The AVOID study

Audit to quantify the VOlume of disease on axillary ultrasound in the axIlla, by assessing the cortical thickness and number of abnormal noDes, to support surgical management of the axilla

Study Protocol Version 3
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British Society of Breast Radiology

ABS ASSOCIATION OF BREAST SURGERY

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1. Background

For patients newly diagnosed with invasive breast cancer and a normal B-mode axillary ultrasound (US), current standard management of the axilla dictates that those scheduled for primary surgery will proceed with a surgical sentinel lymph node biopsy (SLNB) at the same time as the cancer resection. Similarly, patients with a benign biopsy of B-mode US morphologically indeterminate/ abnormal lymph nodes will also have a SLNB as part of their primary surgical treatment. For patients confirmed on needle biopsy to have lymph node involvement after a B-mode axillary US lymph node biopsy, the recommendation is to continue with an axillary lymph node dissection (ALND). However, a recent review of the UK surgical breast screening audit data demonstrated that around 40% of women who underwent ALND had a low malignant nodal burden defined as 2 or fewer macrometastatic lymph nodes[1].

It Is now accepted practice that patients with isolated tumour cells (ITCs) and micrometastases in excised sentinel lymph nodes do not need further axillary treatment and those with and 1-2 macrometastases may not need further axillary treatment. This means that ALND could constitute overtreatment for a significant proportion of patients undergoing primary surgical treatment.

A survey looking at imaging practices across the UK highlighted that breast units have different cortical thickness thresholds to determine if an axillary lymph node is normal or abnormal, which varies from 2mm or more to 4mm. This impacts on the number of women having an axillary lymph node biopsy test and the likelihood of picking up low volume disease if a lower cortical thickness threshold is used. This data was presented at the British Society of Breast

Radiology in 2018. The breast screening data therefore needs to be interpreted with caution with the caveat that there are different thresholds for lymph node biopsy in the UK[2].

The aim of this audit is to standardise the cortical thickness at a national level to help determine the threshold when needle biopsy of the lymph node is required. We are asking units what their current cortical thickness threshold for axillary biopsy is and we are collecting data on all axillary needle interventions performed in the context of a biopsy proven cancer. The data collected will include benign axillary biopsies as well as malignant biopsies. Collecting the data at this level will help us determine a national cortical thickness threshold and help standardise practice across the UK. It is important when we determine the threshold that we recognise there will be false negatives at SLNB but this should not translate to a completion axillary clearance for low volume disease. It is important to standardise practice to support future audits and research centred around axillary management.

2. Aims and objectives

The primary aims of the AVOID national audit are:

1. Describe current clinical practice with regards to the ultrasound lymph node cortical thickness threshold required to prompt biopsy at different institutions across the UK.
2. Describe the association between cortical thickness threshold used and the volume of malignant lymph node disease found with axillary lymph node dissection.

3. Methods

This is a prospective national collaborative audit. Each participating centre will obtain local audit approval with a confirmatory email showing approval. Participation and data entry will be taken as approval for (anonymised) data to be used for publication purposes. The study will take place in England, Wales, Scotland and Ireland (Northern Ireland and The Republic of Ireland).

3.1 Patient inclusion and exclusion criteria

Inclusion criteria

All patients with a new diagnosis of primary invasive breast cancer (B5b) undergoing an axillary lymph node core biopsy. This includes patients having primary surgery, neo-adjuvant chemotherapy and neo-adjuvant endocrine therapy.

Exclusion criteria

Patients with a new diagnosis of recurrent or metastatic breast cancer.

3.2 Participation identification and recruitment

Breast Units will be asked to nominate a local lead for the audit and data collection. Each unit will be asked to collect information from 25 consecutive cases where the axilla has been biopsied in patients newly diagnosed with invasive breast cancer.

Potential patients will be identified prospectively by the breast radiology department. Prospective data entry would occur on a weekly basis, following the MDT meeting.

Simple demographic, procedure and process data will be contemporaneously collected for each participant. Data will be recorded in an anonymised format using a unique alphanumeric study identification number on a secure web-based database (REDCap) designed by Vanderbilt University(21-23) (http://www.projectredcap.org/).

It is vital that a secure record is kept locally of NHS numbers and corresponding RedCap ID. This will be necessary for a 'staged' data collection and future outcome studies.

To register for the study, participating units are requested to email shelley.potter@bristol.ac.uk to request access to the online database. Each unit will then be designated a unit ID (e.g. MFT), which will be used as a prefix for the patient ID (e.g. MFT001). It is of vital importance that a local secure record is kept within each participating NHS Trust of the RedCap ID with corresponding NHS numbers for future identification of patients. It is vital that this list is kept by the nominated audit lead for each trust.

4. Case Record Form

Attached are the REDCap fields that we will be collecting

4.1 Data capture phases

It is likely that the data capture will occur in several phases.

Phase 1 – This will ideally be prospective where possible. This will 'register' the patient to the study and classify the patient's management.

Phase 2 – This can be collected prospectively or retrospectively where possible.

5. Data management and storage

Data collection will occur in accordance with Caldicott II principles. All units will prospectively register the audit with their local audit offices prior to commencing data collection. Data for each patient will be pseudo-anonymised using a unique alphanumeric study identification number. This key will be kept locally within each participating NHS trust. No patient identifiable data will be recorded centrally on redcap for the purpose of the audit.

Study data will be collected and managed using REDCap electronic data capture tools hosted at University of Bristol. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. More information about the consortium and system security can be found at http://www.projectredcap.org/.

6. Data analysis

All data analysis for this audit will occur centrally using the data uploaded to redcap and will be led by the steering group. All individual units will have access to their own data and will be able to perform their own analyses. Local collaboratives and hospital Trusts will have ownership of their own data and will be able to present it locally if they so wish.

Simple summary statistics will be calculated for each outcome and regression analysis used to control for predictive variables. Data will be tested for distribution and differences between groups using unpaired t-tests, Mann-Whitney U tests and Chi squared tests as appropriate. There is no power calculation for this audit.

7. Publication and authorship policy

All presentations and publications will be made on behalf of the AVOID Study Research Collaborative.

Three levels of authorship are proposed based on degree of study participation:

7.1 Named authors

Named authors will be required to meet the International Committee of Medical Journal Editors (ICMJE) criteria (www.icmje.org) for authorship based on the following four criteria:

1. Substantial contribution to the conception or design of the work; or the acquisition, analysis or interpretation of the data for the work and
2. Drafting the work or revising it critically for important intellectual content and
3. Final approval of the version to be published and
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The ICMJE states '*when submitting a manuscript authored by a group, the corresponding author should specify the group name if one exists and clearly identify the group members who can take credit and responsibility for the work as authors. The byline of the article identifies who is directly responsible for the manuscript and MEDLINE lists authors*

whichever names appear on the byline. If the byline includes a group name, MEDLINE will list the names of individual group members who are authors or who are collaborators, sometimes called non-author contributors, if there is a note associated with the byline clearly stating that the individual names are elsewhere in the paper and whether those names are authors or collaborators.'

It is anticipated that between six and eight individuals will be named on each publication followed by the wording 'on behalf of the AVOID Research Collaborative'. All citable collaborators will be listed at the end of the paper and their roles identified.

7.2 Citable collaborators

Citable collaborators will have made a considerable contribution to the study but will not have met the ICMJE criteria for authorship (non-author contributors). These will include trainee or consultant leads at each centre and other trainees or team members (including consultant surgeons, clinical nurse specialists or research nurses) who have recruited at least 10 complete case records to the study.

7.3 Acknowledged collaborators.

Acknowledged collaborators will include members of the clinical multidisciplinary team who contributed patients to the audit but did not personally collect data or recruit patients and trainees who have made a lesser contribution to patient recruitment and data collection than that required for citable collaborator status. Trainees who are acknowledged contributors will also receive a certificate of participation for inclusion in their portfolios.

The final reports will be prepared in accordance with the STROBE(24) (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

8. Audit Governance

1. The main aim of the AVOID prospective audit is to collect data reflecting current clinical practice. In addition, an exploratory analysis will be conducted to establish the optimal lymph node cortical thickness biopsy threshold required to limit surgical overtreatment of the axilla.

A unit lead will be identified, who will coordinate the audit locally, in keeping with local protocol and policies. It is assumed that all breast cancer patients will be discussed at MDT.

The named unit project lead will act as the principal investigator for each unit. Audit approval will need to be sought from the Clinical Audit Department for the project prior to commencing data collection, and the audit reference number emailed to nisha.sharma2@nhs.net. Dr Sharma will then complete the RedCap request form for access to the database and the individual will receive an email from the RedCap database team.

Each unit participating in AVOID will retain full ownership of its own data. Authorship on publications will follow the guidance in section 7, above. Summary statistics will be calculated

for each participating region and fed back to individual units to allow comparison with national averages and ranges. Overall audit results and results from individual centres will be fed back to the BSBR.

9. Audit Management

The Audit Steering Committee (ASC) will

i) maintain oversight of the AVOID national audit. This will include management and data ownership of global data entered onto RedCap.

ii) assess future applications for access to the AVOID dataset with regards to putative research or audit projects. The committee will be advised on these applications by the Audit Advisory Group.

iii) lead future applications to grant awarding bodies in order to conduct ethically approved research / outcomes studies using the AVOID dataset.

iv) work with the audit advisory group to respond to any potential future challenges to the audit

10. References

1. Meeting Abstracts from the British Society of Breast Radiology Annual Scientific Meeting 2022. Breast Cancer Research. 2023;25(S1):73.

2. Guidance on screening and symptomatic breast imaging. 4th edition. RCR 2019.