Implementation of echocardiographic contrast agents into clinical practice: a United Kingdom National Health Service Survey on behalf of the British Society of Echocardiography

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Aims
The administration of echocardiographic contrast agents has been shown to improve accuracy and be cost-effective in patients with suboptimal endocardial definition. We sought to investigate the implementation of contrast agents in clinical practice.

Methods and results
An electronic questionnaire was devised to determine the use of contrast ultrasound agents in clinical practice and sent electronically to echocardiography departments at each national health service hospital within the UK. Out of 198, 107 departments responded (54%). Out of 673,121 echocardiograms, 25,834 (3.8%) were performed with contrast. Out of 551 echocardiography machines, 358 (65%) were suitable for contrast use. Of the sonographers, out of 711, 112 (15.8%) could perform i.v. cannulation and 42 (5.9%) could administer contrast independently. The median time for an echocardiographic examination was 30 min (inter-quartile range 30–45 min). Significant predictors of contrast use were the presence of a consultant cardiologist with subspecialty training in echocardiography (odds ratio 8.7, \( P = 0.004 \)), the presence of a stress echocardiography service (odds ratio 2.3, \( P = 0.004 \)), and the presence of a physician during the day (odds ratio 3.0, \( P = 0.04 \)). Reasons for impediment in administering contrast were staff training (34.6%), extra time required for a contrast study (29.9%), and the expense of contrast (18.7%).

Conclusion
The use of echocardiographic contrast agents within routine echocardiographic practice in the UK is limited to <4% of all transthoracic echocardiographic studies. Major barriers to the implementation of contrast use are the absence of cardiac imaging specialists directly supervising echocardiography departments and the training of sonographers to independently administer contrast.

Keywords
Contrast • Echocardiography

Introduction
Between 10 and 15% of patients undergoing standard transthoracic echocardiography have suboptimal left ventricular endocardial definition.¹,² In patients referred for stress echocardiography a higher proportion (up to 25%) may have two or more poorly visualized segments.³ Furthermore, in those with suboptimal images, a large proportion of myocardial segments are not visualized well.¹ This can lead to an inaccurate quantification and assessment of left ventricular function. An accurate assessment of the LV ejection fraction is critical in the management of multiple pathologies. In patients with heart failure, eligibility for treatment with cardiac resynchronization therapy and prophylactic implantable cardiac defibrillators is based on an ejection fraction of <35%.⁴,⁵ Chemo-therapy regimens are known to be cytotoxic with a potential to cause left ventricular impairment. Cessation of these agents is

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recommended if the ejection fraction during treatments falls by >10%.6 The use of echocardiographic contrast agents has been shown to enhance the visualization of left ventricular wall segments, improve the quantification of the LV ejection fraction, reduce inter-observer variability, and be more cost-effective as a result of less downstream investigations.1,7 Recent guidelines recommend the use of echocardiographic contrast agents where two or more segments are not well visualized9,10. Despite the evidence base and guideline recommendations for the use of contrast agents in routine echocardiographic practice, there are no data identifying the implementation of guidelines into clinical practice.

Methods

Identification of echocardiography departments within the UK
A database of all United Kingdom National Health Service (NHS) Trusts was created from the NHS website (www.nhs.uk). Each NHS trust may be composed of several hospitals. Therefore each trust was contacted by telephone to establish which of its constituent hospitals had an echocardiography department. The clinical head of the echocardiography department in each hospital was identified and the contact e-mail address was obtained.

Questionnaire design
A questionnaire was designed to identify the prevailing practice of contrast echocardiography use within the UK. Thirty-two questions were formulated to identify data in four core areas.

Core areas and data acquired
(1) Contrast use and workflow patterns
   (a) The number of echocardiograms and stress echocardiograms performed with and without contrast.
   (b) The workflow organization for patients who need contrast including the type of list, time duration of studies and any extra time allocated for contrast studies.

(2) Training of staff
   (a) Number of sonographers able to perform i.v. cannulation and administer contrast.
   (b) The medical staffing in the echocardiography department.

(3) Facilities
   (a) The type of department (tertiary centre or district general hospital).
   (b) The number of echocardiography and contrast capable echocardiography machines.
   (c) The type of contrast available for use in the department.

(4) Contrast protocols
   (a) The presence of a departmental policy on contrast administration.
   (b) The requirement of patient to read a patient information sheet and sign a consent form.

Questionnaire mailing
The questionnaire was placed into an electronic template using commercial online software. The questionnaire was e-mailed to the head of echocardiography at each designated hospital. Non-respondents to the initial e-mail were sent a reminder at weekly intervals.

Statistics
Data are reported as a median and inter-quartile range or number and percentage. Multiple logistic regression analysis was used to identify predictors of the use of echocardiographic contrast agents. All tests of significance were two sided. A probability value (P) of <0.05 was considered significant. Statistical analysis was performed using StatsDirect Version 2.5.7 (StatsDirect, UK).

Results
A total of 198 acute NHS hospitals with echocardiography departments were identified. One hundred and ten (55.6%) of echocardiography departments responded. Of these, three questionnaires were not fully completed and therefore excluded. Therefore data from 107 (54%) departments were used for the final analysis. From this cohort, 30 departments (28%) were tertiary centres, and 77 (72%) were district general hospitals.

Contrast use
The total number of echocardiograms performed per year was 673,121 (median of 6000 per department, inter-quartile range 4500–10,000). Of these 25,834 (3.8%) were performed with contrast (median 100 per department, inter-quartile range 20–400). Seventy-four departments performed stress echocardiograms. A total of 32,167 stress echocardiograms were performed (median 255 per department, inter-quartile range 30–500). Of these 21,417 (66.6%) were performed with contrast (median 76 per department, inter-quartile range 43–100).

Facilities
The total number of echocardiography machines operated by the 107 departments is 551 (median 5 and inter-quartile range 3–6). Of these 358 (65%) machines (median 3 per department) had software allowing contrast settings (Table 1). Eighty-one departments (75.7%) used only Sonovue contrast. Eleven departments (10.3%) used both Sonovue and Optison and 15 departments (14%) used Optison only.

Table 1 Number of ‘contrast capable’ echocardiography machines per department

<table>
<thead>
<tr>
<th>Number of ‘contrast capable’ echocardiography machines</th>
<th>Number (%) of departments</th>
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<tbody>
<tr>
<td>0</td>
<td>4 (3.7)</td>
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<tr>
<td>1</td>
<td>9 (8.4)</td>
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<tr>
<td>2</td>
<td>24 (22.4)</td>
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<td>3</td>
<td>22 (20.5)</td>
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<tr>
<td>4</td>
<td>25 (23.3)</td>
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<tr>
<td>5</td>
<td>11 (10.2)</td>
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<td>6</td>
<td>7 (6.5)</td>
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<tr>
<td>7</td>
<td>3 (2.8)</td>
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<tr>
<td>8</td>
<td>1 (0.9)</td>
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<tr>
<td>9</td>
<td>1 (0.9)</td>
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</tbody>
</table>
Staff and training

There were a total of 711 sonographers [median 6 per department (inter-quartile range 5–9)] employed. Of these 112 (15.8%) could perform i.v. cannulation and 42 (5.9%) could administer contrast independently. The number of sonographers who could obtain i.v. access or administer contrast varied between departments (Tables 2 and 3). In 88 departments (82.2%), only doctors could administer contrast. In 18 departments (17%) both sonographers and doctors could administer contrast and in one department (0.9%) only a sonographer administered contrast. Doctors were present for the full duration of the working day in 68 departments (63.6%). The designated head of the department was a consultant cardiologist with subspecialty training in echocardiography in 76 departments (71%), general consultant cardiologist in 5 departments (4.7%), sonographer in 22 departments (20.6%), and 4 departments (3.7%) reported no direct head of department.

Work-flow

The median time for a complete echocardiographic examination was 30 min (inter-quartile range 30–45 min). Fifty-four departments (50.4%) allowed extra time for contrast studies. The median extra time allowed was 15 min (inter-quartile range 10–15 min). Thirty-six departments (33.7%) could administer contrast to any patient undergoing an echocardiogram if required. Forty-three departments (43%) arranged a special list for patients who required contrast. Nineteen departments (17.8%) could arrange a contrast study if needed although did not routinely administer contrast. Nine departments (8.4%) did not administer contrast in any patient.

Protocols

A protocol for the administration of echocardiographic contrast agents was used by 54 departments (55.1%). Twenty-nine departments (29.6%) required patients to read an information sheet prior to the administration of contrast and 23 departments (23.4%) required patients to sign a consent form agreeing to the use of contrast agents.

Monitoring of the LV ejection fraction in patients undergoing serial measurements

Twenty-three departments (21.5%) routinely used two-dimensional (2D) visual estimates to monitor the ejection fraction in patients undergoing serial monitoring of LV function. Forty-nine departments (45.8%) routinely used the 2D Simpson’s Biplane method. Twenty-three departments (21.5%) used the 2D contrast-enhanced Simpson’s Biplane method and 12 departments (11.2%) used 3D volumes.

Barriers to the introduction of contrast into the echocardiography laboratory

The most common reason cited for difficulties in the introduction of contrast agents into routine echocardiographic was staff training in 37 departments (34.6%), extra time required for contrast study in 32 departments (29.9%), expense of contrast in 20 departments (18.7%), safety of contrast agents in 9 departments (8.4%), and the lack of suitable echocardiographic machines in 9 departments (8.4%).

Predictors of contrast agent use

A logistic regression analysis was performed to identify predictors of the use of contrast agents within an echocardiography department. The type of hospital (tertiary or district general), ≥ 5 echocardiography machines, ≥ 6 sonographers, the presence of sonographers who could perform i.v. cannulation, the presence of sonographers who could administer contrast, time duration of a study ≥ 30 min, the presence of a physician throughout the duration of the working day, the presence of a consultant cardiologist with subspeciality training in echocardiography, and the presence of a stress echocardiography service were entered in to the logistic regression model.

Significant predictors of the use of contrast were the presence of a consultant cardiologist with an interest in echocardiography [odds ratio 8.7 (inter-quartile range 2.0–38.0) \( P = 0.004 \), the
presence of a stress echocardiography service [odds ratio 2.3 (inter-quartile range 2.1–47.4) \(P = 0.004\)] and the presence of a physician during the day [odds ratio 3.0 (inter-quartile range 1.1–12.9) \(P = 0.04\)].

The only significant predictors of the use of contrast in >10% of echocardiograms were the presence of a sonographer able to perform i.v. cannulation [odds ratio 7.2 (inter-quartile range 1.3–38) \(P = 0.02\)].

**Discussion**

This is the first study to examine the integration of contrast echo-


cardiography into routine clinical practice within a large cohort of echo-
cardiographic departments. Several previous studies have
identified between 10 and 15% of routine echocardiograms
having incomplete endocardial border visualization. In this
study, only 3.8% of studies were undertaken with contrast en-
hancement. Thus, at least 60% of patients with suboptimal
images did not receive contrast administration. Only one-third of
echocardiography departments could administer contrast routinely
in patients whose echo windows were suboptimal at the same visit.
Of concern is that 8.4% of departments do not administer contrast
at all. These figures are disappointing given the wealth of evidence
pointing to improved accuracy, cost effectiveness, and reduced re-
quirement for further investigations associated with the use of con-
trast agents. In contrast, more than two-thirds of stress
echocardiograms were performed with the aid of contrast
enhancement.

Several barriers to the routine implementation of contrast use in echocardiography departments were identified by the survey. The administration of contrast requires a team approach to manage several processes and steps required to achieve the optimal benefit to patients. This requires obtaining consent from the patient, achieving i.v. access, administering the contrast, optimizing machine settings for contrast use, and interpretation of the study by the sonographer or physician.

**Administration of contrast and staff training/supervision**

The logistic regression model shows that the administration of contrast to >10% of studies was associated with the presence of at least one sonographer in the department who could perform i.v. cannulation. Overall, the proportion of sonographers who can perform i.v. cannulation (15.8%) and administer contrast agents (5.9%) were small. Within the UK there are no licensing or training schemes for sonographers who wish to perform i.v. cannulation or administer contrast, although local protocols may exist.

Logistic regression also showed the presence of a cardiologist with subspecialty training in echocardiography, the presence of a stress echocardiography service and the presence of a doctor throughout the working day were predictors of the use of con-
trast. Both in the UK and USA there is a wide variation in the supervision, training, and support provided to sonographers in echocardiography departments. Although a dedicated cardiologist with expertise in echocardiography may be present in academic centres, this may not be the case in smaller, non-academic centres. In this study, 29% of echocardiography departments did not have a cardiologist with subspecialty training in echocardiography. Another important consideration for contrast echocardiog-


raphy is the administration of contrast, albeit very rare, may result
in an allergic reaction and, therefore, requires a physician in attend-
ance within the department. In this study, 36.4% of departments
did not have a physician present during the working day to oversee contrast administration. Indeed, almost one-third of departments reported that the lack of staff trained in contrast echocardiography was a barrier to the use of contrast. This serves to highlight the need for specialist training, supervision and support of echocardiography departments by specialist medical staff to provide an optimal service which is unlikely to be provided by a general cardiologist.

**Work-flow and facilities**

The median time duration of a study was 30 min. Despite this, the
duration of an echocardiogram was not a significant predictor of
the use of contrast. This is potentially because almost half of
departments provided extra time if contrast was needed. However, almost one-third of departments thought that the extra time required for a contrast enhanced study was a barrier towards the use of echocardiographic contrast agents. A possible explanation for the conflicting view maybe that departments which allow extra time for contrast enhanced studies may only use contrast in patients where image quality is almost un-
interpretile. This very small volume of patients may not impede work-flow in the department. Time may be more of a constraint if departments adopted a more liberal and appropriate use of con-
trast in the 10–15% of patients in whom more than two segments are not visualized.

**Reimbursement**

Nearly one in five departments stated that the reason for limited
contrast use was the expense of the contrast agent. In the UK, a
provider does not get additional reimbursement for the use of
contrast agents during echocardiography. Several studies have
shown that the use of echocardiographic contrast agents reduces
the number of un-interpretable studies with reduced referrals
for other diagnostic tests. Overall these studies showed
that, despite the extra initial expense, contrast agents prod-
ced a net saving per patient.

**Protocols and consent**

This overview of UK practice suggests a protocol for the adminis-
tration of echocardiographic contrast agents was in place in 51% of
departments, 29% required patients to read an information sheet
prior to the administration of contrast, and 23% required patients
to sign a consent form agreeing to the use of contrast agents. In a
retrospective review of adverse effects related to 66,164 adminis-
tered doses of two contrast agents, Wei et al. found adverse
reactions to contrast in just 0.01% of cases. Multiple studies have
confirmed contrast administration to be safe, although there is a very small risk of allergic reactions and minor adverse
effects. Neither the American Society of Echocardiography or
European Association of Echocardiography guidelines mandate
signed patient consent to undergo contrast echocardiography. The Inter-societal accreditation commission standards for laboratory accreditation require a written policy for the use of contrast agents. A protocol may be helpful for staff in order to reinforce the indications for contrast echocardiography, ensure the safe use of contrast agents and improve work-flow patterns for contrast studies within a department.

**Stress echocardiography**

This survey also identified almost 70% of stress echocardiograms that were performed with the use of contrast compared with only 3.8% of resting transthoracic studies. Furthermore, logistic regression demonstrated that departments performing stress echocardiography was a predictor of the use contrast during their routine transthoracic studies. The result is not surprising as, in the UK, a physician is almost always present during stress echocardiography and there is a high likelihood they will be a cardiologist with an interest in stress echocardiography. The nature of the investigation means there will almost always be an i.v. access line in situ and contrast is usually administered by sonographers in the presence of a physician. Finally, there are numerous stress echocardiography workshops where the use of contrast is encouraged even where resting windows are optimal because of the probability that image quality may deteriorate after stress.

**Limitations**

The data obtained for this study were in the form of an electronic survey. Not all echocardiography departments within the UK responded to the survey or fully completed the survey, although we believe that a sample size of 107 departments (54% of the total number of echocardiography departments within the UK) is approximately representative of current practice. It is possible departments who do not use contrast were less likely to respond to the survey and therefore are under-represented and therefore the overall nationwide use of contrast may be even lower than we report. The data were dependent on reliable information provided by heads of echocardiography departments and there was no other external verification of this information.

**Summary**

The use of ultrasound contrast agents within routine echocardiographic practice in the UK is limited with <4% of studies performed with contrast enhancement. Major barriers to the implementation of contrast use are the absence of senior medical specialists in echocardiography directly supervising echocardiography departments, training, and accreditation of sonographers to independently administer contrast and perform i.v. cannulation and re-imbursement of contrast costs.

**Conflict of interest:** R.S. has received honorarium for lectures from Bracco and sits on the advisory board for GE healthcare. R.K. and G.L. have received educational meeting support from Bracco. S.B. has no conflicts of interest to declare.

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