This document is part of my dissertation: MSc in Medical Ultrasound (Echocardiography), Imperial College London, awarded in 2015.

Results, conclusions and appendices have been removed.

Declaration

This is to declare that this project is entirely my own work and has not been submitted to this or any other university.

……

Catherine Stowell

TABLE OF CONTENTS

Abbreviations

AR – Aortic Regurgitation
AS – Aortic Stenosis
AHA – American Heart Association
ASE – American Society of Echocardiography
AVA - Aortic Valve Area
BMI – Body Mass Index
CI – Confidence Interval
CMR – Cardiac Magnetic Resonance
DTTE – Diagnostic Transthoracic Echocardiogram
EAE - European Association of Echocardiography
ECG - Electrocardiogram
EF – Ejection Fraction
GI - Gastrointestinal
HFNEF – Heart Failure with Normal Ejection Fraction
IVC – Inferior Vena Cava
LA – Left Atrium
LV – Left Ventricle
MR – Mitral Regurgitation
MS – Mitral Stenosis
MCE – Myocardial Contrast Echocardiography
NHS – National Health Service
PASP – Pulmonary Artery Systolic Pressure
PH – Pulmonary Hypertension
PRF – Pulse Repetition Frequency
RA – Right Atrium
RF – Regurgitant Fraction
RVSP – Right Ventricular Systolic Pressure
RWMA – Regional Wall Motion Abnormalities
SD – Standard Deviation
TR – Tricuspid Regurgitation
TTE – Transthoracic Echocardiography
TOE – Transoesophageal Echocardiography
UK – United Kingdom
VTTE – Vscan Transthoracic Echocardiography

Abstract

Background: In the United Kingdom, approximately 100,000 patients per year are referred for a resting transthoracic echocardiogram (TTE) prior to non-cardiac surgery, and numbers are increasing. A preoperative screening tool would help to relieve pressure on echocardiography departments, and avoid unnecessary delays to surgery. No published studies have analysed the performance of pocket echocardiography for this purpose. The present study assesses whether pocket echocardiography, in the hands of experienced operators, can effectively screen preoperative non-cardiac patients so that those with a normal result could proceed to surgery without full TTE. It also estimates the potential cost savings of this strategy.

Methods: Adult patients referred for resting TTE at the department prior to non-cardiac surgery were recruited between [data removed]. Patients were scanned as normal on full TTE, and then with a pocket-sized echocardiography device (GE Vscan) by a different echocardiographer. The full TTE was reported as normal; the Vscan was reported onto a tick-box reporting form. Operators were blinded to each other's findings. The two reports were compared, and a level of agreement (Kappa) obtained.

Results: 70 patients were recruited, of which 67 had image quality suitable for creating a Vscan report. Overall sensitivity was 77%, and specificity was 93%. For patients aged 65 years or older, gynaecology patients, and outpatients, sensitivity was 100%. Specificity was also high, at 94%, 92% and 97%, respectively. Cost savings for Vscan screening of preoperative non-cardiac patients is estimated at £44.89 per patient.

Conclusions: This study has identified a population for whom yield on full TTE is particularly low, and the cost-effectiveness ratio of screening by pocket echocardiography particularly high. In addition, there are some subgroups of patients where sensitivity and specificity are >90%, and cost savings per patient exceed £48 per patient.

Word Count: 27,659

CHAPTER 1: INTRODUCTION

1.1 Background

Preoperative TTE is firmly established as an invaluable tool for risk stratification in patients undergoing non-cardiac surgery (Subramani & Tewari, 2014). Cluer (2014) extrapolated figures from McMartin's (2014) HealthQuality Ontario review and estimated that there are approximately 50,000 resting transthoracic echocardiography (TTE) studies performed preoperatively in the United Kingdom every year. Pearse (2013) states that over one million adults per year undergo non-cardiac surgery in the NHS, with about 10% of these at high risk of complications (Pearse et al., 2012). Assuming conservatively that only the high-risk patients were referred for a preoperative resting TTE, this would in fact bring the estimate closer to 100,000.

With the number of individuals aged 65 and above increasing, as well as the growing number of individuals with cardiovascular risk factors such as obesity (Kristensen et al., 2014) and adult congenital heart disease (Gatzoulis & Webb, 2003), "the number of patients with significant perioperative cardiac risk undergoing non-cardiac surgery" can only be expected to rise (BMJ, 2014). Clearly, this puts immense pressure on echocardiography departments.

In the context of our Echocardiography Department, there was a steady increase in the overall number of scans performed between 2004-2011. The number of scans performed finally reached a plateau of [data removed] scans per year from the second quarter of 2011 onwards. It is worth noting that the number of available scanning slots is limited not only by the number of examination rooms and staff, but also by the department's teaching of Imperial College Masters students and visiting cardiac fellows. Therefore, it is not implied that the number of scans is

representative of other departments in the UK, but may be representative of the overall pattern of increased demand over time.

[Figure 1 has been removed and can be supplied only with departmental permission]

1.2 Costs

Cost-benefit analyses of echocardiography in the UK non-cardiac preoperative setting are currently absent, and even the costs of performing an echocardiogram are difficult to define. Marwick (2005) defines costs associated with echocardiography as fixed costs (capital, depreciation, servicing), variable costs (such as consumables), 'stepped' costs (staff salaries), and induced costs (from complications arising from the test). Clearly, calculating all of these variables accurately is a complex task, but Marwick (2005) found that in the Australian model, "government or insurance company reimbursements are a reasonable approximation to cost" within the public healthcare domain. This figure has indeed been adopted as the estimate of the cost of a resting transthoracic echocardiography (TTE) in other studies (Neale et al., 2015). Assuming this to be accurate for the trusts within the NHS in the UK, the approximate cost to the Imperial College Healthcare NHS Trust for an echocardiogram is £87 (EchoTech, 2015; NHS England, 2009).

Marwick (2005) states that besides optimally managing these costs, overall cost-effectiveness can be improved "by controlling referrals" and "identifying situations where echo provides… the same outcome as a more expensive technique." Marwick's final point can also be applied to alternative forms of the echo examination itself, were outcomes shown to be similar to a full echocardiogram in answering specific clinical questions.

1.3 The case for pre-operative screening of non-cardiac patients

There are doubts as to the appropriateness of a large proportion of echocardiography referrals prior to non-cardiac surgery (Bhatia et al., 2012; Vigoda et al., 2011), with ramifications not only for the resources of echocardiography departments, but (contentiously) also for patient health. Jettoo et al. (2011), for example, found that hip fracture patients suffered an average surgery delay time of 2.6 days whilst waiting for an echocardiogram, and highlights the potential consequences on morbidity and mortality in this particularly time-sensitive group of patients.

Yet, the overall consensus is that TTE is a valuable tool for risk stratification prior to non-cardiac surgery, with studies showing evidence of changes in management decisions and patient outcomes following preoperative TTE (Canty et al., 2012a; Canty et al., 2012b), including in aforementioned hip fracture patients (Canty et al., 2012c). It seems likely that the conflicting reports as to the effectiveness of TTE stem from a number of factors. Differences between institutions must be considered, particularly given contrary reports of delays to surgery. There is also great diversity across preoperative patient populations in terms of surgery type, age, gender, and the prevalence of cardiac pathology within these groups. In populations with a very low probability of cardiac pathology, a comparison of costs with benefits of preoperative TTE will inevitably yield poor results (Kimura et al., 2002).

There is little doubt that better adherence to established referral criteria is needed for the benefit of patient health and healthcare resources (Vigoda et al., 2011), but an additional possibility for reducing the demand on resources of echocardiography departments (staff, scanning rooms and equipment) is to screen patients scheduled for a preoperative TTE quickly and inexpensively, in order to identify those without serious cardiac risk who may proceed directly to surgery. With

recent technological improvements and the miniaturisation of ultrasound technology (Cardim et al., 2010), this is now a viable possibility.

A number of studies have sought to compare the effectiveness of handheld systems to traditional TTE performed on a 'high end' ultrasound machine in a variety of clinical settings. Given, however, the importance of well-established and invaluable techniques such as spectral and tissue Doppler; specialist areas such as stress testing (Picano et al., 1991); the growth of 3D imaging which is set to "become an integral part of a complete echo examination" (Roelandt, 2009); and the potential clinical application of newer techniques such as speckle tracking (Beynon, 2011), any study focusing on the potential for handheld scanners to *replace* the work of 'high end' TTE would be asking the wrong question.

Just as today the literature fills with studies on pocket-sized devices, previously the discussion focused on the potentials of laptop-style echocardiography (Vourvouri et al., 2005). This equipment was never used widely as an echocardiographic screening tool, perhaps due to the fact that, besides portability, it did not offer anything fundamentally different to a full echocardiogram.

Unlike laptop-based mobile echocardiography, pocket-sized machines are designed – at least at the time of writing – to perform a limited set of functions at a much reduced price, and therefore lend themselves well as an echocardiographic screening tool. Although the potentials of truly handheld echocardiography as a screening tool were first put forward by Roelandt and colleagues in 1978, other technological advances – particularly the shift to digital beamforming and phased array transducers (Hoskins et al., 2010) – delayed realisation of this goal.

1.4 Previous Studies

Cullen et al. (2014) compared the performance of the leading pocket ultrasound device, the GE Vscan, with full TTE, in the hands of experienced echocardiographers under normal clinical conditions. Their rationale was that previously published studies had enrolled fewer than 50 participants, and had not been used to perform a full examination. However, they were testing the hypothesis that the Vscan device could *replace* full TTE; inevitably, the hypothesis was rejected. In addition, the authors did not take any steps to demonstrate that observed discordance went beyond normal interobserver variability in their laboratory.

Erkoyuncu et al. (2013) described the Vscan as a 'disruptive innovation,' explaining that "disruptive innovations introduce a new performance trajectory and improve performance along parameters *different* from those traditionally valued by mainstream customers." In other words, to judge the Vscan against the current gold standard for performance of a full echocardiogram on the general patient population – and not to use it as a tool to answer a specific question – is not particularly productive.

As previously mentioned, preoperative non-cardiac patients may be one more appropriate application for this technology. Canty et al. (2012a) found that focused echocardiography on a full-service machine performed well as a preoperative screening tool in non-cardiac patients, and in March 2015, Neale et al. published the first cost-benefit analysis of focused echocardiography in the preoperative setting. Both papers referred to a limited protocol, using only B-mode and colour flow Doppler and performed by an anaesthetist.

The B-mode and colour Doppler images generated by pocket echocardiography systems have been shown by a number of authors to be of equal (Frederiksen et al., 2010; Leibo et al., 2011;

Khan et al., 2014) or near equal (Testuz et al., 2013) suitability for echocardiographic interpretation on adult patients as those obtained from full sized scanners. Handheld systems have also shown strong agreement with full echocardiography on a number of parameters, when performed by experienced operators (Frederiksen et al., 2010; Khan et al., 2014). Thus, the ability of the handheld scanner to perform a basic cardiac scan is not in question, but its ability to detect significant abnormality as effectively as full sized 'high end' ultrasound equipment to be used as a potential screening tool for preoperative non-cardiac patients has yet to be fully explored (Cluer, 2014). In the context of the findings of Canty et al. (2012) and Neale et al. (2015), such a screening tool would have powerful implications.

Cavallari et al. (2015) recently published a study comparing the "conclusiveness" of handheld and full sized echocardiography in preoperative non-cardiac patients. 'Conclusiveness' was defined as the proportion of studies in which a "satisfactory diagnosis" was reached. These authors found no significant difference between the two methods. However, patients were scanned with a full *or* a handheld device, but not both. Hence, there was no gold standard comparison, nor was a follow-up on perioperative outcomes performed.

The present study includes a comparison with a gold standard, because the performance of pocket echocardiography in preoperative non-cardiac patients has yet to be fully explored. Specifically, it is not clear that all preoperative non-cardiac patients are appropriate candidates for handheld screening. Kimura et al. (2002), for example, found that certain patient subgroups benefited more from screening than others. In fact, the very patients recruited in the study by Cavallari et al. – only patients referred by a cardiologist – were previously found by Kimura et al. to have one of the poorest cost-effectiveness ratios with pocket echocardiography in their study, due to the relatively high prevalence of significant cardiac disease which would require more detailed investigation by TTE.

Although significant cardiac disease was only reported in 33% of patients in the Cavallari et al. study, there exists the potential that prevalence may have been under- or overestimated, particularly as groups were not matched by age, gender or referral request. The prevalence of significant cardiac pathology was higher for every single measure on full echocardiography versus handheld, which those sceptical of the performance of handheld echo could well argue may represent a number of missed findings. Without the crucial comparison with an echocardiographic gold standard, such criticisms cannot be addressed.

1.5 Summary

There has been a huge amount of interest in handheld echocardiography to date, and its ability to detect a number of significant pathologies is firmly established. Studies which have judged handheld devices against full echocardiographic systems on the ability to perform a full, quantitative echocardiogram, have inevitably found handheld devices to be lacking. Perhaps, however, the inability to quantify pathology is unproblematic – and even advantageous – in the appropriate setting.

Yet, it must be remembered that this new technology is still in its infancy. Appropriate applications are still being defined, and cost-benefit analyses such as that published by Kimura et al. (despite looking at focused echocardiographic screening in general and not handheld devices in particular) contribute greatly to this task. The present study seeks to identify a further patient subgroup who can benefit from this technology, but comparison with the current echocardiographic gold standard has to remain a fundamental component. To do so is not to judge handheld echocardiography against an impossibly high standard, but to allow findings to be kept in perspective.

The hypotheses of the present study are as follows:

1. Significant cardiac pathology can be detected by pocket echocardiography, such that it can be used safely as a screening tool for preoperative non-cardiac patients referred for TTE (Cluer, 2014).
2. Pocket echocardiography, used as a screening tool in the hands of experienced operators, would deliver significant time and cost savings for the preoperative non-cardiac surgical population.

1.6 Definitions

It is recognised that universally agreed terminology is still being defined. Recent recommendations from the ASE state that, due to their limited functionality, examinations using pocket-size devices should not be referred to as 'echocardiography' without further clarification as either 'limited' or 'focused,' which is dependent upon both the application and the competence of the user (Spencer at al., 2013). A position statement by the EAE (Sicari et al., 2011) avoids associating the term 'echocardiography' with pocket-sized devices at all.

The present study examines the concept of a pocket-sized device in the hands of professional echocardiographers, as a screening tool complementing full echocardiography. At no point is it implied that findings can be extrapolated to untrained or lesser qualified individuals, or even to alternative applications. Hence, the terms 'pocket echocardiography' and 'VTTE' are used freely to refer to any portable devices employing B-mode and colour Doppler imaging. 'Full echocardiography' or diagnostic TTE ('DTTE' (Cluer, 2014)) refers to the current echocardiographic gold standard.

CHAPTER 2: METHODOLOGY

The methodology remains unchanged from Cluer (2014) (Appendix 1), with regard to patient recruitment, image acquisition, and reporting. An addition to the original study is the inclusion of a second rater, which will be discussed in detail below.

2.1 Equipment: The handheld device used for the study was the GE Vscan. This is classified by the ASE as a 'Focused Cardiac Ultrasound' (FCU) device. The Vscan is equipped with a 1.7 – 3.8 MHz phased array transducer, with harmonic imaging enabled as standard. Imaging modes are B-mode and colour flow Doppler; there is no M-mode or spectral Doppler capability.

A unique Vscan ID is generated for each new study, and an automatically detected single cardiac cycle or two-second cine loop clip can be saved for each patient (there is no ECG capability). These are stored on a removable miniSD card, and can be exported in mpeg format if required.

The full-sized devices present in the laboratory are the GE Vivid 9, GE Vivid 7, Philips iE33, and Toshiba Artida 3000.

2.2 Recruitment:

Inclusion criteria were all patients ≥18 years, referred for preoperative resting TTE for non-cardiac surgery between [data removed for purposes of confidentiality]. Exclusion criteria are no consent, or withdrawal of consent, and renal patients attending for pre-transplant workups.

2.3 Protocol: Qualifying patients were informed about the study, and verbal consent obtained. Their TTE was performed as normal by any one of six available echocardiographers,

with or without student involvement, following the department's stringent protocol (Appendix 3). The handheld study was performed alone by a different echocardiographer. Each operator was blinded to the results of the other.

2.4 Reporting: The handheld study was reported immediately after performing the study and without any interaction between operators, with access to the saved cine loops directly on the Vscan device. Findings were reported qualitatively, using the tick-box form designed by Cluer (2014) (Appendix 4), which recorded image quality (adequate or not), age, gender and surgery, before splitting each aspect of the examination into categories, similar to those used in the full study report. Any study rated as having inadequate image quality was excluded from statistical data analysis, but *was* included in analyses related to cost-effectiveness.

Within each category, findings were colour coded as significant or not significant (Table 1). The rationale behind each of these cut-offs is discussed in detail below.

Table 1: Categories and their corresponding thresholds for preoperatively significant abnormality, adapted from Cluer (2014).

Category	**Threshold for referral to full TTE**
LV Systolic Function	Moderate & Severe Impairment
LV Hypertrophy	Moderate & Severe Hypertrophy
LV Size	Moderate & Severe Enlargement
LA Size	None
RV Systolic Function	Mild, Moderate & Severe Impairment
RV Size	Moderate & Severe Enlargement
RA Size	None
Aortic Stenosis	Moderate & Severe Stenosis
Aortic Regurgitation	Moderate & Severe Regurgitation
Mitral Stenosis	Moderate & Severe Stenosis
Mitral Regurgitation	Moderate & Severe Regurgitation
Tricuspid Valve	Moderate & Severe Regurgitation; any degree of Stenosis
Pulmonary Valve	Moderate & Severe Regurgitation; any degree of Stenosis
Aortic Root	Moderate & Severe Dilatation
Pericardial Effusion	Small, Medium or Large
IVC Collapse (RA Pressure)	Collapse < 50%
RWMA	Any
Other significant findings	Any

2.5 Perioperative significance of valvular heart disease

The 2014 ESC/ESA guidelines on non-cardiac surgery recommend preoperative echocardiography for any patient with known or suspected valvular heart disease.

The preoperative significance of valvular regurgitation depends upon the mechanism (primary or secondary), whether the patient is symptomatic or not, and their left ventricular function. Symptomatic aortic or mitral regurgitation, impaired left ventricular function and functional mitral regurgitation all pose independently significant perioperative risk which would require changes to patient management (Kristensen et al., 2014).

The question is whether or not regurgitation can be adequately graded using pocket echocardiography, given the plethora of advanced methods now available? These include measurements which are technically possible but practically infeasible within the remit of rapid pre-operative screening, such as measuring regurgitant jet area (Muzzi et al., 2003) or vena contracta width (Zhou et al., 1997; Quéré et al., 2003). This is in addition to a number of methods requiring adjustment of the colour Doppler pulse repetition frequency, and/or spectral Doppler for calculation of regurgitant volumes and fractions (Zoghbi et al., 2003) which are currently beyond the limitations of this system.

Given that echocardiographers often rely on qualitative methods for initial judgements of regurgitation severity (Khanna et al., 2005) and the availability of colour Doppler on the GE Vscan, the lack of quantitative methods would seem unproblematic as long as thresholds for referral were sufficiently sensitive. Following the recommendations of the ACC/AHA, it has been assumed for the purposes of this study that anything at, or above, moderate regurgitation is considered a significant preoperative finding and would warrant referral for a full TTE prior to surgery.

For valvular stenosis, the ESC/ESA and ACC/AHA 2014 guidelines recommend close haemodynamic monitoring for patients with severe aortic or mitral stenosis undergoing surgery, making its preoperative detection very important. With mild stenosis, however, “non-cardiac surgery can be performed with relatively low levels of risk” (Kristensen et al., 2014). For this reason, stenosis of the mitral or aortic valves must be moderate or severe to be considered a significant preoperative finding.

Stenosis of the tricuspid or pulmonary valves, when not of tumour or congenital origin, is invariably due to rheumatic disease, carcinoid disease or infective endocarditis (Armstrong &

Ryan, 2010). In almost all cases, it will be accompanied by significant regurgitation, and the two have been combined on the reporting sheet designed by Cluer (2014). Anything at, or above, moderate regurgitation, and/or the presence of any degree of stenosis, is considered to be a significant finding for right-sided valves.

2.6 Perioperative significance of right heart assessment

Pulmonary hypertension (PH) is a significant perioperative risk factor in non-cardiac surgery (Minai et al., 2013), and both the ACC/AHA and ESC/ESA preoperative non-cardiac guidelines recommend a thorough preoperative assessment in patients known to have the disease, regardless of severity, for optimal haemodynamic monitoring during and after surgery. Both classify severe PH, right ventricular dysfunction and intermediate- to high-risk surgery as additional risk factors.

Pulmonary hypertension is defined as mean pulmonary artery pressure at rest of ≥ 25mmHg at right heart cathetarisation (Gibbs et al., 2009). Echocardiography alone cannot diagnose PH (Gibbs et al., 2009), with some milder degrees of pulmonary arterial hypertension (PAH) or PH secondary to lung disease particularly problematic given that the only sign on 2D echo may be subtle RV dysfunction. Due to this fact, Cluer (2014) classified RV impairment of 'mild' or above as a significant finding.

An additional (but non-specific) B-mode indicator of elevated right heart pressure is a dilated right atrium. A poorly collapsing inferior vena cava is a more specific, and arguably less subjective, indicator of elevated right heart pressures; so for this reason, failure to collapse >50% was considered to be a significant preoperative finding, warranting referral to TTE for more accurate estimation of pulmonary artery systolic pressures (PASP).

2.7 Perioperative significance of left ventricular size and function

A common referral request for echocardiography is an assessment of left ventricular (LV) systolic function. The 2014 ACC/AHA guidelines for non-cardiac surgical patients state that information obtained regarding isolated LV systolic dysfunction of an asymptomatic patient may not add "incremental information that will result in changes in management and outcome" (Fleischer et al., 2014). The 2014 ESC/EAE guidelines similarly deem information on LV dysfunction of mild or moderate severity to be of "limited predictive value."

The guidelines themselves are not without critics. A number of authors have called for an assessment of LV systolic and diastolic function in all patients undergoing high-risk non-cardiac surgery (Flu et al., 2010; Groban & Kitzman, 2010). These recommendations are based on the 2010 study by Flu et al. of 1,005 vascular surgery patients, finding that 50% of these had left ventricular dysfunction, 80% of whom were asymptomatic. Under current ACC/AHA guidelines, these individuals would not be referred for a preoperative echocardiogram. The implications of this condition were striking: 17% of patients experienced perioperative events within 30 days of surgery, of which 90% had some form of LV dysfunction detected by echocardiography, 41% of them asymptomatic.

Other authors, such as Saito et al. (2012), recommend determination of LV function prior to non-cardiac surgery according to the risk inherent within the patient's own medical circumstances (for example, in the elderly), as opposed to the risk classification of the surgery itself (Table 2).

Table 2: Risk classification for a number of non-cardiac surgical procedures, taken from ACC/AHA (2014) and Saito et al. (2012)*.

TYPE OF SURGERY	RISK CLASSIFICATION
Peripheral vascular surgery	High
Intra-thoracic and intra-peritoneal surgery, carotid endarterectomy, head and neck surgery, orthopaedic surgery, prostate surgery	Intermediate
Superficial procedures, endoscopic procedures, cataract surgery, breast surgery, ambulatory surgery, plastic surgery	Low

*This list is neither exhaustive nor without need for qualification. For example, Flu et al. (2010) made a further distinction between endovascular (intermediate risk) and open vascular surgery (high risk). The ACC/AHA (2014) themselves note that surgical method and urgency of surgery also have a significant bearing on risk level.

In light of these unresolved debates, in the present study any LV systolic dysfunction of moderate or greater severity is considered a significant finding. Diastolic dysfunction cannot be directly assessed using pocket echocardiography, the implications of which are discussed below.

2.8 Summary

The 2014 ACC/AHA Guidelines provide clear guidance as to when a preoperative echocardiogram is indicated, but which echocardiographic information is actually relevant preoperatively is less clearly defined. Whether a finding is considered significant or not depends not only upon the current medical consensus, but on a number of other factors, including the type of surgery, comorbidities, and the overall result of the echocardiogram. It is for reasons such as these that any attempt to classify abnormality as significant or non-significant will always have a degree of arbitrariness. Cluer's answer to the problem was to make categories "intentionally

conservative," and this study has followed the category recommendations set out by Cluer (2014). The only exception to this was to exclude right and left atrial size from the list of significant findings. Even this judgement is not without controversy given that LA size has been shown to be a good predictor of perioperative events such as atrial fibrillation, which occurs in between 5-10% of non-cardiothoracic surgeries (Danelich et al., 2014). In addition, this decision to classify LA enlargement as a non-significant finding meant that the only indirect (and non-specific) sign of diastolic dysfunction was LV hypertrophy. Although this is in line with the fact that assessment of diastolic function is not included within the guidelines, again, this decision is controversial given its powerful prognostic implications (Groban, 2010).

By keeping the reporting form consistent with Cluer (2014), there exists the added benefit of allowing retrospective data to be combined with prospective data, in order to obtain a data set consistent with sample size calculations (Appendix 2). The only modification was that, in the original tick-box form designed by Cluer (2014), there was a box in which the operator was to estimate their time taken to perform the study. As the study progressed, it became clear that this field was not being consistently completed by all operators, and was omitted from further versions of the form; as all Vscan cine loops are timestamped, the time between the first and last save could, in any case, be recorded. It is recognised nonetheless that this ignores the time taken to obtain the first parasternal view (estimated by Freeman (2012) to be 30 seconds by an experienced operator, and likely to be less on the Vscan device where image optimisation is limited to only depth and gain controls), which will be addressed later.

The full study was reported using ProSolv Cardiovascular (Fujifilm) software. Once finalised by the operator, it was converted onto a tick-box form in order to be directly comparable with the Vscan report. Due to the inherent subjectivity in converting descriptive, qualitative data into a categorical format, a conservative approach was taken to ensure consistency and objectivity. For

example, where a regurgitant lesion may have been described as “mild-moderate,” it was cautiously coded as moderate.

2.9 Second Rater Test

Many previous studies have attempted to test handheld echocardiography within the ‘real life’ clinical setting, where the examination is performed and reported by the same operator. However, these studies have largely failed to acknowledge the influence of interobserver variability. A full inter- and intra- operator test, involving the rescanning of each patient, was not possible to perform within the setting of a working echocardiography laboratory. However, 38 studies (selected by random number generator) were rerated by one of the echocardiographers over a period of three months, providing some measure of inter-rater and intra-rater variability.

It was also considered important to gain some idea of whether discordance arose from the differences in reporting methods as opposed to the scanning techniques themselves. For this reason, full studies were rerated directly onto the same tick-box form on which the Vscan studies were reported.

The full studies were reviewed in ProSolv, but the rater was instructed not to open the previous report. Measurements could be performed at the rater’s discretion.

Given that only a proportion of all of the studies were rerated, results are interpreted with reference to the level of agreement between DTTE and VTTE for this subgroup of patients, where this differs from the overall Kappa of the study.

2.10 Time Analysis

A measure of image acquisition time was obtained for a full non-cardiac preoperative TTE, and the mean time spent across all types of resting TTE in the department. Scan duration was obtained from the first and last cine loop or image frames stored for each patient, which are displayed to the nearest second.

Sample 1: All of the time stamped full examinations already included in this study, excluding any with student involvement.

Sample 2: All of the full examinations performed during 1st – 5th September 2014, which is outside of Imperial College teaching time. Excluded alongside paediatric studies, were those with more than one operator or without timestamps.

Time taken to complete a Vscan study was also obtained by comparing the first and last acquisitions on the device, which are displayed to the nearest minute. Mean scan time across all operators, and changes in scan times with experience for individual operators, were recorded.

2.11 Cost-effectiveness

Kimura et al. (2002) performed a cost-benefit analysis for a limited echocardiographic examination, in order to find which patient subgroups offered the best 'return' on an echocardiographic screen. As well as prevalence (termed "yield" in their study), Kimura et al. (2002) also calculated a cost-effectiveness ratio: the number of cases eliminated through screening, divided by the number of false negatives.

Cost-benefit analyses are commonplace for transoesophageal echocardiography (TOE), stress echo and contrast echo (particularly myocardial contrast echocardiography (MCE)), but tend to express cost effectiveness in terms of dollars per life-years saved (Shaw et al., 2006; Fleishmann & Weeks, 2012). The cost-effectiveness ratio applied by Kimura at al. in 2002 is more appropriate to the present study design, but what constitutes an acceptable ratio is not defined by these authors, except to state that a ratio of 7.8 was "high."

Due to this lack of clear definition, an additional measure of cost-effectiveness was performed, whereby the cost per VTTE screen was estimated and (hypothetical) financial cost-savings of this method calculated. Consenting patients otherwise excluded from the study due to non-diagnostic Vscan image quality *were* included in this analysis, in order to keep findings relevant to the main research question, although this has not always been in the case in the literature. Abe et al. (2013), for example, found that pocket echocardiography performed excellently as a screening tool for AS; however, any patient deemed as having Vscan image quality insufficient for rating of stenosis was excluded from the study. Clearly, a high level of agreement in the context of a large number of excluded patients would not have the same meaning as a high level of agreement across *all* patients, and the same is true for any cost-benefit analysis.

CHAPTER 3: STATISTICAL ANALYSIS

A sample size calculation was performed prior to commencing this study, and can be found in Appendix 2.

Statistical analysis was performed using IBM SPSS Statistics (Version 22), and a Cohen's Kappa coefficient calculated for each comparison performed, in order to obtain a measure of inter-observer agreement. SPSS uses Siegel & Castellan's 1988 variant of Cohen's Kappa (Hallgren, 2012).

Kappa is calculated by:

$$\kappa = \frac{P_o \ -Pc}{1-Pc}$$

Where P_o is the proportion of agreements and P_c is the proportion of agreements expected by chance (Sim & Wright, 2005).

The Kappa coefficient is influenced by the prevalence of disease (Sim & Wright, 2005), which is not subsequently corrected for by SPSS. For this reason, a prevalence index will be calculated, with a high or low (close to 1 or 0) index suggesting potential underestimation of Kappa. Results should be interpreted with caution particularly in any areas where strong agreement is not found (Burn, 2008).

Figure 2: Example of a typical cross tabulation.

	Pathology	No Pathology
Pathology	a	b
No Pathology	c	d

The prevalence index is the difference between the number of positive and negative agreements, divided by the number of ratings.

$$\text{Prevalence index} = \frac{|a-d|}{n}$$

Where $|a\text{-}d|$ is the absolute value of the difference between the frequencies of cells *a* and *d* (Figure 2), and *n* is the number of paired ratings (Sim & Wright, 2005).

The prevalence index is of greater value than the 'true' prevalence of each respective disease in the population (were such data available), because the very nature of a particular disease or trait as common or rare "will predispose clinicians to diagnose or not to diagnose it, respectively" (Sim & Wright, 2005).

A bias index is automatically calculated by the version of Kappa used by SPSS, and adds to sensitivity and specificity of findings.

$$\text{Bias index} = \frac{|b-c|}{n}$$

Where $|b\text{-}c|$ is the absolute difference between cells *b* and *c*. If the bias index is large (close to 1), this would indicate that VTTE is disagreeing much more when DTTE is positive than negative, or vice versa. It would give some indication on whether the VTTE does less well when the echocardiogram is truly negative or positive. A bias-adjusted Kappa is automatically generated by SPSS, so clearly no attempt to amend Kappa will be made in light of the bias index.

Similarly, an adjustment for prevalence goes beyond the scope of this paper, but the implications of the prevalence index on current results and future work will be discussed.

In summary, percentage agreement, prevalence and bias indexes will accompany the results by way of qualification (Byrt et al., 1993) but no adjustment of the overall Kappa will be made in light of these influences. Kappa will be interpreted as:

Value of κ	**Strength of agreement**
< 0.20	Poor
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Good
0.81-1.00	Very good

(Lund Research, 2013)

Sensitivity, specificity, positive and negative predictive values are all commonly quoted in the literature, and overall values for these measures will be included in the results.

Sensitivity is the ability of the test to correctly identify all those with disease, so is calculated as $\frac{a}{a+c}$ (Figure 2). Specificity is the ability of the test to correctly identify all those without disease; $\frac{d}{b+d}$. These two measures are a reflection of the test itself (Parikh et al., 2008).

Positive predictive value and negative predictive value are influenced by the prevalence of the disease, such that positive predictive value = number of true positives / (number of true positives + number of false positives), and negative predictive value = number of true negatives / (number of true negatives + number of false negatives). The utility of positive and negative predictive

values assumes that the prevalence in the study is representative of the general study population (Parikh, 2008).

Continuous data are expressed as mean ± standard deviation. Where a monotonic relationship exists, the strength of the relationship between continuous variables is assessed using Spearman's rank correlation coefficient, r_s, where 1 is a perfect positive correlation and -1 would be a perfect negative correlation. Degrees of freedom (n-2) will be quoted alongside r_s, accompanied by the significance level (*p* value).

An association between nominal variables is assessed using either Chi Square or Fisher's Exact Test (where expected frequencies are below five).

For all statistical tests, a *p* value of <0.05 was considered to be significant.

CHAPTER 5: DISCUSSION

5.1 Demographics & Disease Prevalence

Overall prevalence of significant cardiac disease was low (19%), and in some individual categories it was so low that the performance of VTTE could not be fully assessed. While this represents one of the major weaknesses of the study in answering the first research question, the low prevalence of pathology, and the associated implication that the majority of patients sent for preoperative echocardiography should not have been referred in the first place (Cluer, 2014), only strengthens the argument for a screening process.

Contrary to previous reports that have suggested a greater prevalence of pathology in patients aged 65 and over (Kimura et al., 2002), in this sample there was a slight trend in the other direction (Table 3, Section 4.2). Gynaecological patients represent one of the largest patient subgroups (21% of the sample), but with one of the lowest rates of disease prevalence (7.7%). When these patients were excluded (Table 6, Section 4.3), there was no age difference in the prevalence of pathology.

The prevalence of cardiac disease was higher in males than females, but this difference was not statistically significant when assessed with Fishers Exact Test (Section 3).

Of the patients referred prior to gynaecological surgery, there was one false positive, which was the result of VTTE grading the level of tricuspid regurgitation as “moderate/severe” but DTTE grading it as “mild.” The only DTTE positive result for significant pathology was a patient due for termination of her pregnancy because of worsening symptoms of peripartum cardiomyopathy. It could be argued that, although technically undergoing non-cardiac surgery, the fact that

planned surgery was a direct result of a *cardiac* pathology means that this case should not have been included within the study. At the very least, it is clear that such a patient would be sent directly for a full TTE and would not be a candidate for Vscan (although, interestingly, she was first correctly diagnosed the night before by a Registrar with a Vscan device). The only other referral for full TTE from this subgroup would have come from a patient with a bioprosthetic aortic valve. Again, such a patient would realistically be referred automatically for full TTE (Kristensen et al., 2014), and would never be a candidate for preoperative VTTE.

If these patients are excluded from the sample, then it is clear that the prevalence of any significant finding in patients due for gynaecological surgical procedures was 0%. This raises questions about the appropriateness of referrals from this department, but also indicates a patient population very appropriate for screening, given the VTTE's overall high specificity (93%) and negative predictive value (96%), which is 92% and 100% respectively for this subgroup of patients.

5.2 Cost-Benefit Analysis

The prevalence of disease by gender, age, surgery type and whether the patient was an inpatient or outpatient is important in the context of a cost-benefit analysis. Kimura et al. (2002) found much lower rates of pathology in females, outpatients, those referred by noncardiologists, and patients under 65 years of age. The findings of this study mainly support those of Kimura et al., except for the final point, where significant pathology was in fact more prevalent in patients under 65 in the current study.

It is thought that almost all of the patients in this study were referred by noncardiologists, with the exception of the patient attending prior to pregnancy termination (and in whom significant cardiac pathology was indeed present). It seems likely that referral practices are by far the greatest influence upon prevalence of significant cardiac pathology in the preoperative non-cardiac population, and the apparent inappropriateness of a large number of referrals for echocardiography prior to non-cardiac surgery was previously commented on by Cluer (2014). Examples of seemingly inappropriate referral reasons included "pre-assessment for left hepatectomy. No cardiac history," "pre-operative workup. Planned for a cyst-gasterectomy and cholecystomy. No known cardiac problems." Many more simply stated "pre-op," with no referral reason given. It is impossible to know whether these referrals were indeed inappropriate, but given the request form and the low prevalence of pathology in the sample, it seems likely that a significant portion of referrals did not adhere to published guidelines. This is a known issue which is certainly not unique to our hospital, and has been discussed in Section 1.3.

In the present study, 70% of the sample would (hypothetically) not have been referred for full echo. Patients who would have been referred are tabulated in Appendix 7 (Table 1). 4.3% of patients (5.7% of un-referred patients) would have had significant findings which would have been missed. The overall cost-effectiveness ratio of VTTE was 17.67. The low prevalence of significant cardiac disease makes this ratio exceptionally high, and the case for screening very powerful.

Certain subgroups had even higher cost-effectiveness ratios. The percentage of patients aged 65 years or older which would have required referral for full TTE was 25.6% (9 with significant pathology according to VTTE, 2 with image quality unsuitable for VTTE). A cost-effectiveness ratio could not be calculated because there were no false negatives (no 'costs,' as defined by Kimura et al., 2002). The financial cost, however, can be calculated (Table 17, Section 4.9).

The cost of a VTTE screen is calculated in Appendix 8 as £20.98 per patient. The cost of a full TTE has been previously stated as £87 (Section 1.2). Hence, instead of a total cost of £3,828 for the 43 patients aged 65 and over, the total cost of VTTE screening would be £1,880.12 (43x£20.98, plus 11x£87 for the full TTEs which would need to be performed); a cost-saving of £44.27 per patient.

The cost savings for gynaecological patients would be similar. Out of 15 patients, 4 would have been referred for full TTE (2 for findings which require a formal TTE, 1 false positive, and 1 due to difficult imaging on VTTE); a saving of £42.83 per patient.

An even higher saving is seen for outpatients (n = 44, including one outpatient who was not included in Table 15 due to poor image quality) at £48.22 per patient; an even more important finding given that outpatients made up 66% of the non-cardiac preoperative echocardiogram requests in this study.

Cost savings across the entire preoperative non-cardiac sample would be £44.89 per patient, or a total cost to screen and refer only those deemed in need of full TTE of £2,947.60 vs. £6,090 with the current method. This >50% financial saving comes at a cost of a 4.3% rate of a false negatives across the entire sample.

It is clear from Table 17 Section 4.9 that outpatients, gynaecological patients and the over 65s all present strong cases for screening, with considerable echocardiographic cost savings per patient, and with minimal risk to the patient. Arguably, the false negative rate across the entire study (<5%) is such that there is a strong case for screening of *all* non-cardiac preoperative patients. If known cardiac disease and prosthetic valves are contraindicated, cost savings per patient increase further, to £46.24.

In reality, the number of preoperative non-cardiac scans performed annually is likely to be higher than the conservative estimate in Appendix 8 (due to reasons discussed in Section 4.2), and the cost per VTTE screen would be lower. It may also be the case that full TTE costs are higher than estimated. Gianstefani et al. (2013) estimated the cost of performing a portable TTE to be £88 for the King's College Trust; the cost of full TTE, given its higher purchase price and servicing costs, would therefore be higher.

The benefits of VTTE screening also go beyond the initial cost savings, and include elimination of delays to surgery, step-up and step-down in treatment plans (Neale et al., 2015), and potentially an associated impact on morbidity and mortality of patients (Canty et al., 2012a; Canty et al., 2012b; Canty et al., 2012c). Accurate quantification of the full costs and benefits of VTTE screening for non-cardiac surgical patients has never been performed in the NHS setting, and would be an important addition to the literature.

5.3 Time Analysis

DTTE scan times during the first week of September 2014 varied widely, presumably due to the range of referral reasons and degrees of pathology. A more relevant measure of DTTE scan times for preoperative non-cardiac patients is obtained from the study sample directly, with a mean full TTE scan time of 11:28 minutes, with the caveat that scan times again vary widely (standard deviation of 8:25 minutes).

Interestingly, full TTE was performed an average of 03:41 minutes faster in patients with significant pathology (in the non-cardiac preoperative context). Pathology is clearly on a continuum and a patient deemed as not having significant pathology in the non-cardiac

preoperative setting may nevertheless still have mild lesions which need careful investigation and/or quantification. This same trend was seen on VTTE (albeit far less pronounced – a mean difference of only 14 seconds). This nevertheless implies that operators have a tendency to spend longer to ensure that they have not diagnosed a false negative, but a more detailed study would be necessary to test this hypothesis.

Preoperative non-cardiac patients appear to be quicker to scan (mean difference of 01:19 minutes between the general scans and preoperative noncardiac scans) than the average patient, the reasons for which also would need to be the subject of further investigation. Possible reasons are the complexity and range of cardiac disease present. Whilst non-cardiac preoperative patients with significant pathology tended to be scanned more quickly than those without, this patient group had few of the serious and time-consuming cardiac pathologies frequently seen in the department (such as aortic stenosis or pulmonary hypertension).

Both DTTE samples represent shorter scanning times than in the published literature. Kimura & DeMaria (2003), for example, found in their study that the mean scanning time was 26 ± 5.4 minutes. However, this 'scanning time' also included performance of *all* calculations during the examination itself, as well as performance of each measurement twice. At our hospital, this level of scrutiny tends to be performed in the reporting room on dedicated software.

Kimura & DeMaria's (2002) study also did not utilise harmonic imaging, which may have resulted in a slower examination time given that harmonic imaging has been shown to improve border delineation (Turner & Monaghan, 2006), almost certainly reducing the time taken to visualise endocardial borders and place calipers.

Mean VTTE scan times varied between operators. When pathology was controlled for, there was a negative correlation between scan time and Vscan experience (Figure 8, Section 4.4), which was weakly statistically significant. Previous studies have found this to be highly significant ($p<0.01$), though crucially with inexperienced operators (Prinz et al., 2012). It seems likely that as the operators in the present study were all experienced echocardiographers, the learning curve was not as pronounced.

It is important to note that the mean scanning time calculated in the present study for both VTTE and DTTE, given that it was calculated as the time between the first saved cine loop or still, did not include patient preparation or cleaning time, or time taken to obtain the first view. This time *is* included in the oft-cited 40-45 minute examination time (Wharton et al., 2015), which crucially also includes reporting time; this is another aspect of the examination which was not measured in the present study.

It could be argued (particularly given the relatively short DTTE scan times observed), that much of the time-saving benefit of VTTE in the present study arises from the tick-box reporting method, and not from the equipment itself. While reporting time was not measured in the present study, given that scanning time took an average of only 12.5 minutes of the 40-45 minute full TTE exam time, it is thought that mean reporting time would be >20 minutes. In contrast, observed reporting time for VTTE using the tick-box form is qualitatively estimated at 1-2 minutes. Any attempt to introduce VTTE as a preoperative screening tool should not underestimate the influence of the reporting method on the results in this study (discussed in Section 5.5). Gianstefani et al. (2013) also used a simplified grading sheet for pocket echocardiography, and found a reduction in scanning and reporting time of 66% compared with portable TTE.

An assumption of the study was that each operator would perform approximately the same number of VTTE and DTTE scans throughout the duration of the study (Cluer, 2014). This was found not to be the case. Two operators left during the course of the study, and two new echocardiographers joined the team during the latter half of the study. However, not only did the members of staff change over the course of the study, but patterns quickly emerged as to people's favourite 'roles' (DTTE or VTTE operator) which exacerbated the imbalance. This is a potential weakness of the study.

5.4 Operator Experience

Three patients had images considered too poor for any diagnosis to be made. All three of these patients were recruited during the first four months of the study; within the first 28 scans performed, where the most active operator had Vscan experience of seven patients and the least active only one patient. Previous studies have suggested a rapid increase in Vscan image quality with experience (Prinz et al., 2012), as well as the previously discussed reduction in scanning time. The Prinz et al. (2012) study was with inexperienced operators and it may not be valid to extrapolate to experienced echocardiographers; however, it certainly is possible that there was a period of adaptation. If introducing a preoperative non-cardiac screening programme, it may be that the proportion of patients referred for full TTE due to non-diagnostic image quality would similarly reduce with increased familiarity with the equipment and/or an understanding of its capabilities, and that the cost-effectiveness ratio of VTTE can be expected to increase further with time.

Prinz et al. (2012) additionally found improvements in the diagnostic accuracy of handheld ultrasound with experience; however, it is not thought that such a trend would be observed with

experienced echocardiographers. Certainly in the present study, there was no relationship between number of VTTE examinations performed and occurrence of false positives or false negatives.

5.5 Second Rater Test

It was deemed important to compare the results of the second rater test with the same sub-group of patients, and not with the Kappa coefficient for the full sample of patients, because disease prevalence and distribution varied between the sub-sample and the full sample, as well as between operators. This is likely due to the low prevalence of pathology in general, such that one abnormal result had a strong influence.

The overall level of inter-rater agreement between the DTTE operator and the second rater, and VTTE and the second rater, were practically identical to the level of agreement between DTTE and VTTE for this same sub-sample of patients. The same was found for the intra-rater results.

These results suggest that a strong influence upon agreement within the study may be the differences between the ProSolv reports and the tick-box reporting sheet. A separate measure of inter-rater variability within department is needed for these influences to be separated.

The much smaller sample size of the inter-, and particularly intra- rater tests, is also a contributory factor. It is suggested that this component of the study be extended to include all of the patients within the present study.

An individual breakdown by pathology was not considered useful due to the small sample size, and the fact that there were no or only one significant pathology per category in the sub-sample, as rated by either DTTE or the second rater. The only exception to this was for mitral regurgitation, for which there were three instances of disagreement. On two occasions, the second rater diagnosed moderate/severe MR, in contradiction with both the DTTE and VTTE reports. On a third occasion, the second rater graded MR as mild/moderate, again in contradiction to both the DTTE and VTTE reports. This again suggests that there is a complex interplay of influences of interrater variability, different reporting forms, and equipment, which warrants further investigation.

An independent measure of inter-rater variability would be particularly important here, in order to establish whether some operators are more prone to diagnosing a condition than others. As mentioned above, some operators were new to the department, and although all were level three experienced echocardiographers, experience ranged from three years to over twenty.

There are some weaknesses in the current inter- and intra- rater test design. First of all, many of the DTTE images would have online measurements saved on them. Secondly, if significant pathology was present, this may be made obvious by the extra attention given to it. Finally, it is not known to what extent the same methods (specifically, qualitative or quantitative) were used to grade severity for each of the second rater tests, as this was left to the rater's own discretion (Section 5.5).

VTTE performance breakdown

The following section will address each category on the tick-box report in turn, split into areas which underperformed ($\kappa < 0.675$), and equalled or over-performed ($\kappa \geq 0.675$), the level of agreement for the study as a whole. It will conclude with consideration of those measures which were not assessed, and their relevance in the preoperative context.

5.6 Underperformers

- **Aortic Regurgitation**

Agreement between DTTE and VTTE for significant aortic regurgitation was not above that which would be expected by chance ($\kappa = -.031$). Yet, agreement across the full AR dataset (Appendix 7) was very good ($\kappa = 0.70$). This suggests that VTTE was good at detecting the presence of aortic regurgitation, but poor at correctly grading the severity.

Both false negatives in the study were for patients who were identified as abnormal overall by VTTE; one due to the presence of significant aortic stenosis, and the other due to significant mitral and tricuspid regurgitation. There were no isolated cases of significant AR, so it cannot be known if the VTTE grading would have been more cautious in this situation. Equally, there were no cases of severe AR within the sample (both false negatives were for AR graded 'moderate' by DTTE).

Moderate AR is not considered a risk factor for non-cardiac surgery in the current guidelines (Fleischer et al., 2014), so it could be argued that neither of the false negatives would have had negative consequences for the patient (Cluer, 2014). Borderline chronic moderate-severe AR

would be a concern preoperatively, and has been shown to have a major impact upon mortality and morbidity in non-cardiac surgical patients when accompanied by significant LV dilatation and/or dysfunction (Lai et al. 2010; Nishimura et al., 2014). VTTE has performed well on the latter two parameters (κ =0.66 and κ = 0.79, respectively), hence it appears that the risk of VTTE failing to identify preoperatively significant AR is low.

Although the preoperative significance of the two false negatives is low, it is important to identify potential reasons for their occurrence. Kutty et al. (2009) compared colour Doppler echocardiography to Cardiac Magnetic Resonance (CMR) calculations of regurgitant fraction (RF), and found considerable RF% overlap between each classification made by qualitative echocardiography (i.e. between mild and moderate, and between moderate and severe). They found that the distinction between moderate and severe was particularly troublesome. This finding has been supported by the present study, where distinctions between normal and mild were generally very good (Appendix 7).

Quantitative methods for AR grading are not without their problems (Lancellotti et al., 2010a), but it is the combination of various qualitative and quantitative methods which supports the echocardiographer's grading of severity. Colour Doppler jet width has been shown to be influenced by a number of factors independent, or relatively independent, of the severity of regurgitation – such as machine settings (PRF, colour gain), pressure gradients, compliance of the receiving chamber, and eccentricity of the jet (wall-impinging jets or jets travelling out of the imaging plane will appear smaller). Therefore, it is not surprising that this method alone was only sufficient insofar as confirmation of presence/absence of AR – but not in accurate grading of severity.

- **Tricuspid Valve**

There was moderate agreement ($\kappa = 0.57$) between the DTTE and VTTE for the tricuspid valve, with a tendency to overestimate the level of regurgitation, consistent with previously published literature (Testuz et al., 2012).

Any degree of tricuspid stenosis, and/or tricuspid regurgitation (TR) of moderate or greater severity, were considered a clinically significant finding. There was one false negative finding in which tricuspid regurgitation was rated as "mild-moderate" on the DTTE report, but marked as "normal/mild" on the VTTE tick sheet. In fact, "mild" was even circled by the operator (contrary to form filling instructions which asked raters to only tick the appropriate box for this category!), presumably in an attempt to communicate that the level of TR was worth noting. Due to a decision to make ratings intentionally conservative (Cluer, 2014), the DTTE report stating "mild-moderate" was coded as moderate/severe, thus resulting in apparent disagreement between the two systems.

The process of transferring written formal reports into the tick box format is an imperfect method because, were the DTTE operator presented with the same choices during reporting, it cannot be known whether they would have rated the TR as normal/mild or moderate/severe. The second rater test provides some insight into this. When this study was re-rated (and by the same operator that wrote the original DTTE report) and the second rater was presented with the same choices as the original VTTE operator, the second rater concurred with the VTTE report – and not with their original DTTE. This suggests that such disagreement is more a product of the study design than of the Vscan device itself.

- **Atrial Size**

Agreement on left atrial and right atrial dilation was far below the overall level of agreement, at $\kappa = 0.22$ and $\kappa = 0.46$, respectively. It was also exceptional in that agreement between DTTE and VTTE was far below the level of agreement between the original DTTE operator and the second rater ($\kappa = 0.760$ for inter-rater agreement, $\kappa = 1$ for intra-rater agreement) (Tables 13-17, Appendix 7). Agreement between the second rater and VTTE was $\kappa = 0.051$ for LA dilation, and $\kappa = 0.27$ for RA dilation. This strongly suggests that VTTE is inherently poorer than DTTE at estimating LA and RA size (possibly due to its inability to measure volumes), and the level of discordance in the present study was *not* a product of normal interobserver variability.

Isolated left or right atrial enlargement is extremely rare (Armstrong & Ryan, 2010), with no documented significance in the non-cardiac preoperative context. LA dilation is more commonly secondary to left ventricular dysfunction, or organic or functional mitral regurgitation (Kisslo, 2009). RA dilation would invariably be due to volume and/or pressure loading, and would be associated with significant TR and/or a dilated, non-collapsing IVC, or various degrees of RV dysfunction. In the present study, all 3 cases of significant MR on DTTE were accompanied by LA dilation, and all 3 cases of significant RV dysfunction (due to pressure overload, with estimated RVSP >40mmHg in all instances) were accompanied by RA dilation (Tables 8-9, Appendix 7).

A qualitative assessment of this measure by expert operators on handheld echocardiography is absent from the literature. LA and RA size were not considered significant in the non-cardiac surgical context, and hence the significance of the discordance in the present study is minimal.

- **Regional Wall Motion Abnormalities**

VTTE performance was fair (κ=0.4) in the identification of the presence or absence RWMA. Good endocardial definition is essential to the identification of wall motion abnormalities (Otto, 2013), and reports are mixed as to VTTE's performance in this area. Prinz & Voigt (2011) found image quality to be comparable between pocket echocardiography and high end systems, and agreement for RWMA was good (κ=0.73) in their study.

One reason for the comparatively poor agreement in the present study may simply be due to reporting methods. The VTTE reporting form specifically requested a comment on the presence or absence of RWMA, but there is no such field *as standard* as part of the full report. Where significant RWMA are reported, they are either mentioned in the "left ventricle" field, or a 16-segment diagram can be optionally added to the report to grade abnormal segments. As two of the four false positives were in patients who had a history of myocardial infarction stated on their referral form, it is possible that the DTTE operator felt it unnecessary to report a known abnormality.

The second rater test was designed to distinguish true discordance from that due to the difference in reporting methods or normal interobserver variability. Agreement between the DTTE report and the second rater was high ($\kappa = 0.834$, $p<0.005$), which initially suggests that VTTE is inherently poorer at accurately identifying RWMA.

However, agreement between DTTE and VTTE was also high ($\kappa = 0.787$, $p<0.005$) when only the patients for whom a second rating was performed were compared, as was agreement between the second rater and VTTE ($\kappa = 0.779$, $p<0.005$) (Tables 10-12, Appendix 7). This first indicates that the limited sample of patients who were re-rated appear not to be representative of the

sample as a whole, and this test needs to be extended and repeated. Most importantly, however, it means that it cannot be concluded that VTTE shows significantly greater discordance when identifying RWMA than normal interobserver variability.

In comparison with other studies' measures of interobserver variability in RWMA assessment, however, the performance of VTTE across the full data set of the present study does not appear to differ from normal interobserver variability. Hoffman et al. (2006) found a similar level of agreement ($\kappa = 0.41$) between different observers assessing RWMA on standard (unenhanced) echocardiography as the present study found between DTTE and VTTE. Blondheim et al. (2010) found that interobserver and intraobserver reliability was fair for the visual assessment of normal or akinetic LV wall segments by experienced operators, but poor for hypokinetic segments. This suggests that visual assessment can detect significant pathology with reasonable accuracy, but is much less reliable at identifying subtle abnormalities.

One study by Gianstefani et al. (2013) actually found agreement between pocket echocardiography and portable (laptop-style) TTE to be very high for assessing RWMA ($\kappa = 0.946$), but there were key differences between this study and the present study. First, they included the American Society of Echocardiography 16-segment model on their reporting form. Secondly, they compared the Vscan with laptop TTE (not full TTE). Finally, as they only included patients referred for a focused question (i.e. the query was specifically for RWMA on all patients that RWMA was assessed), the full report would also be addressing the same issue *and* reporting in the same way, ensuring that the results were directly comparable. This would have contributed the high agreement.

The significance of RWMA preoperatively depends upon the patient's medical history. In patients with known ischaemia or past myocardial infarction, RWMA in known abnormal

segments is clearly less of a concern than new abnormalities, or RWMA in patients in whom there is no past history of ischaemic heart disease.

Finally, it is noted that the mere presence/absence of RWMA may not be the most appropriate measure of agreement, due to the great variability in its location and severity. RWMA were considered on an individual basis by Cluer (2014), which may be a more appropriate approach. Future work could include a 16-segment diagram on both VTTE and DTTE reports, allowing for direct comparison of wall motion scores.

5.7 Over-performers

- **Aortic Stenosis**

Aortic stenosis has classically been considered a significant perioperative risk factor for non-cardiac surgical patients (Fleisher et al., 2014). The perioperative risk of aortic stenosis in non-cardiac surgical patients depends both upon the severity of the stenosis and the risk level of the surgical procedure (Tashiro et al., 2014). Although recent studies have found this risk to have dropped dramatically compared with previous decades (Tashiro et al., 2014; Agarwal et al., 2013), it is only with awareness of the condition and its severity that patients can be appropriately managed. Accurate detection and grading of aortic stenosis severity by echocardiography is therefore vital. This is particularly relevant in the context of a potential relaxation of guidelines (Osnabrugge et al., 2014; Tashiro et al., 2014). Although the ESC/ESA guidelines currently recommend aortic valve repair or replacement to be performed in asymptomatic patients prior to high-risk surgery wherever possible, the ACC/AHA guidelines have changed during the course of the present study and now state that it is “reasonable” for non-cardiac surgery to proceed despite

severe (asymptomatic) AS (Fleisher et al., 2014). This could potentially lead to more patients attending for echocardiography prior to non-cardiac surgery, with underlying AS.

In addition, the detection of AS during physical examination relies on non-specific signs, such that the condition is not easily distinguishable from an innocent murmur by non-cardiologists (Abe et al., 2013). The potential for referral to echocardiography departments of patients without significant pathology is therefore high.

Given the above, it is important that VTTE performs well in detecting moderate/severe aortic stenosis so that such patients would be referred for full TTE for quantification of valve area, peak velocity, and mean gradient (Samarendra & Mangione, 2015). It is therefore unfortunate that the present study contained only one patient with significant aortic stenosis. Yet, the high level of agreement ($\kappa = 1$) found for this measure in the present study is in line with previous work.

Abe et al. (2013) performed a focused study, using pocket echocardiography in the hands of experienced echocardiographers, to grade the severity of aortic stenosis based on cusp mobility and calcification. They found excellent agreement ($\kappa = 0.85$) between pocket and high-end echocardiography, with high sensitivity and specificity for not only detecting significant AS but also for correctly grading its severity. High concordance was also found by Khan et al. (2014), where aortic stenosis was simply graded as present or absent.

A number of studies have found pocket echocardiography to perform excellently in detecting AS, but with a tendency to underestimate its severity (Andersen et al., 2011; Prinz et al., 2012; Testuz et al., 2013). A possible explanation for the higher levels of agreement in the Abe et al. and Khan et al. studies compared to these is that both employed alternative methods for assessing the aortic valve. In the Abe et al. study, assessment of the aortic valve was the primary objective, and

echocardiographers used a visual scoring system. In the Khan et al. study, the aortic valve was simply graded normal or stenotic, with no grading of severity.

From the current literature and the present study, it can be concluded that the ability of pocket echocardiography to *detect* significant stenosis is excellent. Its ability to accurately grade stenosis is less clear, but this is neither surprising (given its lack of quantitation) nor relevant to the question, when any stenosis >mild would be referred for full TTE anyway.

- **Pericardial Effusion**

Agreement between DTTE and VTTE was perfect for the detection of pericardial effusion (κ = 1). Any size of pericardial effusion was considered significant in the context of the present study. This is an area in which pocket echocardiography has been shown to perform well (Testuz et al., 2012; Prinz & Voigt, 2011). Only one patient presented with a pericardial effusion in the present study, which was rated as moderate/large by both DTTE and VTTE. No conclusions can therefore be drawn about the ability of VTTE to correctly grade small pericardial effusions, although one examination did identify a "trivial" pericardial effusion which was (correctly) rated as insignificant on the tick-box form.

- **Left Ventricular Size & Systolic Function**

Agreement was good on left ventricular size (κ = 0.66), with the only discordance a false positive, in which VTTE classified dilatation as 'moderate' but DTTE classified it as 'mild.' Given that Vscan operators were instructed to perform a qualitative screen only, it may be that a more cautious approach was taken in respect to dimensions.

Prinz and Voigt (2011) found practically perfect agreement for LV dimensions ($\kappa = 0.99$), but crucially, dimensions were quantitatively measured on both systems. Given that the resolution of the GE Vscan was never in doubt (Khan et al., 2014), such high agreement is not surprising.

Assessment of LV systolic function is one of the parameters in which the Vscan, in the hands of experienced operators, has been shown to excel (Testuz et al., 2012; Biais et al., 2012). Qualitative assessment of LV systolic function has been shown to perform favourably with 2D quantitative methods (McGowan & Cleland, 2003; Gudmundsson et al., 2005), so much so that quantification by ejection fraction and/or wall motion scoring is often not performed for patients with normal systolic function. In this sense, a qualitative 'screen' for systolic dysfunction is already commonplace.

In the present study, agreement was good, but not as high as in previous work. In studies by Testuz et al. (2012) and Biais et al. (2012), agreement was found to be very high ($\kappa = 0.89$ and $\kappa=0.87$, respectively), but it is important to note that these studies were performed in the acute care setting, where higher grades of LV dysfunction are far more likely than in preoperative non-cardiac patients. Focused cardiac studies in general have been shown to perform better with more severe levels of pathology, but are less accurate at discerning subtle differences, perhaps due to lack of quantitation.

There was one false negative in the current study. As noted by Cluer (2014), this false negative would *not* have resulted in the patient being sent directly for surgery, as the study itself was correctly identified as 'abnormal' due to significant aortic stenosis. This one false negative result had a particularly strong impact upon the Kappa statistic, given the low prevalence of significant pathology in the sample (prevalence index 0.03). As discussed in Section 3, a very low

prevalence index is an indication that agreement may have been underestimated by Siegel & Castellan's 1988 version of Kappa, which adjusts for bias but not prevalence.

In agreement with previous work (Silcocks et al., 1997), the qualitative distinction between individual grades of LV dysfunction was suboptimal, and the level of agreement falls to $\kappa = 0.46$ when all four grades of dysfunction are included in the analysis (Table 2, Appendix 7). This once again suggests that previous 'failures' of pocket echocardiography (e.g. Cullen et al., 2014) had more to do with the research question and study design, than the technology itself. The question should not be "can pocket echocardiography accurately grade LV systolic dysfunction," but can it accurately detect *significant* LV dysfunction for a given clinical scenario.

- **Right Ventricular Size & Function**

Agreement between DTTE and VTTE on significant right ventricular enlargement was 100% in the present study, but unfortunately, no patients with significant dilatation were recruited. Agreement between grading of normal and mildly dilated right ventricles was moderate (Table 7, Appendix 7).

Agreement between DTTE and VTTE on RV systolic function was excellent ($\kappa = 0.85$). This is unsurprising given that even mild dysfunction was classified as clinically significant; however, even an analysis of the full data set showed very good ($\kappa = 0.70$) agreement between DTTE and VTTE (Table 6, Appendix 7), meaning that VTTE performed well at not only distinguishing between normal and any degree of impairment, but also at discerning the differences between mild and moderate/severe dysfunction. This is impressive, given the lack of TDI or M-Mode TAPSE with the Vscan.

The assessment of RV systolic function with pocket-sized devices is poorly represented in current literature. Cullen et al. (2014) did include it in their study, and found only two cases of discordance in their sample of 190 patients, although a Kappa statistic was not provided. Testuz et al. (2012) also included it in their protocol, finding good agreement ($\kappa = 0.69$).

It is worth noting that qualitative methods in general for assessing the severity of pressure-loading have been shown to perform favourably. Howard et al. (2012) state that experienced echocardiographers are able to accurately grade RV function as mild, moderate or severely impaired on the basis of a qualitative assessment of right ventricular contractility, dilation and hypertrophy. Lange et al. (2013) used qualitative methods to predict pulmonary hypertension (PH) at right heart catheterisation with similar accuracy to estimation of right ventricular systolic pressure, using right ventricular enlargement as the primary indicator.

One study by Kitada et al. (2013) did address the detection of PH with the Vscan device. They found strong agreement between the Vscan and full TTE on the presence of pulmonary hypertension, but worryingly, 5 patients with PH were missed by Vscan. However, all of these had RVSP estimated by full TTE $\leq$ 46mmHg. Given the findings of the present study and research discussed above, it seems highly likely that VTTE would perform excellently in screening for preoperatively significant levels of PH, but further research is needed in this area specifically before it can be definitively concluded that significantly elevated right heart pressures (>mild) would be detected on a VTTE screen. Given its large number of PH queries and the expertise of its echocardiographers, our department would be ideally suited to conduct such a study.

- **Mitral Valve**

There were no cases of mitral stenosis in the sample, and there were no false positives for mitral stenosis. For mitral regurgitation, agreement between DTTE and VTTE was good ($\kappa = 0.65$). Previous studies (Kono et al., 2011; Testuz et al. 2013) have found that the Vscan has a tendency to overestimate the severity of mitral regurgitation, but this was not found to be the case in the present study.

The false negative arose from the Vscan operator grading the severity of MR as 'normal/mild,' and the DTTE operator grading as 'mild-moderate' (see images, Appendix 5), which had to be coded as 'moderate' for statistical analysis. As previously discussed in reference to tricuspid regurgitation, it is possible that, if faced with the same choice of rating scale ('normal/mild' or 'moderate/severe'), the DTTE operator would also have picked the non-significant category. Indeed, the second rater test also rated the level of MR as non-significant, in agreement with VTTE.

The false positive occurred in a patient who was found to have a Barlow's-type mitral valve. This was identified on VTTE, with the referral for full TTE box ticked and the note "MV prolapse with eccentric MR. ?Barlows." It seems likely that, given the eccentricity of the MR jet, the VTTE operator conservatively graded the regurgitation as moderate-severe with the caveat that this warranted further investigation by DTTE. Thus, whilst this case weakens the performance of VTTE from a statistical point of view, it is encouraging for the use of VTTE as a preoperative screening tool in the hands of knowledgeable and experienced operators. Differentiating between primary and secondary causes of MR is vital for anaesthetists in the preoperative context, due to different responses to loading conditions (Kristensen et al, 2014).

Interestingly, a similar level of discordance was found for the inter- and intra-rater tests in the grading of mitral regurgitation severity as between DTTE and VTTE for the same group of patients, which suggests that the disagreement may not be an inherent weakness of the Vscan itself. Studies which have looked at the interobserver variability in screening for MR by colour Doppler have reported high agreement, but most report this in the form of a percentage of agreement. For example, Dall'Aglio et al. (1989) reported agreement for presence or absence of MR at 89%, reporting that this was "good." Agreement between DTTE and the second rater was in the present study was also 89%, but $\kappa = 0.341$, which corresponded to only fair agreement.

In terms of the grading of severity (as opposed to mere presence or absence), it is widely accepted that colour Doppler is *not* an accurate method (Lancellotti et al., 2010b; Hamilton-Craig et al., 2015), for the same reasons as discussed in Section 5.5 for aortic regurgitation. It cannot be known whether more quantitative methods, such as calculations of regurgitant volumes, were performed by the second rater in all (or any) of the three studies in which discordance with the original DTTE was found. This is because the second rater was only instructed to use quantitative methods where they felt it was necessary, but the fact that they were reporting onto a simplified reporting sheet may have led them towards a heavier reliance upon qualitative techniques.

Reporting onto the tick-box reporting form has value because, as mentioned previously, it allows discordance due to the differences in reporting methods to be partially resolved. However, this influence cannot be separated from the effects of inter-rater variability with the current study design. Future work may consider establishing a 'benchmark' level of inter and intra-rater reliability for both DTTE and VTTE, using the same reporting method. This would allow the results of the inter-rater test from the present study to provide more insight into the reasons for discordance, in order to more confidently judge their clinical implications.

5.6 Others

- **Left Ventricular Hypertrophy**

Left ventricular hypertrophy has been linked with perioperative ischaemia in non-cardiac surgical patients (Grasso & Jaber, 2014). It was not possible to obtain a statistical measure of agreement for LV hypertrophy, given that no significantly increased LV wall thickness was detected on VTTE. There was one false negative in the study, but as with the false negative for TR (Section 5.5), the second rater concurred with the VTTE report and graded this as "mild," in contradiction with their own original DTTE report which reported it as "mild-moderate." This would again suggest that this particular 'false negative' is not of perioperative significance.

A number of studies have concluded that handheld echocardiography is an accurate method for screening for LV hypertrophy (Vourvouri et al., 2002; Senior et al., 2004; Coletta et al., 2006; Fukuda et al., 2009). However, these studies employed quantitative methods on both devices.

Expert operators in a study by Galderisi et al. (2010) used only qualitative methods for judging the severity of LV hypertrophy with handheld echocardiography, and found very high agreement between operators (κ=0.91). However, in this study, operators were asked to identify only the presence/absence of hypertrophy. Hypertrophy was defined very sensitively, as a septal or posterior wall thickness ≥1.1cm. This would be relatively easy to judge by eye, given the presence of 1cm measurement markers along the y-axis of the Vscan imaging area. This is in contrast with the present study, where operators followed the BSE guideline values of 1.3-1.5cm for mild hypertrophy, and ≥1.6cm for moderate and above (Lang et al., 2005). Using the criteria of Galderisi et al. (2010), the one false negative result in the present study would have been classed as agreement, given that it was a case of the VTTE selecting 'mild' over

'moderate/severe,' as opposed to the pathology being completely missed. However, it was deemed important in the present study not to introduce changes to normal clinical practice, and this included quantitative thresholds of pathology.

Given that mild hypertrophy was over-diagnosed in 16.7% of patients with VTTE, increasing sensitivity for significant hypertrophy would not be a viable solution. It is worth considering that in a 'real life' screening application, operators would not be under instruction not to use quantitative measures. Given the high levels of agreement in previous studies between full echocardiography machines and handheld devices when quantitative measurements were taken, as well as in the Galderisi et al. study where there was a qualitative assessment of wall thickness ≥1.1cm, it seems sensible to consider recommending quantitative measurement in borderline cases, i.e. where the operators feel that wall thickness is close to the Vscan's 1cm measurement markers.

- **Right Atrial Pressure (IVC)**

Inspiratory collapse of the inferior vena cava is often qualitatively assessed by standard echocardiography, although measurements are taken in ambiguous cases. IVC diameter, collapse, and RA size are used to assign an approximate value for right atrial pressure, according to the BSE recommendations (Rudski et al., 2010). Unfortunately, no patients were deemed to have elevated right atrial pressure on DTTE, and no robust measure of agreement was possible.

Excellent agreement has been found when qualitatively assessing IVC size by pocket echocardiography (Khan et al., 2014). Those studies rating pocket echocardiography less favourably on this measure (for example, Leibo et al., 2011) compare quantitative measurements,

without any measure of the normal level of interobserver variability. It is also important to note that the study by Leibo et al. imposed a time limit of 5 minutes on Vscan examinations, which is below the mean and median time required to perform a full VTTE in the present study. As the authors acknowledge themselves, the fact that subcostal views are the last to be taken could have resulted in poorer image quality and agreement on this measure.

Overall agreement was 97%, with the VTTE returning two false positives. These were both in the context of studies which were rated as abnormal overall for a number of other reasons, so the impact of these false positives was minimal.

- **Contraindications to VTTE**

It was clear that the benefits of VTTE screening were not homogenous across all non-cardiac preoperative patients. Possible contraindications to VTTE screening could be referral by a cardiologist, known stenosis (given that any stenosis greater than mild will require quantification), prosthetic valves, and possibly high-risk surgery as defined by Fleisher et al. (2014). It has previously been suggested that a high BMI and inability to assume the left lateral decubitus position should be contraindications for pocket echocardiography (Cluer, 2014; Leibo et al., 2011), but studies have not found a relationship between body mass index (BMI) and image quality on pocket echocardiography to be statistically significant (Leibo et al., 2011; Gianstefani et al., 2013). In the present study, two of the three patients with nondiagnostic VTTE image quality did have a BMI>40kg/m^2 (Cluer, 2014), but the fact that at least five of the patients with acceptable image quality also had a BMI>40kg/m^2, suggests that the relationship between image quality and BMI is more complex.

Known elevated right heart pressures or pulmonary hypertension would be a sensible addition to the above list of contraindications. Minai et al. (2013) recommend a thorough assessment of pulmonary hypertension prior to non-cardiac surgery. In fact, VTTE graded RV dysfunction remarkably well, but as its ability to detect PH specifically is untested (whilst all three patients in the present study with RV dysfunction had elevated RVSP, none were known to have PH) and in light of the fact that VTTE cannot estimate RVSP, Cluer's conservative recommendation to refer patients even with mild RV dysfunction appears justified. Further work to assess the ability of VTTE to detect PH specifically would clearly be a valuable addition to the literature.

A final important area where questions remain is that of diastolic heart failure, or heart failure with normal ejection fraction (HFNEF) (Sanderson, 2014). Ischaemic heart disease and symptomatic heart failure are considered by some to be the most important perioperative risk factors in non-cardiac surgery (Hammill et al., 2008; Flu et al., 2010). Others go further, including *asymptomatic* heart failure for those undergoing high-risk vascular surgery (Flu et al., 2010).

Doppler echocardiography is the "method of choice" for the confirmation of diastolic heart failure (McMurray et al., 2012). The Vscan's lack of spectral or tissue Doppler capabilities make it an inappropriate tool for the assessment of patients suffering from heart failure in the context of a normal or only mildly reduced ejection fraction. However, mild grades of diastolic heart failure have not been shown to have adverse effects in the perioperative patient (Fleischer et al., 2014). Severe diastolic heart failure is frequently (but not always) associated with significant LV hypertrophy (Pirracchio et al., 2007), for which recommendations for screening with VTTE have already been made (Section 5.6). The possibly still remains that HFNEF could go undetected by VTTE, and for this reason, it would clearly be imperative to exclude any patient with known heart failure from VTTE.

Many authors define risk of HFNEF by patient characteristics, such as underlying ischaemic heart disease, untreated hypertension, diabetes, female gender or age. Pirracchio et al. (2007) state that, among heart failure patients, diastolic heart failure is most prevalent in patients aged >70 years. However, it would not make sense to exclude patients aged >70 years from VTTE screening, as the present study found that there was no greater prevalence of pathology with age, and patients aged ≥65 were in fact a subgroup for which VTTE performed excellently (66% of whom were also >70), with a sensitivity of 100%, specificity of 94%, and cost saving per patient of £44.27.

Given the above, if an exclusion is to be made on the basis of risk for HFNEF, it seems sensible to exclude only patients undergoing high-risk surgery (previously defined in Section 2.9) from VTTE. Of the two patients for vascular surgery in the present study (Figure 5), one of these would potentially have fulfilled this criteria.

The fact that no patients with HFNEF (or the previously discussed topic of pulmonary hypertension) were recruited – whilst unfortunate in that questions remain unanswered – also point to the reality that patients with symptomatic HFNEF or PH would be likely to already be under the care of a cardiologist. If referral for TTE from a cardiologist were already made an exclusion criteria for VTTE, then this problem may be circumvented.

RESULTS, CONCLUSIONS AND APPENDICES HAVE BEEN REMOVED FROM THIS DOCUMENT. Please contact catherine@portableultrasoundmachines.co.uk if you require more information.

References

Abe, Y., Ito, M., Tanaka, C., et al. (2013). *A novel and simple method using pocket-sized echocardiography to screen for aortic stenosis.* J Am Soc Echocardiogr. 26(6):589-96.

Agarwal, S., Rajamanickam, A., Bajaj, N. et al. (2013). *Impact of Aortic Stenosis on Postoperative Outcomes After Noncardiac Surgeries.* Circulation: Cardiovascular Quality and Outcomes (6)193-200.

Andersen, G., Haugen, B., Graven, T. et al. (2011). *Feasibility and reliability of point-of-care pocket-sized echocardiography.* European Journal of Echocardiography (12): 665-670.

Armstrong, W. & Ryan, T. (2010). Feigenbaum's Echocardiography, Seventh Edition. Lippincott Williams & Wilkins, Philadelphia, USA.

Bettex, A., Prêtre, R., Jenni, R., Schmid, E. (2005). Cost-effectiveness of routine intraoperative transesophageal echocardiography in pediatric cardiac surgery: a 10-year experience. Anesth Analg. 100(5):1271-5.

Beynon, R. (2011). *Clinical applications of two-dimensional speckle tracking.* Heart, 97(4): 342.

Bhatia, R., Carne, D., Picard, M., Weiner, R. (2012). *Comparison of the 2007 and 2011 appropriate use criteria for transthoracic echocardiography in various clinical settings.* J Am Soc Echocardiogr. 25:1162-1169.

Biais, M., Carrié, C., Delaunay, F. et al. (2012). *Evaluation of a new pocket echoscopic device for focused cardiac ultrasonography in an emergency setting*. Critical Care, 16:R82.

Blondheim, D., Beeri, R., Fienberg, B., et al. (2010). *Reliability of visual assessment of global and segmental left ventricular function: a multicentre study by the Israeli Echocardiography Research Group.* J Am Soc Echocardiogr. 23(3):258-64.

BMJ (2015). *Preoperative echocardiographic risk assessment.* [online]
Available at: http://bestpractice.bmj.com/best-practice/monograph/954.html
Accessed 12th August 2015

Canty, D., Royse, C., Kilpatrick, D. et al. (2012a). *The impact of focused transthoracic echocardiography in the pre-operative clinic*. Anaesthesia (67), pp. 618-625.

Canty, D., Royse, C., Kilpatrick, D. et al (2012b). *The impact of preoperative focused transthoracic echocardiography in emergency non-cardiac surgery patients with known risk or risk of cardiac disease.* Anaesthesia 67(7):714-20.

Canty, D., Royse, C., Kilpatrick, D. et al (2012c). *The impact on cardiac diagnosis and mortality of focused transthoracic echocardiography in hip fracture surgery patients with increased risk of cardiac disease: a retrospective cohort study.* Anaesthesia 67(11):1202-9.

Cavallari, I., Mega, S., Goffredo, C. et al. (2015). *Hand-held echocardiography in the setting of pre-operative cardiac evaluation of patients undergoing non-cardiac surgery: results from a randomized pilot study*. Int J Cardiovasc Imaging 31:995-1000.

Chung, A., Das, S., Leonard, D. et al. (2006). *Women Have Higher Left Ventricular Ejection Fractions Than Men Independent of Differences in Left Ventricular Volume*. Circulation (113):1597-1604.

Cluer, A. (2014). *Preoperative 'Pocket' Echocardiography Trial (POPPET)* (MSc Dissertation). Imperial College London.

Coletta C., De Marchis E., Lenoli M., et al. *Reliability of cardiac dimensions and valvular regurgitation assessment by sonographers using hand-carried ultrasound devices*. Eur J Echocardiogr 2006;7:275-83

Cullen, M., Blauwet, L., Vatury, O. et al. (2014). *Diagnostic Capability of Comprehensive Handheld vs Transthoracic Echocardiography*. Mayo Clinic Proc. 89(6):790-798.

Dall'Aglio, V., D'Angelo, G., Moro, E. (1989). *Interobserver and echo-angio variability of two-dimensional colour Doppler evaluation of aortic and mitral regurgitation.* Eur Heart J, 10(4):334-40.

Danelich, I., Lose, J., Wright, S., et al. (2014). *Practical Management of Postoperative Atrial Fibrillation after Noncardiac Surgery.* Journal of the American College of Surgeons, Vol 219, No. 4, pp. 831–841.

Dawson, D. (2015a). *Departmental Figures*. Unpublished.

Dawson, D. (2015b). *Job Summary* [online]
Available at:
http://jobs.imperial.nhs.uk/job/UK/London/London_Charing_Cross_Hospital/Imperial_College_Healthcare_NHS_Trust/Echocardiography/Echocardiography-v391645?_ts=404
Accessed 2nd August 2015.

EchoTech (2015). *Establishing Value For Money* [online]
Available at:
http://www.echotech.co.uk/i_am_a_commissioner/delivering_efficiency/115_establishing_value_for_money
Accessed 1st August 2015.

Eckel, R. (1997). *Obesity and heart disease*. Circulation(96): 3248-322250

Erkoyuncu, J., Bolscchikov, S., Steenstra, D., et al. (2013). *Constructing and Evaluating 'as-is' and 'to-be' OPM Models for the Healthcare sector for adoption of Vscan*. Procedia Computer Science, 16:413-422.

Feinstein, A. & Cicchetti, D. (1990). *High agreement but low kappa: I. The problem of two paradoxes*. J Clin Epidemiol. 43(6): 543-9.

Fleischer, L., Fleischmann, K., Auerbach, A. et al. (2014). *2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients undergoing Noncardiac Surgery*. JACC Vol 64, Issue 22.

Fleishmann, K. & Weeks, S. (2012). *Image Analysis in Echocardiography*. In: Otto (ed), Practice of Clinical Echocardiography, 4th Edition: Philadelphia: Elsevier Saunders, pp. 236-246.

Flu, W., Kuijk J. Hoeks, S. (2010). *Prognostic Implications of Asymptomatic Left Ventricular Dysfunction in Patients Undergoing Vascular Surgery.* Anesthesiology 6(112):1316-1324.

Frederiksen, C., Juhl-Olsen, P., Larsen, U., Neilsen, D., Eika, B., Sloth, E. (2010). *New pocket echocardiography device is interchangeable with high-end portable system when performed by experienced examiners.* Acta Anaesthesiol Scand, 54(10): 1217-1223.

Freeman, R. (2012). *Exercise Echocardiography*. In: Otto (ed), Practice of Clinical Echocardiography, 4th Edition: Philadelphia: Elsevier Saunders, pp. 268-291.

Fukuda, S., Shimada, K., Kawasaki, T. et al. (2009). *Pocket-sized transthoracic echocardiography device for the measurement of cardiac chamber size and function.* Circ J 73(6):1092-6.

Galderisi, M., Santoro, A., Versiero, M., et al. (2010). *Improved cardiovascular diagnostic accuracy by pocket size imaging device in non-cardiologic outpatients: the NaUSiCa (Naples Ultrasound Stethoscope in Cardiology) study.* Cardiovascular Ultrasound 8:51.

Gianstefani, S., Catibog, N., Whittaker, A. (2013). *Pocket-size imaging device: effectiveness for ward-based transthoracic studies.* European Heart Journal – Cardiovascular Imaging 14:1132-1139.

Grasso, A. & Jaber W. (2014). *Cardiac Risk Stratification for Non-Cardiac Surgery.* [online] Available at: http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/cardiology/cardiac-risk-stratification-for-noncardiac-surgery/Default.htm [Accessed 21st July 2015]

Groban, L. & Dalane, K. (2010). *Diastolic Function: A Barometer for Cardiovascular Risk?* Anesthesiology 112(6):1303-1406.

Gatzoulis, A., Hechter, S., Siu, S., Webb, G (1999). *Outpatient clinics for adults with congenital heart disease: increasing workload and evolving patterns of referral*. Heart (81):57-61.

Gatzoulis, A. & Webb, G. (2003). *Adults with Congenital Heart Disease: A Growing Population*, in Gatzoulis, A., Webb, G. & Daubeney, P. (2003), Diagnosis and Management of Adult Congenital Heart Disease.

Gibbs, S., Stefanidis, A., Li, W. (2009). *Pulmonary Hypertension Clinical Echocardiography.* In: Nihoyannopoulous, P., Kisslo, J. (eds), Echocardiography. London: Springer, pp. 229-249.

Gudmundsson, P., Rydberg, E., Winter, R., Willenheimer, R. (2005). *Visually estimated left ventricular ejection fraction by echocardiography is closely correlated with formal quantitative methods*. International Journal of Cardiology, 101(2):209-212.

Hallgren, K. (2012). *Computing Inter-Rater Reliability for Observational Data: An Overview and Tutorial*. Tutor Quant Methods Psychol. 2012; 8(1): 23–34.

Hamilton-Craig, C., Strugnell, W., Gaikwad, N. et al. (2015). *Quantitation of mitral regurgitation after percutaneous MitraClip repair: comparison of Doppler echocardiography and cardiac magnetic resonance imaging.* Ann Cardiothorac Surg 4(4):341-351.

Hammill, B., Curtis, L., Bennett-Guerrero, E. et al. (2008). *Impact of Heart Failure on Patients Undergoing Major Noncardiac Surgery*. Anesthesiology; 108(4):559-567

Hoffman, R., von Bardeleben, S., Kasprzak, J. (2006). *Analysis of regional left ventricular function by cineventriculography, cardiac magnetic resonance imaging, and unenhanced and contrast-enhanced echocardiography: a multi-center comparison of methods.* J Am Coll Cardiol. 47(1):121-8.

Hoskins, P., Martin, K., Thrush, A. (2010). *Diagnostic Ultrasound Physics and Equipment, Second Edition.* New York: Cambridge University Press.

Howard, L., Grapsa, J., Dawson, D. et al. (2012). *Echocardiographic assessment of pulmonary hypertension: standard operating procedure.* Eur Respir Rev 21(125):239-248.

Imperial College Healthcare NHS Trust (2015). *National Pulmonary Hypertension Services.* [online]
Available at:
http://www.imperial.nhs.uk/pulmonaryhypertension/nationalpulmonaryhypertensionservices/index.htm
Accessed 11th August 2015

Jettoo, P., Kakwani, R., Junejo, S., et al. (2011). *Pre-operative echocardiogram in hip fracture patients with cardiac murmur- an audit.* Journal of Orthopaedic Surgery and Research 6(49)

Kimura, B., Blanchard, D., Willis, C., et al. (2002). *Limited Cardiac Ultrasound Examination for Cost-effective Echocardiographic Referral*. Journal of the American Society of Echocardiography, 15(6):640-6.

Kimura, B. & DeMaria, A. (2003). *Time Requirements of the Standard Echocardiogram: Implications Regarding Limited Studies*. Journal of the American Society of Echocardiography, 16(10):1015-8.

Khan, H., Wineinger, N., Uddin, P. et al. (2014). *Can Hospital Round With Pocket Ultrasound By Cardiologists Reduce Standard Echocardiography?* The American Journal of Medicine, 127.

Khanna, D., Miller, A., Nanda, N., Ahmed, S., Lloyd, S. (2005). *Transthoracic and Transesophageal Echocardiographic Assessment of Mitral Regurgitation Severity: Usefulness of Qualitative and Semiquantitative Techniques*. Echocardiography, Vol 22, Issue 9.

Kisslo, J., Rivera, D., Adams, D. (2009). *Mitral Valve Disease*. In: Nihoyannopoulous, P., Kisslo, J. (eds), Echocardiography. London: Springer, pp. 135-213.

Kono, Y., Fukuda, S., Shimada, K. et al. (2011). *Pocket-Sized Echo for Evaluation of Mitral and Tricuspid Regurgitation.* JACC Cardiovascular Imaging 4(8)921:921.

Kristensen, S., Knuuti, J., Saraste, A. et al. (2014). *2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management*. European Heart Journal (35):2383–2431.

Kutty, S., Whitehead, K., Natarajan, S. et al. (2009). *Qualitative Echocardiographic Assessment of Aortic Valve Regurgitation with Quantitative Cardiac Magnetic Resonance: A Comparative Study*. Pediatric Cardiology, Vol. 30(7):971-977.

Lai, H., Lai, H., Lee, W., et al. (2010). *Impact of chronic advanced aortic regurgitation of the perioperative outcome of noncardiac surgery.* Acta Anaethesiol Scand, 54(5):580-8.

Lancellotti, P., Tribouilloy, C., Hagendorff, A. et al. (2010a). *European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 1: aortic and pulmonary regurgitation (native valve disease).* European Journal of Echocardiography (11): 223–244.

Lancellotti, P., Moura, L., Pierand, L. et al. (2010b). *European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease).* European Journal of Echocardiography 11(4): 307-32.

Lang, R., Badano, L., Mor-Avi, V., et al. (2015). *Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging.* Journal of the American Society of Echocardiography 28 (1): 1-39.

Lang, R., Bierig, M., Devereux, R. (2006). *Recommendations for chamber quantification.* Eur J Echocardiography (7)79-108.

Lange, T., Baumgartner, S., Arzt, M., Preifer, M. (2013). *Qualitative echocardiography parameters for prediction of pulmonary hypertension.* International Journal of Clinical Practice, Volume 67, Issue Supplement s179.

Leibo, M., Israel, R., Lillie, E., Smith, M., Rubenson, D., Topol, E. (2011). *Is Pocket Mobile Echocardiography the Next-Generation Stethoscope? A Cross-sectional Comparison of Rapidly Acquired Images With Standard Transthoracic Echocardiography.* Annals of Internal Medicine, Volume 155, No. 1.

Lund Research Ltd. (2013). *Cohen's kappa in SPSS*. [online]
Available at: https://statistics.laerd.com/premium/ck/cohens-kappa-in-spss-2.php
[Accessed 14th July, 2015]

Lavie, C., Milani, R., Hector, V. (2009). *Obesity and Cardiovascular Disease: Risk Factor, Paradox, and Impact of Weight Loss*. Journal of the American College of Cardiology, Vol 53, Issue 21:1925-1932.

Marwick, T. (2005). *Can we Justify the Cost of Echocardiography? Lessons from Outcomes Research*. Eur J Echocardiography 6, 155-163

McGowan, J. & Cleland, J. (2003). *Reliability of reporting left ventricular systolic function by echocardiography: A systematic review of 3 methods.* American Heart Journal 146(3):388-397.

McMurray, J., Adamopoulos, S., Anker, S. (2012). *ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012.* European Heart Journal 33:1787-184.

Minai, O., Yared, J., Kaw, R. (2013). *Perioperative Risk and Management in Patients With Pulmonary Hypertension.* Chest 144(1):329-340.

Muzzi, R., de Araújo, R., Muzzi, L., Pena, J., Silva, E. (2003). *Regurgitant jet area by Doppler color follow mapping: quantitative assessment of mitral regurgitation severity in dogs.* Journal of Veterinary Cardiology, 5(2):33-8.

Nageuh, S., Appleton, C., Gillebert, T. et al. (2009). *Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography*. Journal of the American Society of Echocardiography, 22(2):107-33.

Neale, D., Williams, D., Canty, D. (2015). *Cost-Benefit Analysis of Focused Pre-Operative Transthoracic Echocardiography in the Pre-Operative Clinic in Patients at Increased Cardiac Risk Presenting for Non-Cardiac Surgery – A Pilot Study*. International Journal of Anesthetics and Anesthesiology, 2(1).

NHS England (2014). *Payment by Results Guidance for 2009-10* [online]. Available at: http://www.healthcare-today.co.uk/doclibrary/documents/pdf/149_PbR.pdf [Accessed 10th August 2015]

Nihoyannopoulos, P. (No Date). *Echocardiographic Services Booklet. Standard Operating Procedures*. The Hammersmith Hospitals NHS Trust.

Nishimura, R., Otto, C., Bonow, R. et al. (2014). *2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary.* Circulation 129(23):2440-92.

Osnabrugge, R., Kappetein, P., Surryus, P. (2014). *Non-cardiac surgery in patients with severe aortic stenosis: time to revise the guidelines?* European Heart Journal 35(35):2346-2348.

Otto, C. (2013). *Textbook of Clinical Echocardiography, Fifth Edition.* Philadelphia: Elsevier Saunders.

Parikh, R., Mathai, A., Parikh, S., et al. (2008). *Understanding and using sensitivity, specificity and predictive values*. Indian J Ophthalmol 56(1):45-50.

Pearse, R., Moreno, R., Bauer, P. et al. (2012). *Mortality after surgery in Europe: a 7 day cohort study.* Lancet 380(9847):1059-1065.

Pearse, R. (2013). *Enhanced Peri-Operative Care for High-risk patients (EPOCH) Trial* [online]. Available at: http://www.epochtrial.org/docs/EPOCH%20Protocol%20v1%200final.pdf Accessed 14th November 2014

Picano, E., Lattanzi, F., Orlandini, A., Marini, C., L'Abbate, A. (1991). *Stress echocardiography and the human factor: The importance of being expert.* J Am Coll Cardiol 17(3):666-669.

Poldermans, D., Bax, J., Boersma, E. et al. (2009). *Guidelines for preoperative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery*. European Heart Journal (30) 2769a.

Popescu, B., Andrade, M. Badano, L., et al. (2009). *European Association of Echocardiography recommendations for training, competence, and quality improvement in echocardiography.* Eur J Echocardiogr 10:893 – 905.

Prinz, C., Dohrmann, J., Buuren, F. et al. (2012). *The importance of training in echocardiography: a validation study using pocket echocardiography*. J Cardiovasc Med, 13(11):700-7.

Prinz, C. & Voigt, J. (2011) *Diagnostic Accuracy of a hand-held ultrasound scanner in routine patients referred for echocardiography*. J Am Soc Echocardiogr 24(2):111-6.

Quéré, J., Tribouilloy, C., Enriquez-Sarano, M. (2003). *Vena Contracta Width Measurement: Theoretic Basis and Usefulness in the Assessment of Valvular Regurgitation Severity*, Current Cardiology Reports, Vol 5, Issue 2:110-115.

Roelandt, J. (2009). *Three-Dimensional Echocardiography.* In: Nihoyannopoulous, P., Kisslo, J. (eds), Echocardiography. London: Springer, pp. 603-618.

Roelandt, J., Wladimiroff, J. & Baars, A. (1978). *Ultrasonic Real-time Imaging with a Handheld Scanner*. Ultrasound in Med. & Biol. (4)93-9.

Rudski, L., Lai, W., Afilalo, J. (2010). *Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography*. J Am Soc Echocardiogr, 23:685-713

Saito, S., Takagi, A., Kurokawa, F. et al. (2012). *Usefulness of tissue Doppler echocardiography to predict perioperative cardiac events in patients undergoing noncardiac surgery.* Heart Vessels 27:594-602.

Samarendra, M., Mangione, M. (2015). *Aortic Stenosis and Perioperative Risk With Noncardiac Surgery*. Journal of the American College of Cardiology 65(3):295-302.

Sanderson, J. (2014). *HFNEF, HFpEF, HF-PEF, or DHF. What Is in an Acronym?* JACC Heart Failure 2(1):93-94.

Senior, R., Galasko, G., Hickman, M. et al. (2004). *Community Screening for Left Ventricular Hypertrophy in Patients with Hypertension Using Hand-held Echocardiography.* Journal of the American Society of Echocardiography, 17(1):56-61.

Shapiro, B., Nishimura, R., McGoon, M., Redfield, M. (2006). *Diagnostic Dilemmas: Diastolic Heart Failure Causing Pulmonary Hypertension and Pulmonary Hypertension Causing Diastolic Dysfunction*. Advances in Pulmonary Hypertension, Vol. 5, No. 1.

Shaw, L., Marwick, T., Berman, D. et al. (2006). Incremental cost-effectiveness of exercise echocardiography vs. SPECT imaging for the evaluation of stable chest pain. European Heart Journal 27:2448-2458.

Sicari, R., Galderisi, M., Voigt, J. et al. (2011). *The use of pocket-size imaging devices: a position statement of the European Association of Echocardiography*. European Journal of Echocardiography (12):85–8

Sim, J., Wright, C. (2005). *The Kappa Statistic in Reliability Studies: Use, Interpretation, and Sample Size Requirements*. Physical Therapy, Volume 85.

Spencer, K., Kimura, B., Korcarz, C. et al. (2013). *Focused Cardiac Ultrasound: Recommendations from the American Society of Echocardiography*. J Am Soc Echocardiogra 26:567-81.

Tashiro, T., Pislaru, S., Blustin, J. et al. (2014). *Perioperative risk of major non-cardiac surgery in patients with severe aortic stenosis: a reappraisal in contemporary practice.* European Heart Journal (35):2372-2381.

Testuz, A., Müller, H., Keller, P. et al. (2013). *Diagnostic accuracy of pocket-sized handheld echocardiographs used by cardiologists in the acute care setting.* Eur Heart J Cardiovasc Imaging 14(1):38-42.

Turner, S. & Monaghan, M. (2006). *Tissue harmonic imaging for standard left ventricular measurements: Fundamentally flawed*? Eur J Echocardiography (7)9-15.

Vourvouri, E., Poldermans, D., Deckers, J. et al. (2005). *Evaluation of a hand carried cardiac ultrasound device in an outpatient cardiology clinic.* Heart 91:171-176.

Vourvouri, E., Poldermans, D., Schinkel, F. et al. (2002). *Left ventricular hypertrophy screening using a hand-held ultrasound device.* European Heart Journal 23:1516-1521.

Vigoda, M., Sweitzer, B., Miljkovic, N., Arheart, K., Messinger, S., Candiotti, K., Lubarsky, D. (2011). *2007 American College of Cardiology/American Heart Association (ACC/AHA) Guidelines on perioperative cardiac evaluation are usually incorrectly applied by anesthesiology residents on evaluating simulated patients.* Anesthesia & Analgesia, 112(4):940-9.

Wharton, G., Steeds, R., Allen, J., et al. (2015). *A minimum dataset for a standard adult transthoracic echocardiogram: a guideline protocol from the British Society of Echocardiography*. Echo Research and Practice, Vol 2., Issue 1.

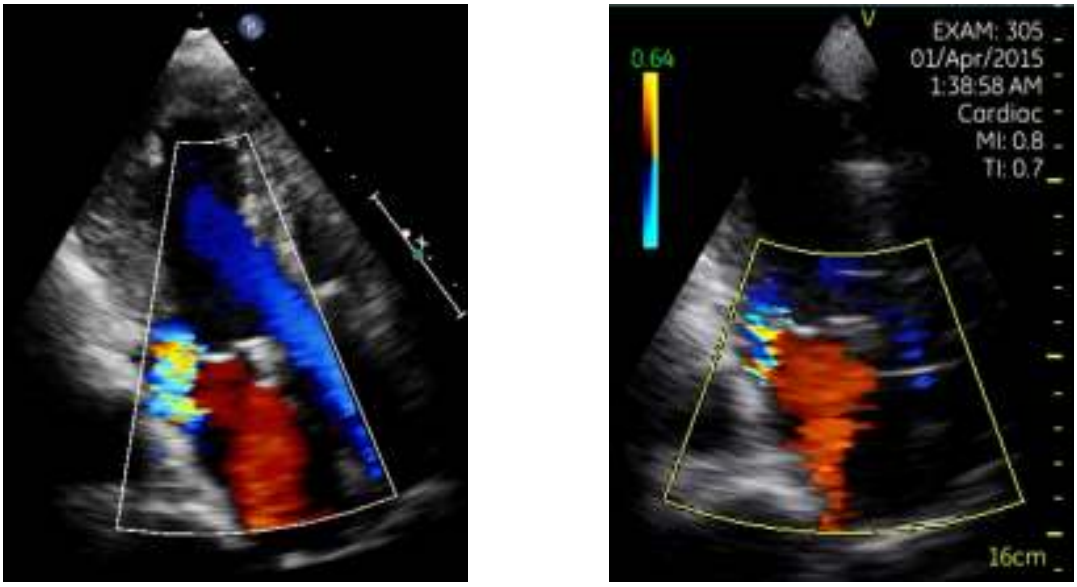
Zhou, X., Jones, M., Shiota, T., Yamada, I., Teien, D., Sahn, D. (1997). *Vena Contracta Imaged by Doppler Color Flow Mapping Predicts the Severity of Eccentric Mitral Regurgitation Better Than Color Jet Area: A Chronic Animal Study.* Journal of the American College of Cardiology. Vol 30, Issue 5:1393-1398.

Zoghbi, W., Enriquez-Sarano, M. Foster, E., Grayburn, P., Kraft, C., Levine, R., Nihoyannopoulos, P., Otto, C., Quinones, M., Rakowski, H., Stewart, W., Waggoner, A., Weissman, N. (2003). *American Society of Echocardiography: Recommendations for Evaluation of the Severity of Native Valvular Regurgitation with Two-dimensional and Doppler Echocardiography.* European Journal of Echocardiography, 4:237-261.

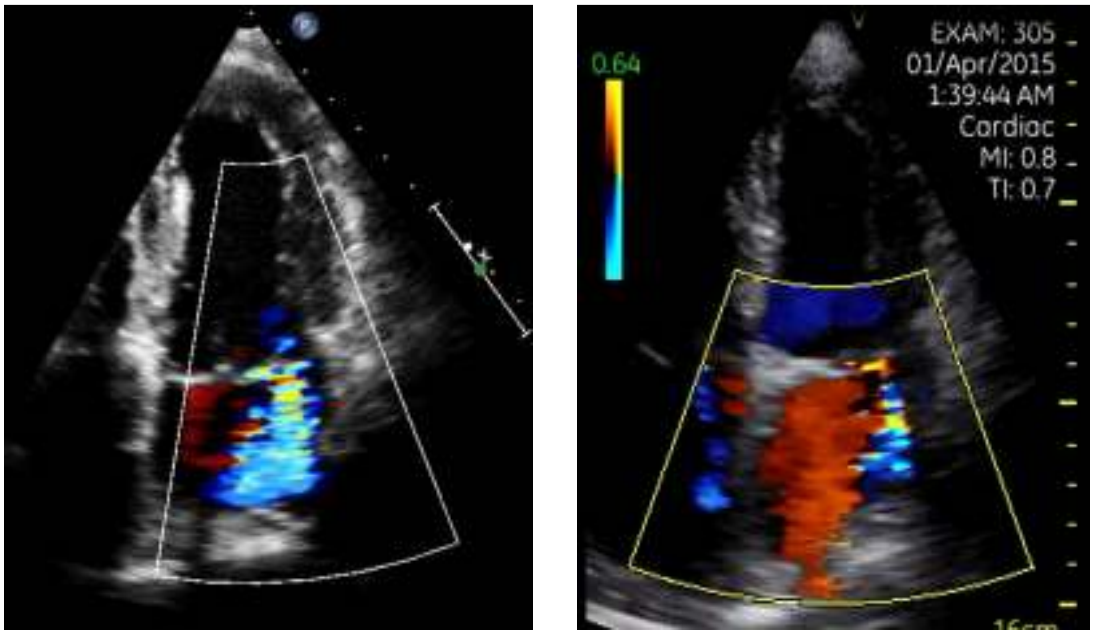
Appendix 5

Mitral Regurgitation:

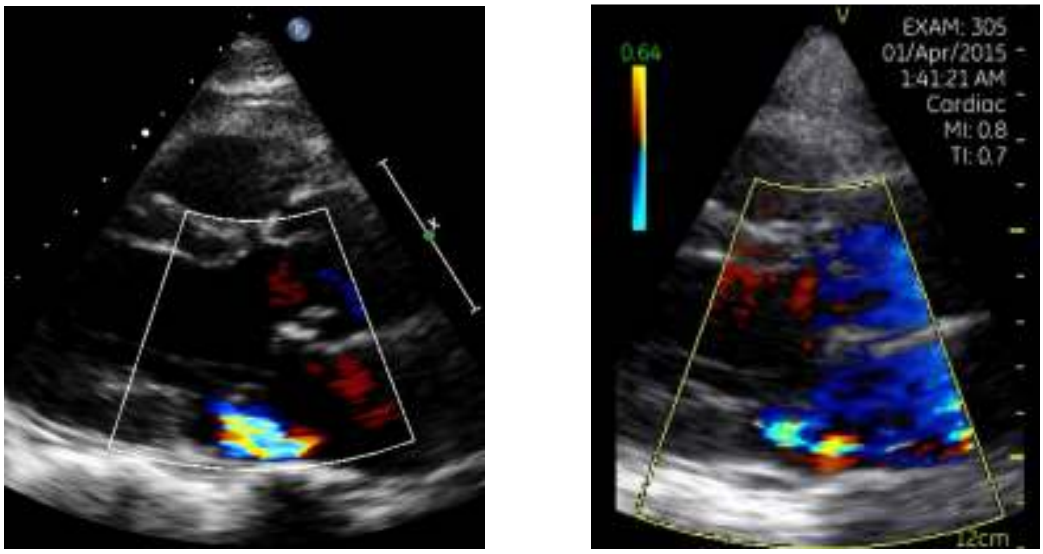
In all instances, the frame depicting the largest regurgitant jet area has been shown.



Above: Apical 3 chamber view shows MR in the same patient, as seen by DTTE (left) and VTTE (right). In this patient, MR was rated as “mild-moderate” by DTTE, but “normal-mild” on VTTE.



Above: Apical 4 chamber view centred on the left ventricle in the same patient, with DTTE on the left and VTTE on the right.



Above: Parasternal long axis view in the same patient, with DTTE on the left and VTTE on the right.

Discordant Results: tricuspid regurgitation, false positive

Figure 1: Parasternal long axis view of the right ventricle (RV inflow view) on the DTTE, with tricpusid regurgitation graded as ‘mild.’

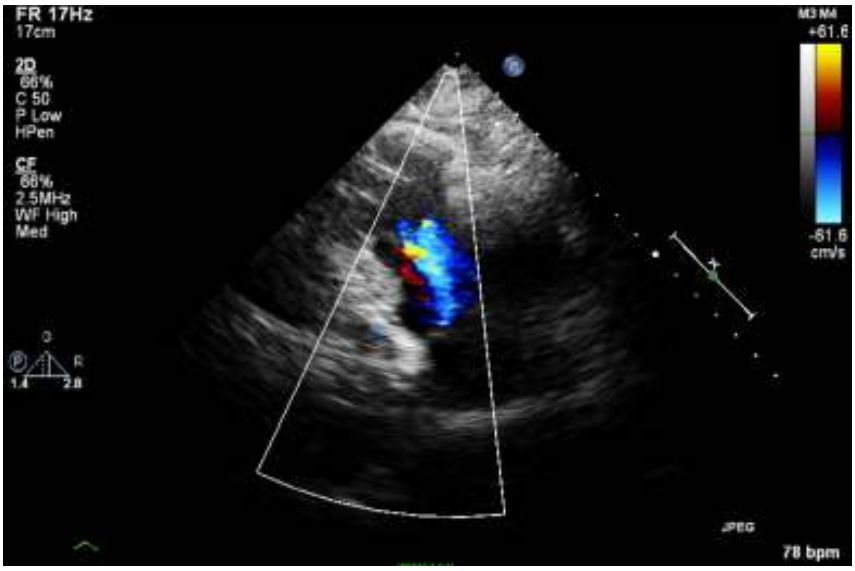


Figure 2: the same view in the same patient using the VTTE, with tricuspid regurgitation rated as ‘moderate.’

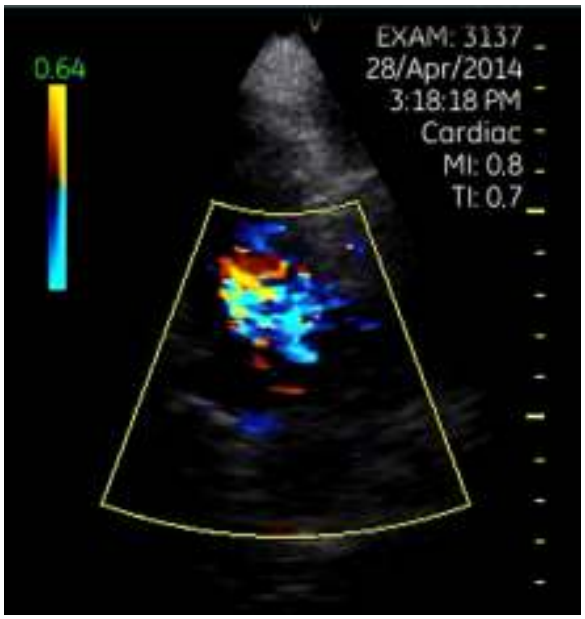


Figure 3: The density of the continuous wave Doppler signal in the same patient on DTTE.