 8 #Thank you

We thank you for completing this survey.

Awaiting the first randomised trial regarding ACT guided heparinization during NCAP (ACTION-1, clinicaltrials.gov: NCT04061798) we aim to provide more detailed insight into antithrombotic strategies during NCAP worldwide with this survey.

If you are interested, we invite you to look into our previous work on antithrombotic strategies during NCAP or on the ACTION-1 website.

Sincerely,

On behalf of the European Vascular Research Collaborative (EVRC) and the ACTION-1 research collaborative,

The ACTION study group:

Arno Wiersema, Vincent Jongkind, Kak Khee Yeung, Lan Tran, Liliane Roosendaal, Max Hoebink

previous research:

Wiersema AM, Jongkind V, Bruijninckx CMA, Reijnen MMPJ, Vos JA, van Delden OM, et al. Prophylactic perioperative anti-thrombotics in open and endovascular abdominal aortic aneurysm (AAA) surgery: A systematic review. European Journal of Vascular and Endovascular Surgery. 2012;44:359–367.

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Appendix 2: invitation E-mail

**attachment: study protocol 'the ACTION survey'* V2.4, dated 2023-03-30*

Dear colleague,

Do you perform non-cardiac arterial procedures (vascular surgery procedures)?

On behalf of the European Vascular Research Collaborative (EVRC), and the ACTION-1 research collaborative, we would like to invite you to participate in the 'ACTION-survey': a worldwide survey on antithrombotic strategies during non-cardiac arterial procedures. This survey will take approximately 10 minutes to fill in.

The purpose of this survey is to obtain detailed insight into the current practice of antithrombotic strategies during NCAP worldwide, potentially identifying the most accepted antithrombotic strategies, knowledge gaps and new research targets. We hope you agree to participate, and fill in the survey via the link below. Also, we would like to ask you to send the link to your colleague vascular surgeons/interventional radiologists/interventional cardiologists to fill in the survey as well. The attached document is the short study protocol.

Please do not hesitate to contact us if you need additional assistance or have any questions.

Thank you for taking the time to consider committing to participate in this project.

Also, on behalf of the European Vascular Research Collaborative (EVRC) and ACTION-1 research collaborative

Sincerely,

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https://www.surveymonkey.com/r/CVQG7MJ