Continuous non-invasive BP monitoring; service evaluation during induction of anaesthesia and haemodialysis

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Abstract

Background

Routine induction of anaesthesia and maintenance haemodialysis are two examples of clinical procedures that exert a direct effect on the cardiovascular system. The exact incidence of haemodynamic instability during such procedures is not well described, as it would have required invasive intra-arterial monitoring, which is not justified for routine use.

As part of two service evaluations, i.e. routine induction of anaesthesia and maintenance haemodialysis, we utilised a noninvasive continuous beat-by-beat haemodynamic monitor, which works using a finger cuff (Finometer), to assess the incidence of haemodynamic instability encountered during these procedures in comparison to the conventionally used intermittent noninvasive blood pressure (NIBP) measurement protocols.

Methods

Using the Finometer, we recorded haemodynamic variables during induction of anaesthesia in 100 patients undergoing elective surgery, and during maintenance haemodialysis in 25 patients with established renal failure.

Firstly, we assessed the feasibility of using the Finometer during induction of anaesthesia and haemodialysis by evaluating its success rate in providing measurements of haemodynamic variables, and by assessing its accuracy in comparison to the readings obtained by the conventional NIBP devices during our service evaluations.

Secondly, we assessed the incidence of haemodynamic instability during both procedures as detected by the Finometer in comparison to the existing conventional intermittent NIBP measurement protocols.

Results and discussion

The Finometer was successful in providing adequate haemodynamic monitoring in 96% and 86% of the attempts to use it in our service evaluations during induction of anaesthesia and haemodialysis respectively.

The Finometer showed comparable accuracy in terms of BP monitoring to the conventional NIBP monitors during induction of anaesthesia and haemodialysis.

A high incidence of significant hypotension as well as significant hypertension was shown during both, routine induction of anaesthesia and maintenance haemodialysis, which were underestimated or even missed by the conventionally used intermittent NIBP monitoring protocols. During induction of anaesthesia, 19% of the patients sustained an episode of hypotension defined as SBP less than 80 mmHg for more than 1 min, and 53% showed a transient increase of the SBP of more than 20% from baseline values. During Haemodialysis, 28% of the patients sustained an episode of hypotension defined as SBP less than 90 mmHg for more than 10 min, and 16% sustained an episode of severe hypertension defined as SBP more than 180 mmHg for more than 10 min.

Conclusion

Haemodynamic instability is commonly encountered during routine induction of anaesthesia and maintenance haemodialysis. Continuous noninvasive finger arterial haemodynamic monitoring is more reliable than the conventionally used protocols of intermittent NIBP monitoring in detecting such haemodynamic instability, thus, providing higher levels of patient safety. Extra and early information about haemodynamic variables, as provided by the Finometer, may provide a better insight on the exact cause of haemodynamic instability, which may aid the physicians in prompt and targeted management.

List of Publications

Abstracts:

Hakim K, Mole J, Mahajan R. Comparison of blood pressure (BP) measurements using arm cuff and Finometry during induction of anaesthesia: 3AP1-8. The European Anaesthesiology Congress. Euroanaesthesia 2010

Hakim K, Mole J, Mahajan R. Conventional intermittent blood pressure (BP) or Finometry in detecting episodes of hypotension during induction of anaesthesia: 3AP1-7. The European Anaesthesiology Congress. Euroanaesthesia 2010

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Table of contents

1 Overview 21

2 Background 23

2.1 Haemodynamic effects of induction of anaesthesia 23

2.1.1 Introduction 23

2.1.2 Cardiovascular effect of drugs commonly used during anaesthesia 23

2.1.3 Cardiovascular effects of airway management during induction of anaesthesia 25

2.2 Haemodynamic response to haemodialysis 26

2.2.1 Introduction 26

2.2.2 Normal Cardiovascular responses to hypovolaemia 27

2.2.3 Determinants of haemodynamic responses to haemodialysis 28

2.3 Effect of haemodynamic changes on patient outcome . 30

2.4 Blood pressure monitoring 32

2.4.1 Introduction 32

2.4.2 Methods of measuring blood pressure 33

2.5 Cardiac Output Monitoring 38

2.5.1 Introduction 38

2.5.2 Principles of Measuring Cardiac Output 39

2.6 Review of cardiac output monitoring devices 44

2.6.1 LiDCO Plus 44

2.6.2 LiDCO Rapid 46

2.6.3 Edwards FloTrac sensor and Vigileo monitor 47

2.6.4 Finometer (Finapres Medical Systems BV, Arnhem, the Netherlands) . 49

2.6.5 Nexfin 58

2.7 Endothelial function monitoring 59

2.7.1 Introduction 59

2.7.2 Pulse wave analysis 60

2.7.3 Interpreting the DVP (Digital volume pulse): 61

2.7.4 Validation of pulse wave analysis for reliability in evaluating the arterial stiffness and endothelial function 62

3 Aim of thesis 63

3.1 Service evaluation 63

4 Generic methods 65

4.1 Devices 65

4.1.1 Finometer 65

4.1.2 Pulse contour analysis 71

4.1.3 Non-invasive blood pressure monitoring (NIBP) 73

4.2 Analysis 74

4.2.1 Student's t test 74

4.2.2 Analysis of variance and Tukey's post hoc test 75

4.2.3 Chi-squared test 75

4.2.4 Bland and Altman technique 76

4.2.5 Linear regression 78

4.2.6 The British Hypertension Society (BHS) protocol for validation of BP devices 79

4.2.7 The Association for the Advancement of Medical Instrumentation (AAMI) protocol for validation of BP devices 82

5 A service evaluation of routine induction of anaesthesia involving an assessment of the adequacy of currently used intermittent noninvasive blood pressure (NIBP) devices in detecting episodes of transient hypotension 83

5.1 Introduction 83

5.2 Aim 85

5.3 Patients and methods 86

5.3.1 Patients 86

5.3.2 Methods 86

5.4 Results: Cohort analysis 96

5.5 Results: Comparison of blood pressure measurements using NIBP and the Finometer during routine induction of anaesthesia 100

5.5.1 Data handling and statistics 100

5.5.2 Results 102

5.5.3 Discussion 111

5.5.4 Conclusion 113

5.6 Results: Haemodynamic changes during routine induction of anaesthesia 114

5.6.1 Data handling and statistics 114

5.6.2 Results 116

5.6.3 Discussion 126

5.6.4 Conclusion 130

5.7 Results: Conventional intermittent blood pressure monitoring or continuous noninvasive haemodynamic monitoring in detecting maximum changes in BP that occur during routine induction of anaesthesia 131

5.7.1 Data handling and statistics 131

5.7.2 Results 132

5.7.3 Discussion 136

5.7.4 Conclusion 137

5.8 Results: An example of the haemodynamic changes during the whole period of anaesthesia as detected by the Finometer 138

5.9 Summary 144

6 A service evaluation of maintenance haemodialysis involving an assessment of the adequacy of the currently used intermittent noninvasive blood pressure (NIBP) devices in detecting BP aberrations.... 146

6.1 Introduction 146

6.2 Aim 147

6.3 Patients and methods 148

6.3.1 Patients 148

6.3.2 Methods 148

6.4 Results: Cohort analysis 157

6.5 Results: Comparison of blood pressure measurements using NIBP and the Finometer during maintenance haemodialysis 158

6.5.1 Data handling and statistics 158

6.5.2 Results 159

6.5.3 Discussion 165

6.5.4 Conclusion 166

6.6 Results: Gross haemodynamic changes in response to maintenance haemodialysis as detected by the Finometer 167

6.6.1 Data handling and statistics 167

6.6.2 Results 168

6.6.3 Discussion 178

6.6.4 Conclusion 180

6.7 Results: Assessment of the Incidence of significant hypotension during maintenance haemodialysis 181

6.7.1 Data handling and statistics 181

6.7.2 Results 183

6.7.3 Discussion 189

6.7.4 Conclusion 192

6.8 Results: Assessment of the Incidence of significant hypertension during maintenance haemodialysis 193

6.8.1 Data handling and statistics 193

6.8.2 Results 195

6.8.3 Discussion 202

6.8.4 Conclusion 205

6.9 Results: Assessment of the sensitivity of the conventional NIBP monitoring in detecting maximum changes in BP in comparison with the Finometer during maintenance haemodialysis 206

6.9.1 Data handling and statistics 206

6.9.2 Results 207

6.9.3 Discussion 212

6.9.4 Conclusion 214

6.10 Summary 215

7 General discussion and conclusion 219

8 Future directions 221

8.1 Use of the Finometer in operating theatres 221

8.2 Use of the Finometer in haemodialysis 222

8.3 Use of the Finometer in intensive care units 223

9 References 224

List of figures

Figure 1. NIBP device..... 34
Figure 2. Finometer screen showing a continuous pulse waveform..... 35
Figure 3. Philips IntelliVue MP30 monitor screen displaying an intra-arterial BP trace in red colour (reproduced from Philips)..... 37
Figure 4. Indicator dilution curve (reproduced from Jonas et al, 1999)[96]..... 40
Figure 5. Thermal dilution curve recorded from the pulmonary artery after the injection of indicator into the right atrium (reproduced from Conway and Lund-Johansen, 1990)[98] 41
Figure 6. Aortic pressure waveform (reproduced from Cerutti et al, 2001)[100] 43
Figure 7. Non-invasive continuous haemodynamic monitor (Finometer) 50
Figure 8. A Pulse waveform (reproduced from Millasseau et al, 2002)[176]..... 61
Figure 9. First step in downloading data from the Finometer via BeatScope 67
Figure 10. Second step in downloading data from the Finometer via BeatScope ... 68
Figure 11. Third step in downloading data from the Finometer via BeatScope 69
Figure 12. Fourth step in downloading data from the Finometer via BeatScope 70
Figure 13. The Pulse Trace device (Micro Medical, Gillingham, Kent, UK) 72
Figure 14. An example of plotted measurements obtained from two devices with the line of equality drawn (reproduced from Bland and Altman, 1986)[184]..... 76
Figure 15. An example of a Bland and Altman plot of differences against averages (reproduced from Bland and Altman, 1986)[184] 77
Figure 16. An example of a linear regression line (reproduced from Petrie et al, 2002)[185] 78
Figure 17. Procedure for sequential validation in the same arm (reproduced from Obrien 1993, et al)[150] 79
Figure 18. Sequential BP measurements according to the BHS protocol (reproduced from Braam 2003, et al)[186] 80
Figure 19. An example of the Finometer's raw data sheets. Haemodynamic data in between the highlighted events were deleted to be able to compress the file for the purpose of demonstration. 92

Figure 20. Pooled data for the SBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages. 103
Figure 21. Pooled data for the DBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages. 104
Figure 22. Pooled data for the MBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages. 105
Figure 23. Pooled data for the dSBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages. 108
Figure 24. Pooled data for the dDBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages. 109
Figure 25. Pooled data for the dMBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages. 110
Figure 26. Finometer trace 1 (patient 81)..... 116
Figure 27. Finometer trace 2 (patient 37)..... 117
Figure 28. Finometer trace 3 (patient 10)..... 117
Figure 29. Graph showing the changes in SBP, DBP, MBP, HR and SV as detected by the Finometer during a whole surgical procedure. Blue lines correspond to NIBP measurements and red lines correspond to actions taken during the procedure ... 140
Figure 30. Graph showing the changes in CO and TPR as detected by the Finometer during a whole surgical procedure. Blue lines correspond to NIBP measurements and red lines correspond to actions taken during the procedure ... 141
Figure 31. Graph showing the changes in SBP, DBP and MBP as detected by the NIBP during a whole surgical procedure. Red lines correspond to actions taken during the procedure..... 142

Figure 32. Pooled data for the SBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages. 161
Figure 33. Pooled data for the DBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages. 162
Figure 34. Pooled data for the MBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages. 163
Figure 35. Graph showing the SBP values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer 171
Figure 36. Graph showing the DBP values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer 172
Figure 37. Graph showing the MBP values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer 173
Figure 38. Graph showing the HR values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer 174
Figure 39. Graph showing the SV values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer 175
Figure 40. Graph showing the CO values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer 176
Figure 41. Graph showing the TPR values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer 177

List of tables

Table 1. BHS criteria for validation of a novel BP device..... 81
Table 2. Cohort characteristics (n = 100) 97
Table 3. Type of surgery (n = 100) 98
Table 4. Anaesthetic drugs and techniques used during induction of anaesthesia (n = 100) 99
Table 5. Assessment of the accuracy of the Finometer by applying the BHS criteria (n of readings = 311)..... 106
Table 6. Mean (SD) of haemodynamic variables during induction of anaesthesia as assessed by the Finometer..... 118
Table 7. Number of patients with episodes of hypotension sustained for more than 1 minute during induction of anaesthesia as indicated by SBP less than 80 mmHg, MBP less than 55 mmHg and a more than 40% decrease from baseline SBP and MBP readings. 119
Table 8. Number of patients sustaining the episode of SBP < 80 mmHg 119
Table 9. Percentage change of lowest BP readings (troughs) from baseline as detected by the Finometer (n = 100) 121
Table 10. The changes in HR, CO, SV &TPR during the BP trough (n = 100) 121
Table 11. Percentage change of highest BP readings (peaks) from baseline as detected by the Finometer (n = 100) 123
Table 12. The changes in HR, CO, SV &TPR during the BP peak (n = 100) 123
Table 13. Hypertensive vs. normotensive hypertensive response to induction of anaesthesia 124
Table 14. Effect of induction of anaesthesia on stiffness index (SI) and reflection index RI (n of readings = 52)..... 125
Table 15. Comparison between percentage changes of lowest blood pressure readings from baseline (NIBP vs. Finometer) (n = 100)..... 132
Table 16. n of readings >30% decrease from baseline as detected by NIBP vs. Finometer..... 133
Table 17. Time lag between lowest blood pressure readings detected by the Finometer and next available NIBP readings..... 133
Table 18. Comparison between percentage changes of highest BP readings from baseline (NIBP vs. Finometer) (n = 100) 134
Table 19. n of readings >30% increase from baseline as detected by NIBP vs. Finometer..... 135

Table 20. Time lag between highest BP readings detected by the Finometer and next available NIBP readings 135
Table 21. Cohort characteristics (n =25) 157
Table 22. Comparison between the NIBP's and the Finometer's pre dialysis and post dialysis BP readings 159
Table 23. Assessment of the accuracy of the Finometer by applying the BHS criteria 164
Table 24. Paired t test for all Finometer's haemodynamic variables pre and post dialysis (n = 25) 168
Table 25. Mean (SD) of haemodynamic variables during routine haemodialysis .. 169
Table 26. Percentage change of lowest BP readings (troughs) from baseline as detected by the Finometer (n = 25) 183
Table 27. The change in HR, CO, SV &TPR during the BP trough (n = 25)..... 183
Table 28. Comparison between predialysis, post dialysis and the averaged values of haemodynamic variables during the hypotension episode (SBP less than 90mmHg) (ANOVA and Tukey's post hoc test) (n = 7) 185
Table 29. Total duration of hypotension episodes of SBP less than 90 mmHg for more than 10 minutes (n=7)..... 185
Table 30. Comparison of pre and post dialysis haemodynamic variables in group 2 (paired t test) 186
Table 31. Comparison of the predialysis haemodynamic variables in both groups (unpaired t test) 187
Table 32. Comparison of the post dialysis haemodynamic variables in both groups (unpaired T test) 188
Table 33. Comparison of different factors for association with hypotensive episodes using an unpaired t test..... 188
Table 34. Percentage change of highest BP readings (peaks) from baseline as detected by the Finometer (n = 25) 195
Table 35. The change in HR, CO, SV &TPR during the BP peak (n = 25) 195
Table 36. Total durations of hypertension episodes of both, SBP more than 160 mmHg and SBP more than 180 mmHg that were encountered for more than 10 minutes..... 197
Table 37. Comparison between predialysis, post dialysis and the averaged values of haemodynamic variables during the hypertension episode of SBP greater than 180mmHg) (ANOVA and Tukey's post hoc test) (n = 4)..... 198

Table 38. Comparison of pre and post dialysis haemodynamic variables in group 4 (paired t test) 199
Table 39. Comparison of the predialysis haemodynamic variables in both groups (un-paired t test)..... 200
Table 40. Comparison of the post dialysis haemodynamic variables in both groups (un-paired t test)..... 201
Table 41. Comparison of different factors for association with hypertensive episodes using an un-paired t test 201
Table 42. Comparison of the 2 sets of NIBP readings that were taken during the whole period of haemodialysis using a paired t test (n = 25)..... 207
Table 43. Percentage change of lowest BP readings (troughs) detected by the Finometer from baseline NIBP readings using a paired t test (n = 25) 209
Table 44. Time lag between lowest blood pressure readings detected by the Finometer and next available NIBP readings..... 209
Table 45. Percentage change of highest BP readings (peaks) detected by the Finometer from baseline NIBP readings (n = 25) 211
Table 46. Time lag between highest blood pressure readings detected by the Finometer and next available NIBP readings..... 211

List of abbreviations

AAMI	Association for the Advancement of Medical Instrumentation
ACEi	Angiotensin converting enzyme inhibitor
ANOVA	Analysis of variance
AP	Arterial pressure
ARB	Angiotensin receptor blocker
ASA	American Society of Anesthesiologists Physical Status Calculation
AVF	Arterio-venous fistula
BHS	British Hypertension Society
BP	Blood pressure
C_2H_2	Open-circuit acetylene uptake
CAD	Coronary artery disease
CaO_2	Arterial oxygen content
CCB	Calcium channel blocker
CGRP	Calcitonin gene related peptide
CI	Cardiac index
CO	Cardiac output
COPD	Chronic obstructive pulmonary disease
CvO_2	Mixed venous oxygen content
CVP	Central venous pressure
Cwk	Total arterial compliance
DBP	Diastolic blood pressure
DM	Diabetes Mellitus
DVP	Digital volume pulse
ESKD	End-stage kidney disease
ETT	Endo-tracheal tube
f-IDH	Frequent intradialytic hypotension
FINAP	Finger arterial pressure
Hb	Haemoglobin
HCU	Height correction unit
HD	Haemodialysis
HR	Heart rate

HTN	Hypertension
IBI	Inter-beat interval
IDH	Intradialytic hypotension
IOH	Intra-operative hypotension
JNC	Joint National Committee
LiDCO	Lithium dilution cardiac output
LMA	Laryngeal mask airway
LVET	Left ventricular ejection time
MAC	Mean alveolar concentration
MBP	Mean blood pressure
N_20	Nitrous oxide
NIBP	Noninvasive blood pressure
NO	Nitric oxide
NSO	Negative surgical outcome
O_2	Oxygen
o-IDH	Occasional Intradialytic hypotension
PAOP	Pulmonary artery occlusive pressure
PAP	Pulmonary artery pressure
PCV	Packed cell volume
PPT	Peak to peak time
PPV	Pulse pressure variation
PR	Pulse rate
PRR	Plasma refilling rate
r	Correlation coefficient
r^2	Square of Correlation coefficient
RI	Reflection index
RRK	Riva-Rocci / Korotkoff
RRT	Renal replacement therapy
SBP	Systolic blood pressure
SD	Standard deviation
SDD	Standard deviation of the mean difference
SE	Standard error of mean
SI	Stiffness index
SV	Stroke volume
SVR	Systemic vascular resistance

SVV	Stroke volume variation
TB	Blood temperature
TB (t) dt	Change in blood temperature as a function of time
TI	Injectable temperature
TPR	Total peripheral resistance
UFR	Ultra filtration rate
VO_2	Oxygen uptake
Zao	Ascending aortic impedance

1 Overview

Episodes of transient hypotension are common during clinical procedures such as induction of anaesthesia or in patients undergoing haemodialysis.[1-3] Recent evidence suggests that hypotension even for one minute is associated with an increased 1 year mortality risk after non-cardiac surgery.[4, 5] Also an increased 2 year risk of mortality has been shown when hypotension is encountered during haemodialysis.[6] The exact incidence and severity of episodes of transient hypotension during anaesthesia or during haemodialysis are not well known, as this would require continuous blood pressure monitoring, which in the current medical practice involves invasive intra-arterial monitoring, a procedure reserved for the more critical patients.[7] During induction of anaesthesia and haemodialysis, it is common practice to monitor BP on intermittent basis via the conventional intermittent non-invasive blood pressure monitors (NIBP), which apply the oscillometric method. NIBP monitors are usually set at 2-3 min and up to 30 minutes intervals during induction of anaesthesia and haemodialysis respectively.

We aimed to evaluate the anaesthetic service at the time of induction of anaesthesia, and the service of haemodialysis in routine clinical settings, by assessing the extent and severity of maximum haemodynamic changes that occur, the existing level of monitoring of these changes, and their possible impact on patient safety.

We used the Finometer for continuous monitoring of the haemodynamics during the two service evaluations. The Finometer is a non-invasive beat-by-beat continuous haemodynamic monitor that uses a finger cuff. It has been shown to be accurate in terms of blood pressure monitoring[8] and reliable in following the trends of change in cardiac output.[9] It is widely used in cardiovascular research [10], but its role in clinical practice, in particular during anaesthesia or during haemodialysis, is not yet established. We assessed the potential of continuous haemodynamic monitoring, as provided by the Finometer, in improving patient safety during these procedures.

From the data collected during these evaluations we have addressed the following:

- Feasibility of using the Finometer during induction of anaesthesia and haemodialysis by assessing its success rate in providing adequate blood pressure recordings, and by comparing the blood pressure measurements obtained by the Finometer against those obtained by the conventional non-invasive blood pressure (NIBP) monitors used in operating theatres and haemodialysis units.
- Evaluation of the haemodynamic changes that occur during induction of anaesthesia and haemodialysis in terms of magnitude and time.
- Comparison of the Finometer and the conventional NIBP monitors in detecting episodes of maximum changes in blood pressure, and assessment of the potential of continuous haemodynamic monitoring in improving patient safety during induction of anaesthesia and haemodialysis.

2 Background

2.1 Haemodynamic effects of induction of anaesthesia

2.1.1 Introduction

General anaesthesia is a state of unconsciousness, amnesia and analgesia initially achieved by the process of induction of anaesthesia, which involves procedures that directly affect the cardiovascular system. These procedures include administration of anaesthetic drugs and management of the airways. Individual effects of these procedures on the cardiovascular system are well known, [11-15] but there is paucity of data describing the overall combined effect in a setting of routine induction of anaesthesia.

2.1.2 Cardiovascular effect of drugs commonly used during anaesthesia

Most anaesthetic drugs are known to cause myocardial depression and / or vasodilatation, thus, resulting in decrease in BP. During routine anaesthesia settings, hypotension is usually treated according to the anaesthetist's clinical judgment of the situation, by administering intravenous fluids and/or vasopressor drugs such as ephedrine and metaraminol.

2.1.2.1 Inhalational anaesthetics

Inhalational anaesthetics are gaseous and volatile agents used mainly for maintenance of anaesthesia, but can also be used for induction of anaesthesia. *Nitrous oxide (N_2O)* is a myocardial depressant, but normally this effect is overcome by the stimulation of the sympathoadrenal response[16] In left ventricular failure, which is associated with high sympathoadrenal activity, hypotension, decreased cardiac output and dose dependent decreased coronary flow may occur in response to N_2O. Therefore its use in patients with cardiac disease is not recommended.[17]

Halothane causes vasodilatation, myocardial depression, a decreased cardiac output and dose dependent hypotension.[13, 18]

Isoflurane causes hypotension, which is mainly due to vasodilatation in muscles and skin.[19]

Sevoflurane affects the cardiovascular system in a similar way to Isoflurane.[20]

In a study by Hanouz and colleagues (1998) the effect of halothane, isoflurane and sevoflurane in equal doses on isolated rat myocardial contractility was evaluated. The three agents produced a dose dependent decrease in myocardial contractility expressed as a percentage decrease of control values of the maximum isometric active force normalised per cross sectional area (AF), the maximum effect on contractility was observed at 2.5 mean alveolar concentration (MAC). Further comparison of the three agents in terms of the maximum decrease in AF which is expressed as a percentage of the control values at 2.5 MAC, showed 15%, 64% and 67% of the control value for halothane, isoflurane and sevoflurane respectively. In summary, Halothane exerted a significantly more potent negative inotropic effect than isoflurane or sevoflurane which exerted similar effects on the inotropicity.[21]

2.1.2.2 Intravenous anaesthetics

Intravenous anaesthetics are mainly used for induction of anaesthesia. They can also be used for maintenance of anaesthesia and sedation.

Sodium Thiopental causes dose dependent hypotension by decreasing the systemic vascular resistance[22] and the cardiac output.

Propofol decreases blood pressure in a similar way to thiopental but the effect is more profound as compared in equipotent doses.[23]

In a study by Rouby and colleagues, comparing the peripheral vascular effects of propofol and thiopental, 5 minutes after injection, showed that the mean arterial pressure decreased by 39% and 21% respectively ($p<0.01$). The systemic vascular resistance index decreased by 44% and 21% respectively ($p<0.05$) showing better haemodynamic stability with Thiopental.[24]

Midazolam causes a dose dependent decrease in blood pressure and vasodilatation.[25]

2.1.2.3 Opioids

Morphine causes arteriolar and venodilatation through depression of the vasomotor centre and also through histamine release. Blood pressure decreases especially when the patient is hypovolaemic or receiving other vasodilator medications. A decrease in heart rate may also occur due to vagal stimulation.[11]

Fentanyl may cause mild hypotension and bradycardia due to vagal stimulation.[26]

Alfentanil is a potent short acting opioid with minimal cardiovascular effects, it is safely used in cardiac surgery.[27]

Remifentanil is similar to Alfentanil in regards to the cardiovascular effects, but with faster resolution of effects on discontinuing the drug.[28]

In a single blinded randomised controlled study, Twersky and colleagues compared the haemodynamic effects of Remifentanil and Fentanyl on 2438 patients. Subjects were randomised to receive either intravenous Remifentanil at a dose of 0.5 μg / kg / min for induction of anaesthesia and a dose of 0.25 μg / kg / min for maintenance of anaesthesia, titrations of the dose during the operation were carried out according to the anaesthetist's judgment, or to receive intravenous fentanyl at a dose and titration that were adjusted also according to the anaesthetist's judgement.

Their results showed that systolic and diastolic pressures were 10-15 mmHg lower in the remifentanil group, heart rate was also 10-15 beats/m lower in the remifentanil group.[29]

2.1.2.4 Muscle relaxants

Muscle relaxants are not known to cause major haemodynamic effects. However, Stevens and colleagues in 1997, reported that rocuronium in contrast to vancuronium blocks the hypotensive effect of balanced induction of anaesthesia.[12]

2.1.3 Cardiovascular effects of airway management during induction of anaesthesia

Laryngoscopy and endotracheal intubation cause a transient reflex sympathetic stimulation, with an associated increase in the plasma catecholamine levels, subsequently increasing the blood pressure and heart rate; this might exert adverse effects especially on patients with coronary artery disease and cerebrovascular insufficiency.[30] Certain drugs used during induction of anaesthesia such as lidocaine, fentanyl, and alfentanil, are known to block this sympathetic response.[31]

2.2 Haemodynamic response to haemodialysis

2.2.1 Introduction

Haemodialysis is the most commonly employed method of renal replacement therapy in patients with end stage kidney disease (ESKD). It became a standard treatment for ESKD in the 1960s [32], and since then major advancements in the technique have been accomplished, which helped improve the quality of the service and patient outcomes. [33] Nevertheless, haemodialysis continues to be associated with complications. Efforts are continuously being undertaken by health care providers to further improve the quality of the service of haemodialysis. Haemodialysis involves withdrawal of blood from the patient's circulation and its passage across an extracorporeal circuit, where it gets in contact with a semipermeable membrane. A dialysis solution (dialysate) composed of a sterilised mixture of water and electrolytes, with sodium chloride concentrations similar to those of normal plasma, is present on the other side of the semipermeable membrane. The dialysate flows in the opposite direction to the blood causing diffusion of waste products from the blood into the dialysate across the concentration gradient created in the semipermeable membrane. Removal of extra fluids from the patient's circulation (ultrafiltration) is carried out by decreasing the pressure on the dialysate side of the machine, causing a pressure gradient across the semipermeable membrane allowing water to pass from the blood to the dialysate. Finally, the cleansed blood is returned back to the patient's circulation.[34] Maintenance haemodialysis is usually prescribed as 3-4 hours sessions, 3 times per week.

Vascular access to haemodialysis is gained by an intravenous catheter, an arterio-venous fistula (AVF) or a synthetic graft.[35] Bicarbonate and acetate are the two types of dialysate solutions available for haemodialysis. Better haemodynamic stability is provided by the bicarbonate dialysate in comparison to the acetate dialysate, as the latter causes a more extensive vasodilatory effect. [36]
During haemodialysis, a large volume of ultrafiltrate is removed from the circulation in a relatively short period of time (3 – 4 hours), which may cause hypotension if the normal compensatory cardiovascular responses to hypovolaemia are not intact.[37]

2.2.2 Normal Cardiovascular responses to hypovolaemia

Physiological compensatory mechanisms in response to hypovolaemia include; increased venous tone; increased heart rate with subsequent increase in cardiac output to overcome the decreased stroke volume; increased total peripheral resistance; redistribution of the blood to the more vital organs.[38] Many dialysis patients have other associated co-morbid conditions that limit their compensatory response to haemodialysis induced hypovolaemia, thus increasing the incidence of developing hypotension during haemodialysis.[39] Significant hypotension is the most common complication of haemodialysis, occurring in 25% to 50% of maintenance haemodialysis sessions.[2, 3]

2.2.3 Determinants of haemodynamic responses to haemodialysis

Blood volume: During haemodialysis, large volumes of fluid are removed from the circulation in a relatively short period of time. Normal cardiovascular compensatory mechanisms are responsible for keeping the patient haemodynamically stable during haemodialysis.[37] The net changes in blood volume are dependent upon the ultrafiltration rate (UFR) and the plasma refilling rate (PRR), which are two opposing forces.[40] The PRR occurs at capillary level and is regulated by the UFR and the dialysate sodium concentration through their effects on the oncotic and hydrostatic pressures.[41] Moreover, the plasma protein concentration, the haematocrit[42] and the interstitial volume cause an increase in the PRR.[37]

Venous tone: Dialysis patients commonly suffer from associated co-morbid conditions that may affect the integrity of their baroreflexes, thus reducing their venous capacity in response to hypovolaemia. [38] Also the use of a dialysate with low sodium content may cause a reduction in the venous tone.[43]

Peripheral vascular resistance: Vascular resistance is an important factor in maintaining blood pressure stability during dialysis induced hypovolaemia.[44]
Factors that affect the integrity of peripheral vascular resistance are:

- Antihypertensive vasodilator drugs e.g. angiotensin converting enzyme inhibitors (ACEi) and calcium channel blockers (CCB) obliterate the vasoconstrictor response to haemodialysis.
- Low haematocrit levels, which cause a decrease in blood viscosity and a consequent decrease in the total peripheral resistance.[45]

Factors that affect the integrity of both, the venous tone and the peripheral vascular resistance are:

- Ingestion of food during dialysis, by redirecting the blood flow to the splanchnic circulation, consequently causing a decrease in the preload and afterload.[46]
- The use of an acetate dialysate causes venodilatation and arterio-dilatation.[47]
- High temperatures cause cutaneous vasodilatation with a reduction in the total peripheral resistance and the venous tone.[38, 48]

Cardiac response: Normal cardiac functions are mandatory for maintaining haemodynamic stability during haemodialysis. The cardiac response to hypovolaemia is brought by the activation of the sympathetic nervous system, initially causing an increase followed by a decrease in the heart rate, also the contractility increases. Those responses tend to be inadequate for optimising the cardiac output in response to the haemodialysis induced decreased stroke volume.[49, 50] The most important factor in maintaining the cardiac output is optimal cardiac filling.[51] Cardiac diseases associated with impaired left ventricular filling such as pulmonary hypertension, tricuspid regurgitation and left ventricular hypertrophy will eventually lead to hypotension in response to haemodialysis.[40]

2.3 Effect of haemodynamic changes on patient outcome

During anaesthesia, as during haemodialysis, extreme values of blood pressure are known to increase the risk of morbidity and mortality. Moreover, Intraoperative hypotension (IOH) has been an area of major interest to researchers recently, for its impact on patient outcome.[5, 52-55]

No definite figure has yet been adopted as a definition of IOH. However the most commonly used is a systolic blood pressure value of less than 80 mmHg, a mean blood pressure less than 55-60 mmHg or a more than 20-25% decrease from baseline values of systolic or mean blood pressure values.[55] In a study by Bijker and colleagues in 2009, a comparison of 16 different definitions of IOH for prediction of 1 year mortality after non-cardiac surgery was performed, results showed a trend of an increased risk of 1 year mortality when there was a more than 1 minute duration of systolic blood pressure values lower than 80 mmHg, mean blood pressure lower than 60 mmHg or a more than 40-45% decrease from baseline values of both systolic and mean blood pressure in the elderly patients.[4]

Monk and colleagues in 2005, studied the effect of IOH on 1 year mortality in non-cardiac patients, results showed an increase in the relative 1 year mortality risk of 3.6% for every minute where the systolic blood pressure was lower than 80 mmHg.[5] Moreover, O'Reilly and colleagues showed that SBP equal or lower than 85 mmHg is an independent predictor of mortality. They also showed a linear relationship between mortality and SBP lower than 90 mmHg.[56]

During induction of anaesthesia, the depressive effects of the anaesthetic drugs, and the cardiovascular responses to airway management, which tends to increase sympathetic stimulation resulting in elevations in blood pressure and heart rate, are usually well tolerated. However, elderly patients, and/or those who are at higher risks of coronary artery disease and cerebrovascular disease are more prone to exaggerated cardiovascular responses with a resultant increase in the incidence of cerebrovascular strokes, myocardial infarctions and sudden deaths.[57, 58]
Patients on maintenance haemodialysis are at more than 30 times higher risks of morbidity and mortality than healthy age matched individuals. That is mainly due to uraemic complications, hypertension[59] and more importantly heart failure which affects 25-50% of patients undergoing maintenance haemodialysis. [60]
Atherosclerosis independent myocardial hypoperfusion is possibly the cause of myocardial stunning, which is a well known complication of maintenance haemodialysis.[61] Recurrent episodes of myocardial stunning eventually lead to chronic heart failure.[62] Myocardial stunning is known to be aggravated by intradialytic hypotension and it can be reverted by better haemodynamic stability during haemodialysis.[63, 64] Shoji and colleagues confirmed that intradialytic hypotension is associated with an increased risk of 2 year mortality.[6]

2.4 Blood pressure monitoring

2.4.1 Introduction

Blood pressure is one of the most important routine measurements in health care, and because of its fluctuating nature, blood pressure monitoring is always needed for the purpose of diagnosis and treatment of hypertension.[65]

Blood pressure variability is a well known character of the cardiovascular system. This can be observed on measuring blood pressure from different arterial sites and the reason for this is the different individual arterial properties.[66] Furthermore blood pressure is constantly changing throughout the day[67] and throughout each respiratory cycle.[68]

This normal variability of blood pressure creates a grey zone that makes it hard for physicians to diagnose hypertension. Researchers are constantly introducing accurate methods for monitoring blood pressure, which are easily applicable, for diagnosis and management of hypertension.[69] Furthermore, cardiovascular disease can be predicted by the extent of blood pressure variability.[70]

2.4.2 Methods of measuring blood pressure

Blood pressure can be either measured indirectly or directly by using the non-invasive or the invasive techniques respectively:

2.4.2.1 Indirect noninvasive method

Ways to measure blood pressure non-invasively:

- Riva-Rocci/Korotkoff, RRK (Auscultatory method)
- Marey (Oscillometric method)
- Peñáz/Wesseling (Finometer)

The auscultatory and oscillometric methods measure blood pressure intermittently at the exact instant of measuring; on the other hand the non-invasive cardiac output monitor (Finometer) provides continuous monitoring of the blood pressure and cardiac output, through implementing the Modelflow® Technology. The Modelflow® estimates the blood pressure and cardiac output through analysing the blood pressure waveform by the use of a nonlinear three-element model of aortic input impedance. The three elements are; the characteristic aortic impedance, the arterial compliance and the systemic vascular resistance.[71, 72]

2.4.2.1.1 Riva-Rocci/Korotkoff (RRK) (Auscultatory method)

This method was discovered by Riva-Rocci in 1896, the Korotkoff criteria followed in 1905.

Applying pressure using an inflatable upper arm cuff that slightly exceeds the systolic blood pressure, will block the brachial artery, the cuff pressure is reflected on a manometer. A stethoscope is applied distal to the arm cuff and over the arterial site. The cuff then is gradually deflated, systolic blood pressure corresponds to the beginning of sounds (Phase I Korotkoff sounds) and diastolic pressure corresponds to either the muffling of sounds (Phase IV Korotkoff sounds) or to the sound disappearance (Phase V Korotkoff sounds). This issue remains unsettled.[73, 74]

2.4.2.1.2 Marey (Oscillometric method)

In 1876 Marey discovered that by applying an inflatable arm cuff, arterial oscillations are detected. The point of maximal oscillations is a reflection of the mean blood pressure, and the points where oscillations begin and end are not exactly corresponding to systolic and diastolic blood pressure values, those values are obtained by approximation. Recent technical modifications to the oscillometric blood pressure measuring devices have increased their accuracy.[75] This method is applied by the noninvasive blood pressure devices (NIBP) that are widely used in routine clinical settings.

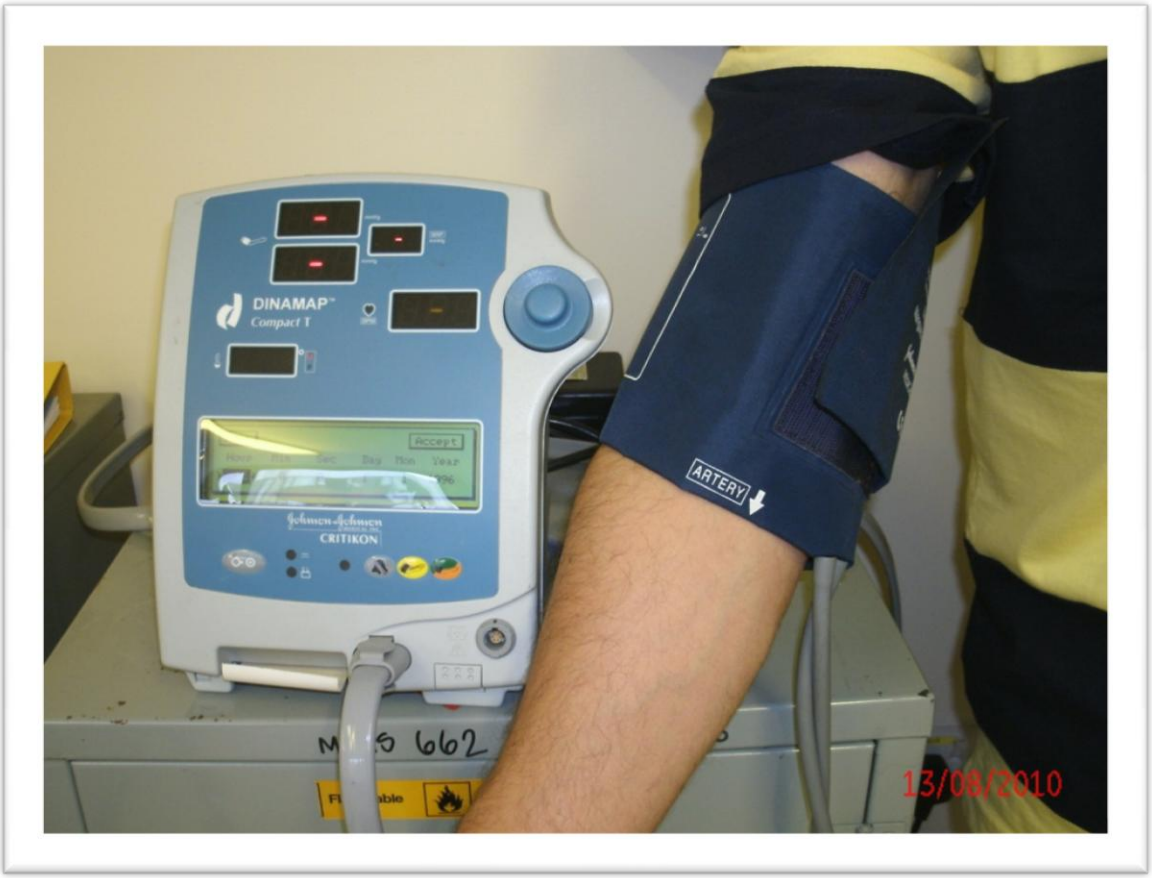


Figure 1. NIBP device

2.4.2.1.3 Peñáz / Wesseling (Finometer)

The Finometer utilises the Peñáz volume-clamp method and the physiocal (physiological calibrating) criteria of Wesseling to obtain a continuous pulse waveform recording.

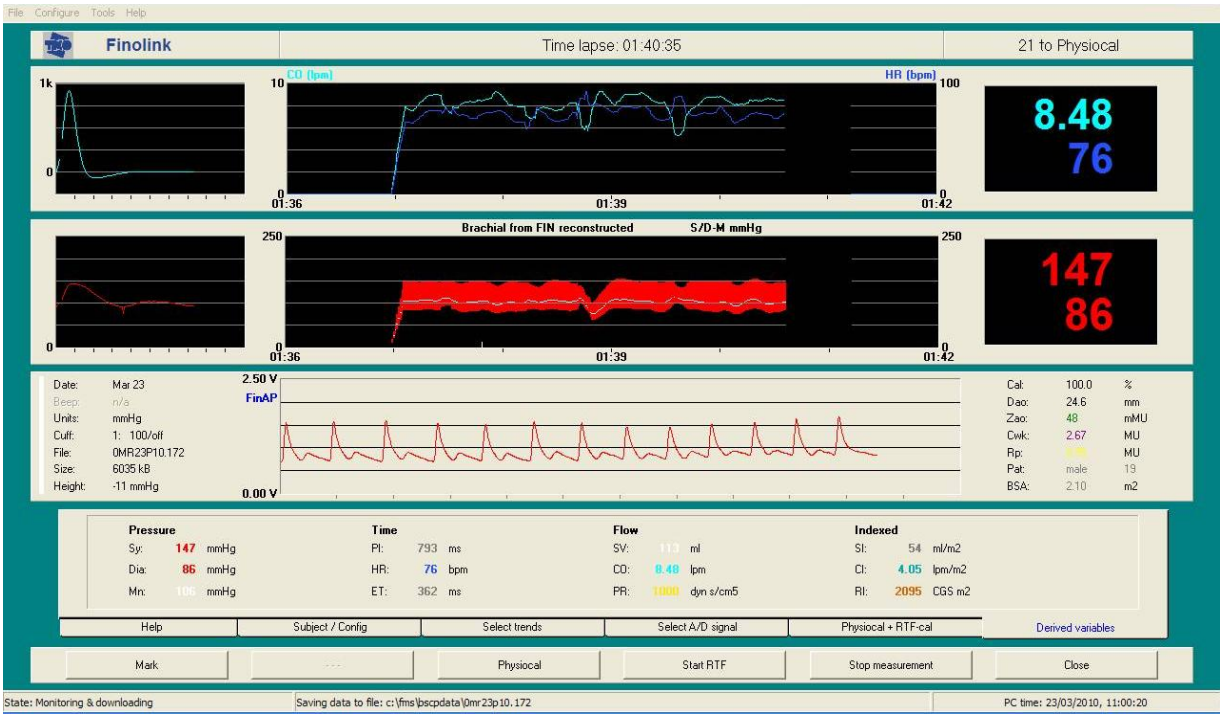


Figure 2. Finometer screen showing a continuous pulse waveform

The Volume-clamp method of Peñáz: The volume clamp method is based on the dynamic unloading of the finger's arterial wall. Its idea is to keep the diameter of the artery continuously constant. A finger inflatable cuff is used, to which an infrared photo-plethysmograph is attached that detects any changes in the arterial diameter. In response to any change in diameter, an electro pneumatic system will act by changing the cuff pressure in response to that change. Accordingly, when the arterial diameter increases following a rise in blood pressure the cuff will inflate and when the diameter decreases following a drop in blood pressure the cuff will deflate, thus keeping the arterial diameter always constant. The cuff pressure is a reflection of the intra-arterial pressure waveform and it's measured by an electronic gauge.[76]

The Physiocal (physiological calibration) criteria of Wesseling: The physiocal criteria of Wesseling states that the intra-arterial pressure will be equal to the recorded finger cuff pressure only in the unloaded diameter of the finger artery, where the transmural pressure is zero. Therefore in order to obtain the accurate arterial blood pressure, the unloaded diameter of the finger artery must be obtained and used as the volume-clamp set point. Physiocal calibrations are made at regular intervals by temporary interruptions to the measuring procedure. The volume-clamp servo loop is opened and the pressure in the cuff is kept midway between the systolic and diastolic blood pressure readings of the previous pulsation. Pressure volume relations are recorded by the plethysmograph and analysed by a computer algorithm that brings the volume-clamp finger artery diameter set point. [77] Ultimately, a pulse waveform is obtained, which is further analysed by the Modelflow algorithm to generate a continuous estimate of the cardiac output. The Modelflow algorithm is discussed in more details in section 2.6.4.

As mentioned before, measuring blood pressure by the auscultatory and oscillometric methods, only provide intermittent blood pressure recordings corresponding to the exact time where the measurements have been taken. On the other hand invasive intra-arterial blood pressure monitoring offers continuous blood pressure measurements, but its invasive nature limits its use to the more critical patients. Blood pressure monitoring using continuous non-invasive technologies such as the Finometer may provide easily applicable alternatives which also has the merit of continuous cardiac output monitoring.[72]

2.4.2.2 Direct invasive method

This invasive method is accomplished by inserting an intra-arterial catheter which is then connected to an external pressure transducer at heart level.[78] Invasive blood pressure monitoring will continuously show the actual intra-arterial pressure and its variability.

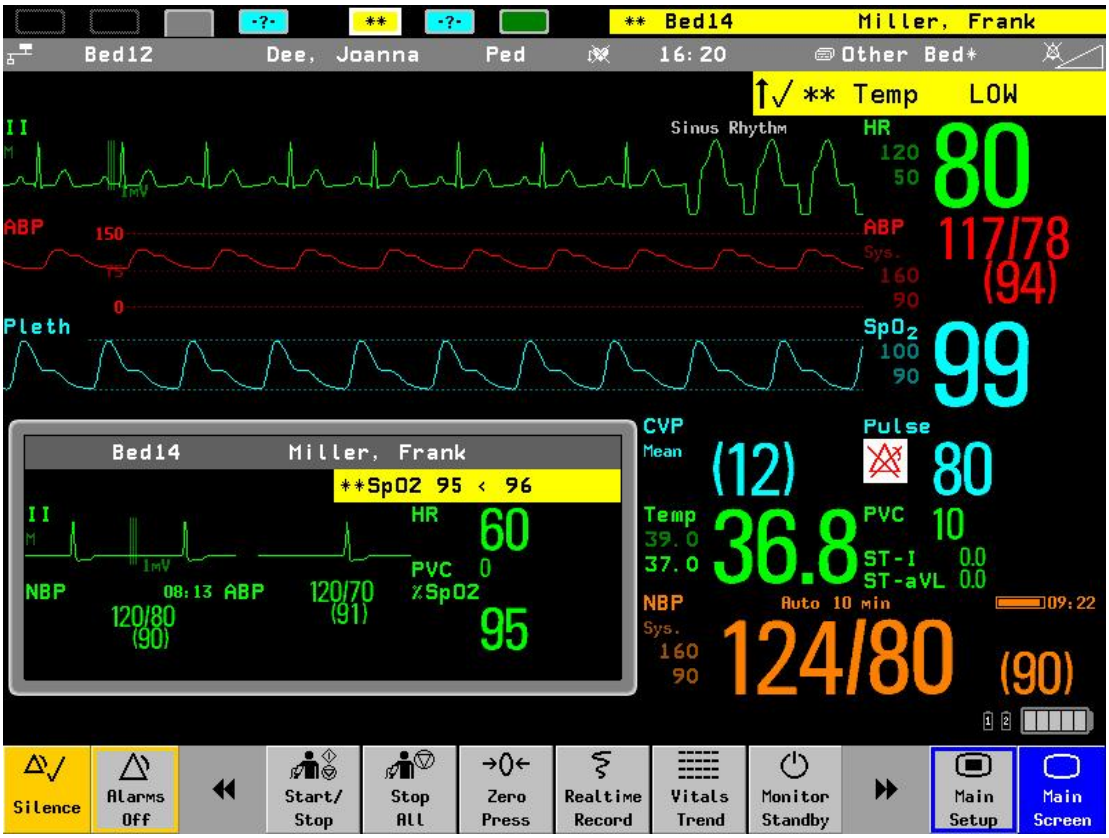


Figure 3. Philips IntelliVue MP30 monitor screen displaying an intra-arterial BP trace in red colour (reproduced from Philips)

2.5 Cardiac Output Monitoring

2.5.1 Introduction

The first trial to discover the circulatory system was in 1733 when Hales inserted a brass pipe into a mare's artery and connected it to a glass tube. He kept observing the arterial pulsations through the transparent glass tube, he then repeatedly disconnected the brass pipe from the artery, left the mare to bleed about a pint of blood each time, reconnected and observed for the effect of bleeding on the arterial pulsations.[79]

In 1970 measurement of the cardiac output was accomplished by the insertion of a balloon tipped pulmonary artery catheter (Swan Ganz Catheter)[80] , and since then its use was widespread in the diagnosis and management of the critically ill.[81] [82] Proper insertion of the flow directed pulmonary artery catheter can provide intermittent accurate estimates of the central venous pressure (CVP), right sided intra-cardiac pressures, pulmonary artery pressure (PAP), pulmonary artery occlusive pressure (PAOP), cardiac output (CO) and systemic vascular resistance (SVR).[83] The pulmonary artery catheter measures the cardiac output by the intermittent thermodilution technique, which is an application of Fick's principle where temperature is used as an indicator, discussed in details in section 2.5.2.1. Pulmonary artery catheters carry the risk of complications related to central venous cannulation such as, bleeding, hematoma, arterial puncture, catheter related sepsis, haemothorax and pneumothorax.[84] Other complications related to the use of the pulmonary artery catheter are: Arrhythmias [85], Thromboembolism[86], knotting[87], pulmonary valvular endocarditis [88], air embolism[89], pulmonary haemorrhage, pulmonary infarction, distal pulmonary artery rupture which could be encountered during insertion or during balloon inflation, and misinterpretation of pulmonary artery catheter data.[83]

It was believed that the pulmonary artery catheter's use was associated with a prevalent mortality rate and it should have been reserved for the highly indicated patients.[90, 91] However more recent trials showed that the use of pulmonary artery catheters does not affect mortality.[82, 92]

The pulmonary artery consensus conference in 1997, disapproved a moratorium for the pulmonary artery catheter and recommended for further randomised controlled studies focusing on further evaluation of pulmonary artery catheters, it also recommended using pulmonary artery catheters in indicated patients after weighing the harms against the benefits by expert hands, if benefits outweigh the harms then it should be used after informing the patient or relatives.[93] The Pulmonary artery catheter is a useful tool for monitoring the haemodynamics of professionally selected patients, when it is properly applied and the data obtained is interpreted competently.[94]

2.5.2 Principles of Measuring Cardiac Output

2.5.2.1 Fick's Principle

Adolf Fick in 1870 discovered that blood flow across an organ can be measured by calculating the arterio-venous concentration gradient of a certain indicator after it has been injected into the blood supply of the organ. Accordingly cardiac output can be measured by calculating the pulmonary arterio-venous concentration gradients of oxygen and carbon dioxide (oxygen consumption and carbon dioxide production).

Eqn1

$$CO = \frac{VO2}{CaO2 - CvO2}$$

VO_2 (O_2 uptake); CvO_2 (mixed venous O_2 content); CaO_2 (arterial O_2 content).

2.5.2.2 Indicator Dilution Technique

George Stewart used the indicator dilution technique to measure cardiac output; he injected a salt solution in the blood supply of different organs and detected the arrival of salt in the blood returning from those organs by electrodes.[95] Hamilton continued what Stewart has started, he used phenolphthalein as an indicator and by blood sampling it was possible to draw the arterial concentration against time curve (Indicator dilution curve). On applying the Stewart/Hamilton equation, cardiac output will be inversely proportional to the area under the curve.

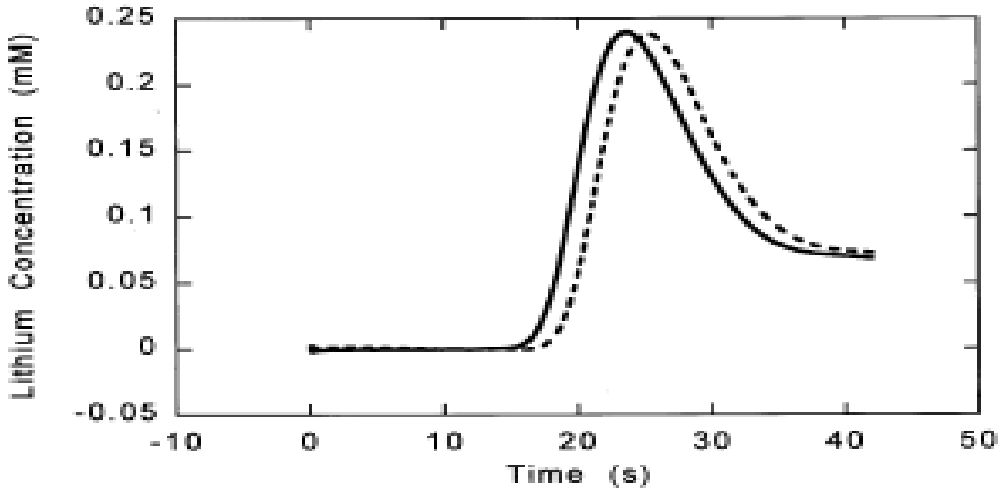


Figure 4. Indicator dilution curve (reproduced from Jonas et al, 1999)[96]

Eqn2 *Applying Stewart/Hamilton equation for thermal dilution*

$$CO = \frac{V(TB) - (TI)\ K1\ K2}{TB(t)dt}$$

V (Volume injected.), TB (Blood temperature.), TI (Injectable temperature.), K1&K2 (Computational constants.), TB (t) dt (change in blood temperature as a function of time.)

Measuring the cardiac output by the use of a thermal indicator was first accomplished by Fegler in 1954 on dogs.[97] Later in 1968 Branthwaite and Bradley measured the cardiac output in man by injecting a thermal indicator in the right atrium through a central line and measured the temperature in the pulmonary artery by using a thermistor tipped pulmonary artery catheter.[81] The thermal dilution technique is considered the gold standard for measuring cardiac output in the clinical setting. However less invasive methods of measuring cardiac output are now showing comparable results.[82]

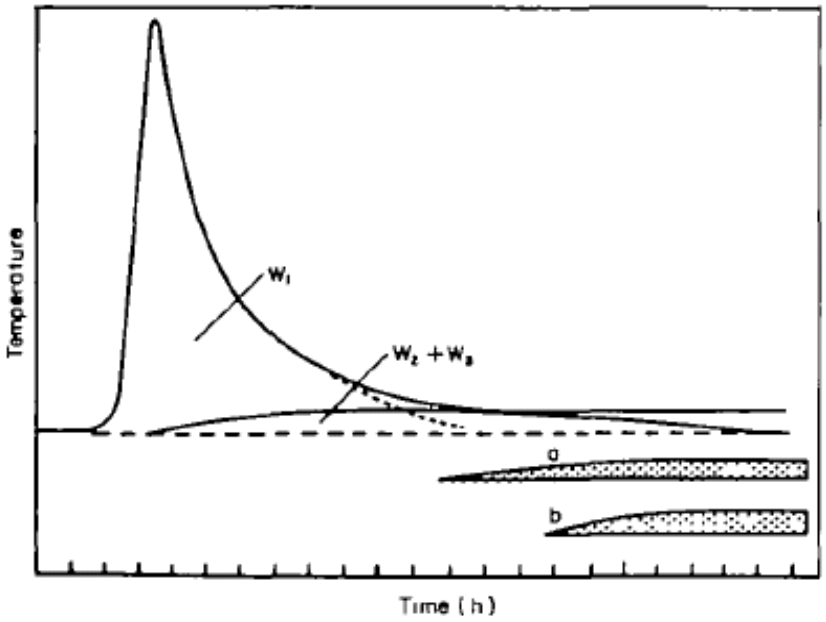


Figure 5. Thermal dilution curve recorded from the pulmonary artery after the injection of indicator into the right atrium (reproduced from Conway and Lund-Johansen, 1990)[98]
W1 (actual thermal dilution curve), W2 + W3 (area of the curve produced by conduction of heat through the catheter wall as a result of injection of thermal indicator), a + b (areas of the curve produced by recirculation of thermal indicator from the superior and inferior vena cava respectively).

2.5.2.3 Arterial waveform analysis

In 1899 Frank explained that the total peripheral resistance can be calculated by measuring the aortic pulse wave velocity and the cardiac output can be derived from the total peripheral resistance and the mean blood pressure.

Eqn3 *Relation between cardiac output, mean arterial pressure and total peripheral resistance.*

$$CO = \frac{MBP}{TPR}$$

Kouchoukos and colleagues in 1970 measured the stroke volume as the area under the systolic part of the aortic pressure waveform which corresponds to the pressure change from the end of diastole to the end of systole. [99]

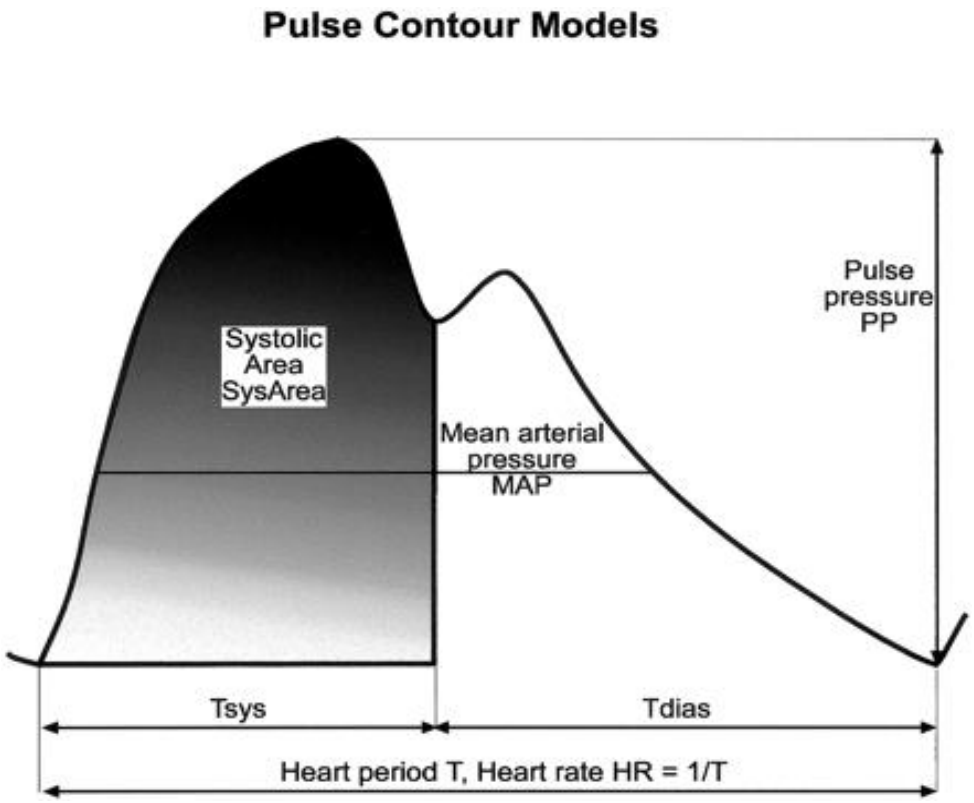


Figure 6. Aortic pressure waveform (reproduced from Cerutti et al, 2001)[100]

Furthermore Wesseling and colleagues studied the pulse wave and were able to extract the cardiac output from it by using the Modelflow technique, which provides computational analysis of the blood pressure wave by using the non linear three-element model of aortic input impedance (described in details later).[71, 101, 102]

2.5.2.4 Doppler Ultrasonography

Doppler Ultrasound can be used to calculate the cardiac index (CI) through measuring the aortic blood velocity and the aortic diameter. It is an accurate measure when compared to the conventional thermodilution technique.[103]

2.6 Review of cardiac output monitoring devices

2.6.1 LiDCO Plus

2.6.1.1 Introduction

The LiDCO Plus is a minimally invasive cardiac output monitor utilising two systems:

- The lithium indicator dilution cardiac output (LiDCO) and
- The Pulse cardiac output real-time (Pulse CO).

The lithium indicator dilution cardiac output LiDCO method is widely validated for its accuracy in terms of cardiac output monitoring.[104, 105] The LiDCO Plus system uses lithium indicator dilution for calibrating the cardiac output estimates generated by the Pulse CO method, once every 8 hours. After calibration, the Pulse CO will provide reliable continuous beat-by-beat measurements of the BP, heart rate (HR), stroke volume (SV), CO, and the preload responsiveness parameters (stroke volume variation (SVV) and pulse pressure variation (PPV)) through analysing the arterial pressure waveform by the computated Pulse CO algorithm.[106]

2.6.1.2 Operation and technology of LiDCO Plus

Lithium indicator dilution LiDCO component measures the cardiac output intermittently by using the indicator dilution technique, where lithium acts as the indicator. The amount of lithium used is small and pharmacologically insignificant; 0.002-0.004 mmol/kg. Lithium can be either injected into a central or peripheral vein.[107] The arterial lithium concentration is then measured by an ion selective electrode which is connected to the patient's arterial line; the arterial blood flowing through this electrode is kept constant at 4 ml/ hour by means of a peristaltic pump. A lithium concentration gradient against time curve is drawn and the cardiac output is estimated from the area under the curve by using the equation:

Eqn4

$$CO = \frac{(\mathrm{Li} * 60)}{\mathrm{A} * (1 - \mathrm{PCV})}$$

Li, lithium dose is expressed in mmol; A, area under the lithium concentration time curve; PCV, packed cell volume which is calculated as follows:

Eqn5

$$PCV = \frac{\text{Haemoglobin concentration in (g/dl)}}{34}$$

Lithium is distributed in plasma, therefore, correction for the packed cell volume is required.[108] The injection procedure is repeated three times and the obtained cardiac output readings are averaged.[109]

The Pulse CO component measures cardiac output continuously on beat-by-beat basis through analysing the whole arterial waveform by using a pulse power algorithm.[106] Unlike Wesseling's pulse contour method which calculates the cardiac output by analysing the systolic part of the arterial waveform.[71] Pulse CO uses a three step pulse power algorithm, which first transforms the arterial pressure waveform into a volume time waveform, second it calculates the nominal stroke volume and the heart beat duration and third it converts the nominal stroke volume and accordingly the cardiac output into accurate values by using a calibrating factor.[108]

2.6.1.3 Validation of LiDCO Plus

Two studies published in 1997 both compared the lithium indicator dilution cardiac output (LiDCO component of LiDCO Plus) with the pulmonary artery catheter thermodilution technique and they both showed comparable results.[104, 105] Furthermore, the Pulse CO component was successfully validated against the thermodilution technique[106] and against the lithium indicator dilution technique after being calibrated.[110]

2.6.1.4 Limitations

LiDCO Plus should not be used in patients weighing less than 40 kg, pregnant and those on oral lithium medications.[111] Also, cardiac output measurements of the LiDCO Plus are unreliable in patients receiving muscle relaxant infusions, as muscle relaxants can cause malfunctioning of the lithium measuring electrode.[108] Furthermore, the need for training staff on performing lithium dilution calibrations, and the time taken to calibrate, add to the limitations.

2.6.2 LiDCO Rapid

A new monitor that has been developed which is technically the Pulse CO component of the LiDCO Plus monitor, steering away from the limitations of the LiDCO Plus, in the sense that it is compact, easily applied in less than a minute, and does not require lithium calibration. This device tracks the trend of change in flow and resistance, providing continuous monitoring of the BP, HR, SV, CO, and also preload responsiveness parameters (SVV and PPV).[112]

2.6.3 Edwards FloTrac sensor and Vigileo monitor

2.6.3.1 Introduction

The Edwards FloTrac sensor/ Vigileo monitor is a minimally invasive reliable continuous cardiac output monitoring device. It provides accurate measurements of cardiac output without the necessity of calibrating against other cardiac output monitoring techniques.[113, 114] The FloTrac sensor is connected to the patient's peripheral arterial line at one end and to two simultaneous monitors on the other end; a standard monitor used for arterial pressure monitoring and the Vigileo monitor. The Vigileo monitor uses a technology that processes arterial signals obtained from the FloTrac sensor together with the patient's characteristic data like the age, sex and body surface area. Calculates the cardiac output (CO), cardiac index (CI), stroke volume (SV), stroke volume index (SVI) and stroke volume variation (SVV) and displays those estimates at 20 second intervals. Furthermore, connecting the monitor to a central venous catheter can provide estimates of the systemic vascular resistance (SVR) and the Systemic vascular resistance index (SVRI).[115]

2.6.3.2 Technology used for cardiac output monitoring

The FloTrac sensor / Vigileo monitor system measures the cardiac output on continuous basis by applying the following formula of arterial pulsatility:[116]

Eqn6

$$\mathrm{CO} = \mathrm{PR} * \mathrm{SD}\,(\mathrm{AP}) * \mathrm{K}$$

SD (AP), the standard deviation of the arterial pressure throughout a 20 second interval; PR, pulse rate; K, constant value that is a reflection of the arterial compliance and the vascular resistance. K is derived from the patient's characteristic data of age, sex, body surface area and the arterial waveform characteristics.[117]

2.6.3.3 Validation

A validation study conducted by McGee and Janvier comparing the Edwards FloTrac / Vigileo system with the intermittent thermodilution technique in a total of 36 cardiac surgery and critically ill patients, showed comparable cardiac output measurements.[118] Another study compared the cardiac output measurements obtained by the Edwards FloTrac / Vigileo system with those obtained by the continuous and intermittent thermodilution techniques in fifty post-operative cardiac surgery patients. Results showed that the Edwards FloTrac / Vigileo system is accurate and reliable.[119]

2.6.3.4 Limitations

The Edwards FloTrac / Vigileo system may provide unreliable measurements in the presence of arterial wave artifacts for example kinking or presence of air inside the tubing system, aortic regurge, severe peripheral vasoconstriction, irregular pulse and the presence of an intra-aortic balloon pump. Its use in paediatric patients is still not studied.[9, 116]

2.6.4 Finometer (Finapres Medical Systems BV, Arnhem, the Netherlands)

Accurate measurements of cardiovascular parameters including the blood pressure and cardiac output provide important tools in clinical practice.[120] Reliable blood pressure measurement is important for the proper diagnosis and management of conditions associated with abnormal blood pressure such as hypertension, in order to minimise the risks of developing complications like coronary artery disease, cerebro-vascular stroke, peripheral vascular disease, congestive heart failure and renal failure.[121] Furthermore, monitoring of the cardiac output is essential for the management of the critically ill and surgery patients.[71]

Until recently the intermittent thermodilution technique was the most commonly used in monitoring cardiac output.[82] However newer less invasive techniques that are showing comparable results are being adopted.[122]

We are of opinion that the Finometer being easily applicable, non-invasive, hazardless, showing comparable results to other established methods as observed in many cardiovascular studies[123, 124] and not missing acute hemodynamic events,[125] may show a good potential for haemodynamic monitoring of patients in intensive care units[122] and routine clinical settings.

The Finometer is a non-invasive beat-by-beat haemodynamic monitor that generates a continuous pulse waveform by means of a finger cuff. As described earlier, it uses the Peñáz volume-clamp method [76] and the physiocal (physiological calibrating) criteria of Wesseling [77] to obtain a continuous pulse waveform recording. The pulse waveform is then analysed by the Modelflow technique, which is a computer analysis of the blood pressure wave by using the non-linear three-element model, providing continuous blood pressure and cardiac output monitoring.[101, 102] Modelflow technique is further discussed in the following section.

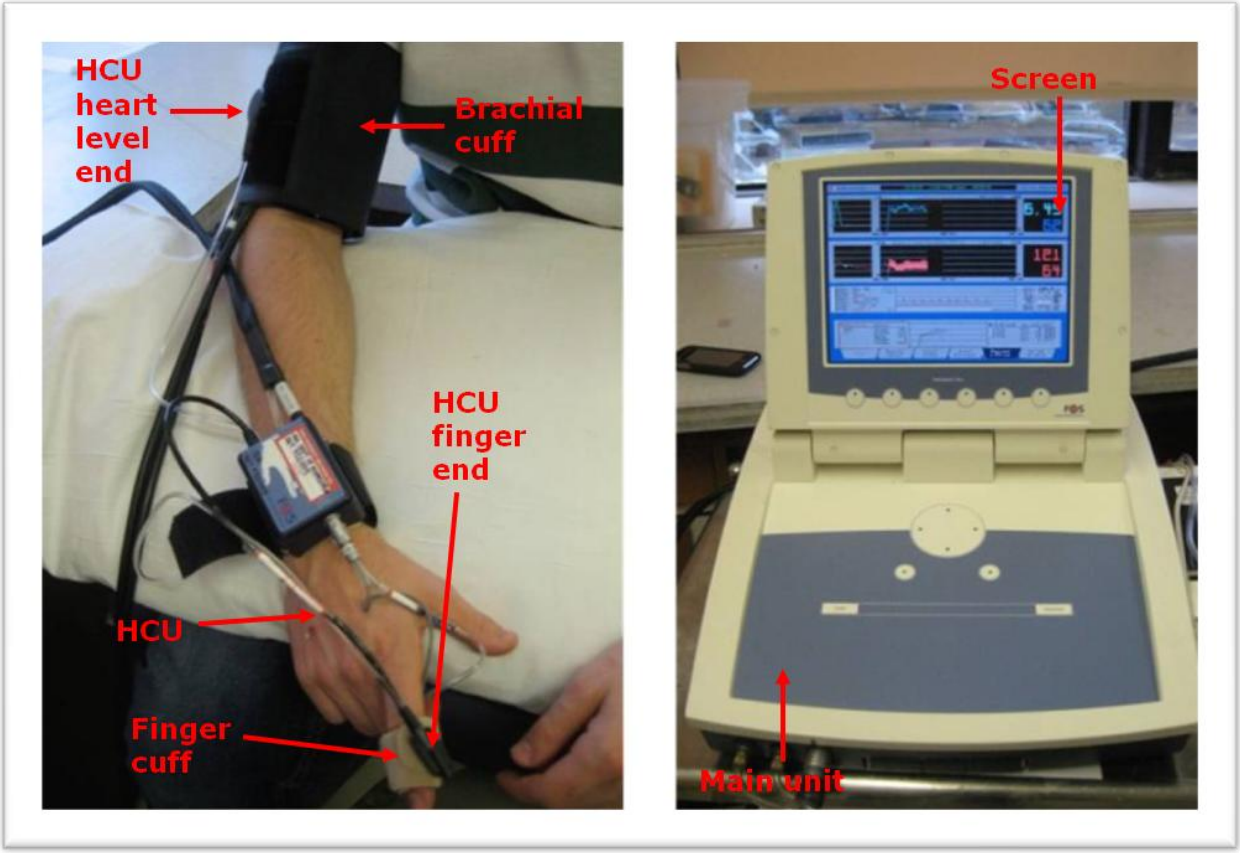


Figure 7. Non-invasive continuous haemodynamic monitor (Finometer)

2.6.4.1 Technology used by the Finometer

The Finometer is composed of:[126]

- Three different sized finger cuffs
- Return-to-flow calibration system using an upper arm Riva-Rocci/Korotkoff (RRK) brachial cuff
- Automatic height correction unit (HCU)
- Main unit and monitor
- Analog input/output box and
- Internal storage for all recorded data with the ability to download on a connected computer or of online downloading to a remote computer

The Finometer offers non-invasive beat-to-beat arterial pressure monitoring via applying the following techniques:

- As described earlier in section 2.4.2.1.3, the Finometer uses the Peñáz volume-clamp method and the physiocal (physiological calibrating) criteria of Wesseling to obtain a continuous pulse waveform recording. The pulse waveform is further analysed by the Modelflow technique, which determines the other derived variables on beat-by-beat basis, namely the CO, SV, TPR, left ventricular ejection time (LVET) which is the time between beginning of upstroke and dicrotic notch, inter beat interval (IBI) which is the time between two beats, ascending aortic impedance (Zao) and total arterial compliance (Cwk).
- The Modelflow technique is a computer based algorithm that analyses the blood pressure waveform by using the non-linear three element model, which represents the three characteristics of aortic input impedance; the aortic compliance, characteristic impedance and systemic vascular resistance. The compliance is a reflection of aortic elasticity, impedance reflects the opposing force created by the aorta towards the blood flowing from the heart and the systemic vascular resistance reflects the resistance to blood flowing from aorta to periphery.[71]

- Reconstructed brachial arterial pressure waveform is then obtained to correct for the arterial blood pressure differences that naturally occur between central and peripheral arteries. The systolic blood pressure tends to be higher peripherally, which is mainly due to propagating pulse wave amplifications which depend on frequency and accordingly on heart rate, while diastolic and mean blood pressures are lower peripherally.[127] In order to overcome this site related blood pressure difference, the Finometer provides a reconstructed brachial arterial pressure waveform, by means of waveform filtering (transfer function) which corrects for the waveform changes resulting from pulse propagation, and by calibrating with the brachial arterial pressure by means of a (Riva-Rocci/Korotkoff) cuff.[128, 129]
- The feature of hydrostatic height correction is available in the Finometer to correct for hand movements to correspond with the heart level.[130]
- Proper size of finger cuff must be used as loosely fitting cuffs will provide inaccurate results.[131]

2.6.4.2 Advantages and uses

The Finometer has an established role in routine cardiovascular research studies involving, blood pressure variability,[132] baroreflex sensitivity,[133] arrhythmias, pacemakers and cardiac resynchronization,[134] exercise, postural effects,[10] tilt tests and neuro-cardiogenic syncope studies.[135] However its use in a cohort of patients in routine clinical practice has not been demonstrated yet.

We suggest that the Finometer might potentially be a useful tool for monitoring cardiovascular parameters in haemodialysis and patients undergoing surgery due to its easy handling and its non-invasive nature when compared to the other invasive methods. In this project we will evaluate the feasibility of using the Finometer in haemodialysis units and operating theatres.

2.6.4.3 Disadvantages and limitations

- *Finger arterial vasoconstriction*

The presence of finger arterial vasoconstriction[127] and cold fingers might affect the integrity of photo plethysmographic readings. Nevertheless, it is usually possible to obtain readings in cases where fingers are cold and cases of vasoconstriction, only when it is severe does it impede the plethysmographic measurements.[77, 136] Studying the effect of hand warming to 44°C temperature on finger blood pressure measurements, showed a decrease in the naturally occurring over estimation of systolic blood pressure,[137] which is observed when comparing central and peripheral arterial pressure readings. It is mainly due to propagating pressure wave amplifications.[127] On the other hand, cooling of the hand produced an over estimation of systolic and diastolic blood pressures, which was reversible with re-warming.[138]

- *Young age less than 6 years*

Use of the Finometer in young age 0-6 is still under development. Tanaka and colleagues compared the finger arterial blood pressure with the brachial blood pressure that is obtained by auscultatory methods. They found that Finapres follows blood pressure trends of change accurately in children[139] Andriessen and colleagues found that the Finometer is feasible for monitoring blood pressure in young age, as pulse waves in young age resemble adult's pulse waves. However the adult physiocal algorithm that is used by the current Finometer needs adaptation to meet with the very young age vascular physiology.[140]

2.6.4.4 Validation of the Finometer

2.6.4.4.1 Introduction

Continuous blood pressure monitoring is invaluable in many critical clinical circumstances.[141] The availability of a non-invasive hazardless device that can provide continuous beat-by-beat accurate measurements or even measurements that follow the trends of the actual blood pressure and cardiac output remains an interesting issue for researchers.[142-144]

2.6.4.4.2 Validation of Finapres (old version of the Finometer) for blood pressure monitoring

Finapres is the older version of the Finometer, deprived of the options of reconstructed return to flow brachial pressure, wave form filtering and hydrostatic level correction.[144] Two studies, one conducted by Van Egmond and colleagues and published in 1985 on a total of 32 patients, 20 of whom were major surgery patients, 5 open heart surgery and 7 intensive care patients. The other study was conducted by Parati and colleagues and published in 1989, 16 uncomplicated hypertensive patients and 8 normotensive were enrolled in the study. Comparing the Finapres blood pressure recordings with the intra-arterial blood pressure in both studies showed that the Finapres provided an accurate estimate of the blood pressure.[145, 146]

A study performed by Aitken and colleagues that was published in 1991 on 10 patients undergoing local resection of choroidal melanomas, a procedure requiring induction of hypotension. Blood pressure obtained by Finapres was compared with the intra-arterial blood pressure, systolic blood pressure and heart rate values were comparable, whilst the diastolic and the mean blood pressures were overestimated.[147]

In another study performed by Farquhar, published in 1991 involving 10 ICU patients and comparing the Finapres with the intra-arterial blood pressure. Finapres showed inaccurate blood pressure estimates, however the trend estimation of the changes was clinically acceptable.[148]

Regarding the study by Aitken and colleagues, they compared the quantitative values and they didn't correlate trend similarities, whereas Farquhar noticed that there was stability in the differences between results.

Considering the inaccurate results obtained by Finapres in both studies, an important issue that needs to be highlighted is that both studies were performed using the older version of the Finometer (Finapres) deprived of the reconstructed return to flow brachial artery pressure which was proven to reduce the pressure differences between the Finometer and intra-arterial blood pressure.[144]

2.6.4.4.3 Validation of the Finometer (new version) for blood pressure monitoring

Hehenkamp and colleagues performed a study to validate Portapres which is the portable version of the Finometer against the standard Riva-Rocci/Korotkoff (RRK) method, 30 normotensive pregnant ladies and 20 pre-eclamptic patients were enrolled in the study and Portapres showed comparable results.[143]

A study focusing on the evaluation of the reconstructed brachial pressure waveform which is an option present in the new version (the Finometer) was performed by Guelen and colleagues and published in 2003 on 37 post coronary angiography patients. Basically, the comparison was made between the *brachial arterial pressure that is brought by the Finometer through applying the RRK method and each of the following*: 1) Original finger arterial pressure, 2) Waveform filtered and level corrected arterial pressure and 3) The return-to-flow calibrated, waveform filtered & level corrected arterial pressure. Observations were; a reduction in the pressure difference between finger and brachial intra-arterial pressures when waveform filtering and level corrections were used. Furthermore when the return-to-flow calibration was added, the reduction in the pressure difference was not as big but still met with the Association for the Advancement of Medical Instrumentation AAMI criteria[149] for evaluation of automated blood pressure devices.[144]

Schutte and colleagues performed a validation study on the Finometer in measuring blood pressure against the Riva-Rocci/Korotkoff sphygmomanometric method. 102 females; 24 were hypertensive, 25 obese normotensive and 35 lean normotensive were enrolled in this study. Results of the Finometer met with the validation criteria of the Association for Advancement of Medical Instrumentation (AAMI)[149] and the British Hypertension Society (BHS).[8, 150] The AAMI and the BHS criteria for validation of BP devices are described in details in sections 4.2.7 and 4.2.6 respectively.

2.6.4.4.4 Validation of the Finometer for cardiac output monitoring

2.6.4.4.4.1 Validation of the Modelflow algorithm

The Modelflow is a computer algorithm present in the Finometer, which estimates the cardiac output on continuous basis from the arterial pressure wave by simulating a non-linear three element model of the aortic input impedance. The three elements of the Modelflow are aortic characteristic impedance, arterial compliance and systemic vascular resistance.[71] Arterial pressure waves are obtained either invasively by the intra-arterial method or non-invasively by finger arterial pressure devices.

A Modelflow validation study was performed by Jellema and colleagues on 32 critically ill patients. The invasive intra-arterial pressure waveform was used to estimate the cardiac output by using the Modelflow technique and values were compared with those of the thermodilution technique. The comparison showed good correlation of results when calibrations were done with the thermodilution technique once every two days.[151]

In another study conducted by Jansen and colleagues, published in 2001 which also compared the cardiac output estimated by Modelflow simulation of invasive intra-arterial pulse waveform and the thermodilution technique, in 54 patients undergoing open heart surgeries. Comparable results were obtained after one calibration only per patient.[152]

2.6.4.4.4.2 Validation of the Finometer

Validation studies of the Finometer in terms of CO monitoring produced mixed results, both accuracy and inaccuracy have been demonstrated. However, there was general agreement on the usefulness of the Finometer in the detection of CO trends. Inaccuracy of the finger arterial pressure (FINAP) has been reported in a study by Remmen and colleagues; they compared CO measurements obtained from the pulmonary artery catheter and the FINAP in 28 healthy subjects. Their results showed no significant correlation between the FINAP and the pulmonary artery catheter CO measurements , the bias was -1.7 L / min, and the 95% limits of agreement ranged between -4.6 L / min and +1.1 L / min ($r = 0.28$ and $p = 0.13$). On the other hand, several studies have shown reliability of the FINAP in monitoring the CO.[153] Harms and colleagues compared 155 SV measurements obtained by the pulmonary artery catheter and the FINAP in 9 healthy individuals who were subjected to orthostatic stress conditions during the study. Their results showed accuracy of the FINAP in comparison with the pulmonary artery catheter ($r = 0.97$ and $p < 0.001$).[154] Tam and colleagues compared 45 CO readings obtained by FINAP

and a respiratory method using open-circuit acetylene uptake (C_2H_2) in 9 healthy subjects. They further performed another comparison after calibration of the FINAP with the C_2H_2. Their results before calibration showed significant correlation between the FINAP and the C_2H_2 ($r = 0.784$ and $p < 0.01$). The bias was 1.83 L / min, and the 95% limit of agreement ranged between -6.23 L / min and +9.89 L / min, the regression line between FINAP and C_2H_2 CO readings showed a slope of more than 1, indicating that the FINAP arterial pressure overestimated the CO in comparison with the C_2H_2. The results after calibration showed that FINAP is accurate in bringing absolute values, the bias was 0.24 L / min, and the 95% limits of agreement ranged from -6.58 L / min to +7.05 L / min ($r = 0.931$ and $p < 0.01$). [155]

Azabji Kenfack and colleagues compared 10048 CO readings measured by the Modelflow noninvasively from the finger (FINAP) and invasively from the radial artery in 7 healthy subjects. The regression line was displaced upwards with a slope significantly higher than 1, indicating that the FINAP overestimated the value of CO in comparison with the radial artery. The bias was 1.44 L / min, and the 95% limits of agreement ranged between -4.12 L / min and +7.01 L / min ($r = 0.603$). [156]

Hirschl and colleagues compared 323 pairs of FINAP and pulmonary artery catheter cardiac index (CI) readings in 46 critically ill patients. The Bias was 0.14 L / min / m^2, and the 95% limits of agreement ranged between -0.6 L / min / $m^2$and +0.88 L / min / m^2 ($p < 0.001$). They also showed that there was a large variation between the FINAP and the pulmonary artery CI readings in 23% of the measurements. [142]

2.6.4.4.5 Summary

The Finometer is fairly accurate in terms of blood pressure monitoring.[8] However, as the current evidence stands, it can be said that it has not been shown to be accurate in generating absolute cardiac output measurements, but it has been shown that it accurately follows the trends of changes in cardiac output.[9]

2.6.5 Nexfin

The Nexfin is the most recent development in finger arterial pressure technology, which has been applied also by the Finometer. It measures the same haemodynamic variables as the Finometer with equal accuracy.[157] The Nexfin in contrast with the Finometer has the merit of being compact and easy to use. Furthermore, it obtains the true brachial arterial pressure by merely correcting for individual characteristics rather than physically taking brachial arterial pressure measurements, thus, allowing a rapid start of the device. It also can provide pulse oximetry and continuous haemoglobin concentration monitoring.

2.7 Endothelial function monitoring

2.7.1 Introduction

The vascular endothelium forms a semi-permeable membrane that acts as a barrier which prevents the larger blood constituents from moving out of the blood vessels and on the other hand allows the movement of water and solutes.[158]

The endothelium also plays an important role in regulating the immune response against pathogens, by producing adhesion molecules that bind to leukocytes enabling them to migrate to inflamed areas.[159]

It is also involved in the process of angiogenesis[160] and very importantly in the regulation of vascular tone through the production of both vasodilator and vasoconstrictor mediators. Vasodilator mediators are: nitric oxide (NO), prostacyclin, bradykinin [161] and endothelium derived hyperpolarising factor. These four vasodilator mediators also inhibit platelet aggregation.[162] Vasoconstrictor mediators are: angiotensin II, endothelin, thromboxane A_2 and prostaglandin H_2.[163]

As discussed above, the endothelium is involved in many vital roles; hence endothelial dysfunction is likely to be a major cause of morbidity and mortality,[164] which urges the need for endothelial function testing. It was found that an easily applicable way of determining the endothelial function is by measuring the tone regulatory function of the endothelium.[165] In endothelial dysfunction, nitric oxide production decreases hence causing an increased vascular tone and stiffness,[164] also an increased incidence of atheroma development.[166]

Arterial stiffness is a reflection of the degree of age related changes and atherosclerosis. Accordingly it is considered an independent risk factor for coronary artery disease. [167] Therefore, the importance of early identification of arterial stiffness in order to adopt preventive measures of atherosclerosis promptly to arrest the disease progression.[168] Carotid – Femoral Pulse wave velocity is considered the gold standard for measuring arterial stiffness.[169]

Pulse wave velocity is the time taken by the blood pressure wave to cover a certain distance between two set points of the arterial system. It is affected by the arterial elasticity, arterial thickness and the blood density. Hence an increase in the arterial stiffness will eventually increase the pulse wave velocity.[170]
Arterial endothelial dysfunction is the first event that occurs in the process of atherosclerosis, its early detection is invaluable for the prevention of atherosclerosis progression. Endothelial function integrity can be estimated by measuring the vasomotor function of arteries after giving intra-arterial injections of drugs that cause the release of endothelial nitric oxide.[171, 172] The use of this procedure is limited by its invasive nature. Recently non-invasive techniques that measure the arterial stiffness and the endothelial function via pulse wave analysis have been developed.[171]

2.7.2 Pulse wave analysis

Photo plethysmography is a simple, noninvasive and accurate way of obtaining a digital volume pulse, from which the stiffness and the reflection indices that correspond to the large artery stiffness and the small artery vasomotor function respectively are generated.[173] Photo plethysmography operates through emission of an infrared light through the capillary bed of the finger tip. Changes in blood volume occurring in the capillary bed during pulsations will eventually change the amount of light absorbed. Those changes in light absorption that reflect changes in blood volume are interpreted and a digital volume pulse waveform is obtained.[174] The digital volume pulse waveform is composed of a systolic component which is a resultant of transmission of the blood pressure wave from the aortic root to the finger (peak A) and a diastolic component (peak B) which is caused by the backwards reflection of the pressure wave from the aorta to the finger after it has been transmitted from the left ventricle to the periphery via aorta (figure 8).[175]

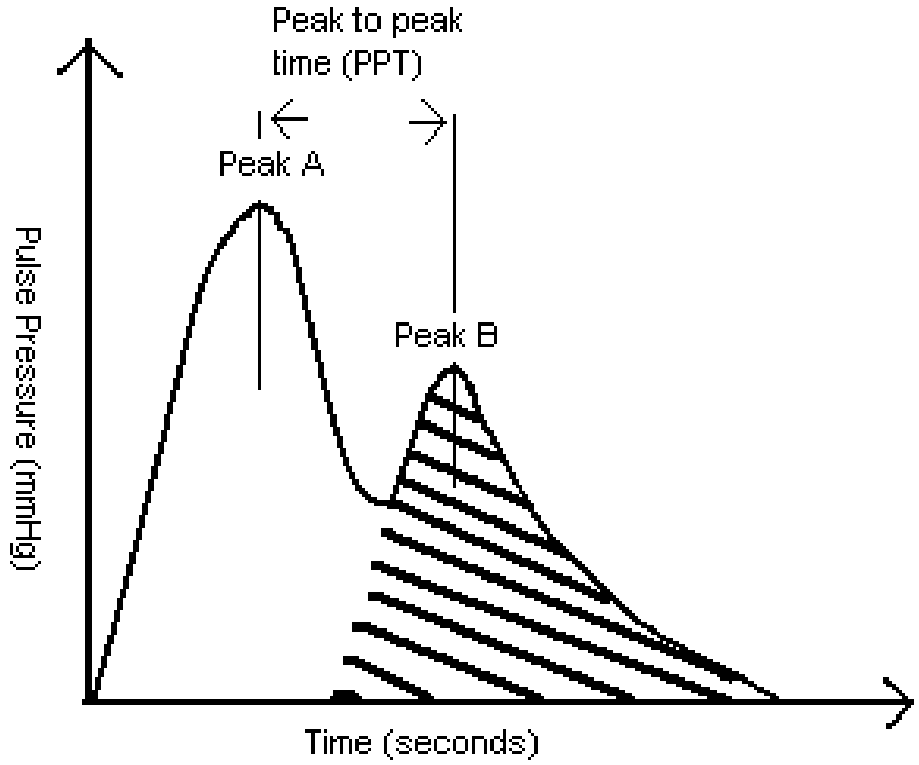


Figure 8. A Pulse waveform (reproduced from Millasseau et al, 2002)[176]

2.7.3 Interpreting the DVP (Digital volume pulse):

The amplitude of the diastolic component of the DVP depends on the intensity of blood pressure wave backwards reflection and is directly related to the endothelial vasomotor function of the small arteries. The time difference between the diastolic and the systolic peaks corresponds to the PWV (Pulse wave velocity) and it depends on the arterial stiffness.

RI (Reflection index) is the ratio between the amplitudes of the diastolic peak (peak B) and the systolic peak (peak A) and is expressed as a percentage. Reflection index is considered a measure of the intensity of pulse wave reflection and the endothelial function (figure 8).[175]

Eqn7

$$\mathrm{RI} = \text{peak B/peak A} * 100\%$$

SI (Stiffness index) corresponds to the pulse wave velocity which is used mainly to measure arterial stiffness in large arteries. SI is calculated by dividing the subject's height in metres by the time in seconds between the systolic and diastolic peaks (PPT) (figure 8).[175, 176]

Eqn8

$$\mathrm{SI} = \mathrm{H} / \text{PPT (Peak to peak time)}$$

2.7.4 Validation of pulse wave analysis for reliability in evaluating the arterial stiffness and endothelial function

Studies comparing the PWV (carotid – femoral) which is considered the gold standard method for measuring the arterial stiffness [169] with the stiffness index (SI) obtained by the DVP showed a good correlation in results. [175, 176] Reflection index (RI) obtained by the DVP was shown to correlate well with the vascular tone in several studies.[175, 177, 178]

3 Aim of thesis

In the context of evaluating BP aberrations during routine anaesthesia service at the time of induction and also during routine haemodialysis, the Finometer was used to determine:

- The gross haemodynamic changes that occur during these procedures
- Whether the Finometer provides extra information, and hence potential for better patient safety, than the non-invasive blood pressure monitors that are currently used in practice

3.1 Service evaluation

This thesis is designed to evaluate the 'standard practice' NIBP monitoring that is conventionally used during two routine clinical situations where BP aberrations are anticipated to happen, namely, induction of anaesthesia and haemodialysis. In view of emerging evidence that both, hypotension and hypertension encountered during induction of anaesthesia and haemodialysis are associated with poor patient outcome [5, 6, 179, 180], we wished to evaluate our current practice of monitoring BP intermittently to see if it provided adequate information about the extent and severity of BP aberrations. The underpinning principal is that correct and timely information regarding BP changes will aid the physician for early diagnosis and management of those haemodynamic mishaps, and eventually improve the level of patient safety.

To evaluate this, the following questions were framed:

- Are blood pressure measurements obtained by the Finometer comparable to those obtained by the conventional non-invasive blood pressure monitors in terms of accuracy?
- Do significant haemodynamic changes occur during routine induction of anaesthesia and maintenance haemodialysis, and do blood pressure values reach the threshold for intervention during these procedures?
- Is the Finometer a better detector of episodes of maximum blood pressure changes as they occur than the conventional non-invasive blood pressure devices?

4 Generic methods

4.1 Devices

This section describes the procedures of operating the devices that were used in both our service evaluations of routine induction of anaesthesia and maintenance haemodialysis.

4.1.1 Finometer

The Finometer has been discussed in details in sections 2.4.2.1.3 and 2.6.4

4.1.1.1 Procedure of operating the Finometer

We attached the brachial cuff to one of the patient's arms, and attached the appropriate sized finger cuff to either the index or the middle finger of the same arm; we always made sure that the finger cuff cables were along the palm side of the finger. The finger cuff size is considered appropriate when both of its longitudinal edges are in line, this means that that they neither overlap nor be apart. Finometer was then switched on and patient data including age, sex, weight and height were entered.

The height correction unit (HCU) is formed of a transparent thin tube containing water with two ends; a finger end and a heart level end. It is connected to the Finometer by a thin cable. Both the finger and the heart level ends of the HCU were initially brought together to employ height correction system during monitoring.

When started, Finometer delivers an un-calibrated finger arterial pressure waveform. Calibration with the brachial BP, can take approximately 2 minutes. A reliable continuous beat-by beat haemodynamic monitoring is provided thereafter.

Indicating the Finometer's readings at specific times when relevant events happened, such as the start and end of the procedure, was accomplished by pressing the [mark] button. This has allowed us to review the Finometer's readings corresponding to those events after having retrieved the data from the Finometer.
After data has been collected from the patient, the Finometer was switched off and the brachial and finger cuffs were then disconnected from the patient (Figure 7).

4.1.1.2 Procedure of data retrieval from the Finometer

Retrieval of the data from the Finometer was done on the same day of data collection, to ensure that work does not accumulate especially since vast amounts of data were available per patient. It also needs to be mentioned that the Finometer can store up to 24 hours worth of haemodynamic data, and it tends to overwrite when its memory is full. Retrieval of data was done using the BeatScope version 1.1a software (product of Finapres Medical Systems BV, Arnhem), which was installed on a laptop. The Finometer and the laptop were switched on, and connected to one another via an RS232 cable.
[Finometer research] mode was selected from the options on the Finometer screen. The BeatScope program that was installed on the laptop was opened, and data from Finometer downloaded (figure 9).

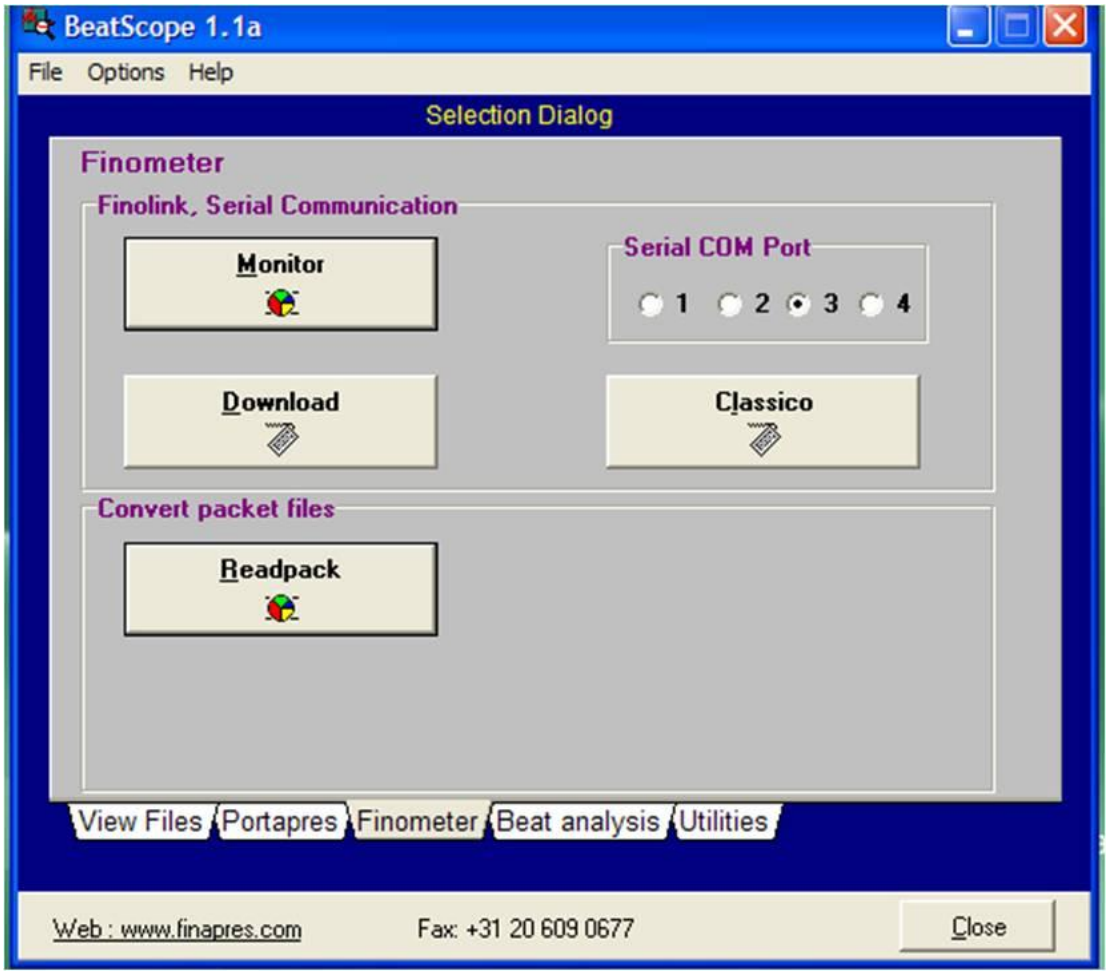


Figure 9. First step in downloading data from the Finometer via BeatScope

A 4 hour haemodialysis file approximately took 30 minutes to download (figure 10).

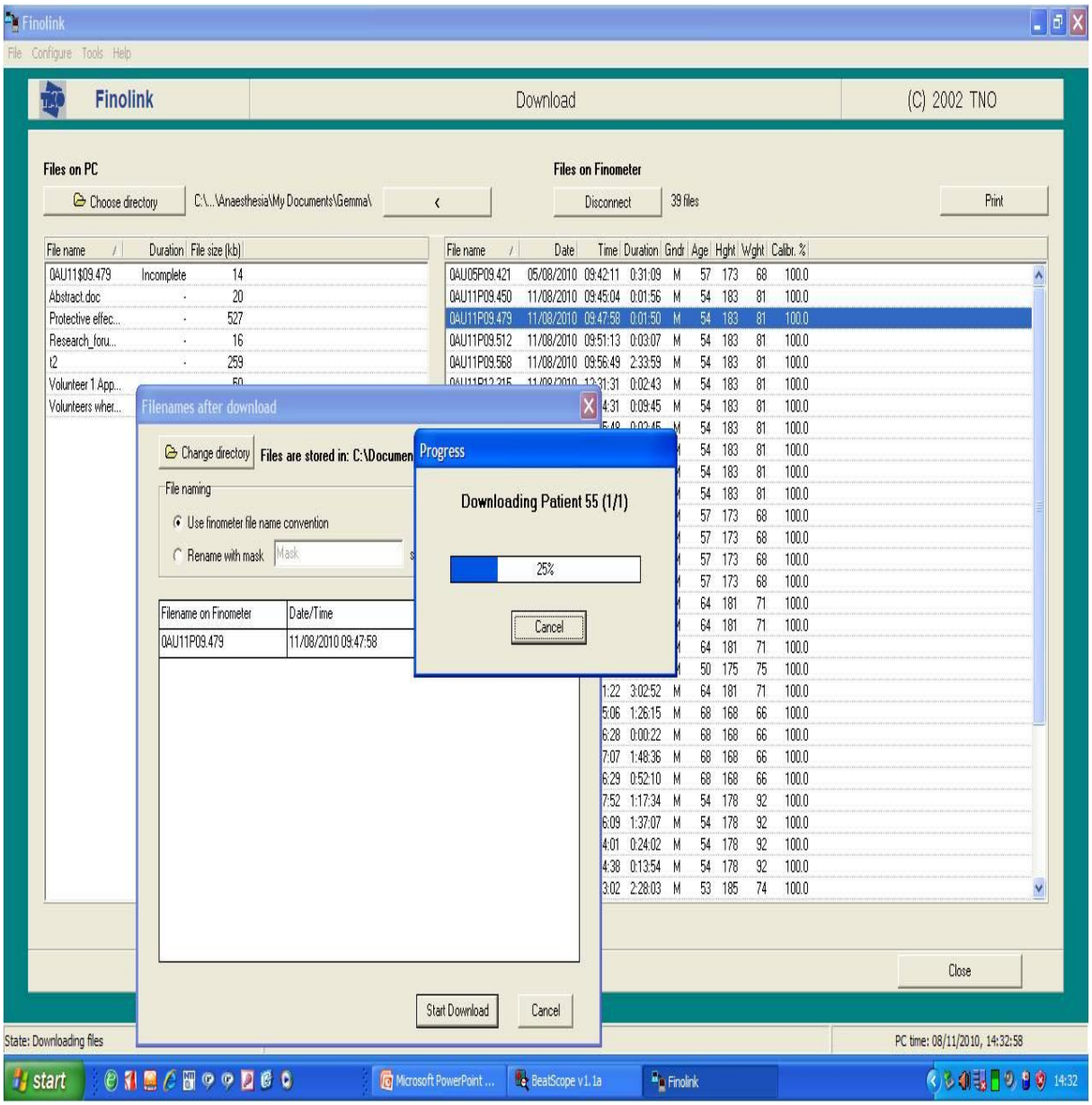


Figure 10. Second step in downloading data from the Finometer via BeatScope

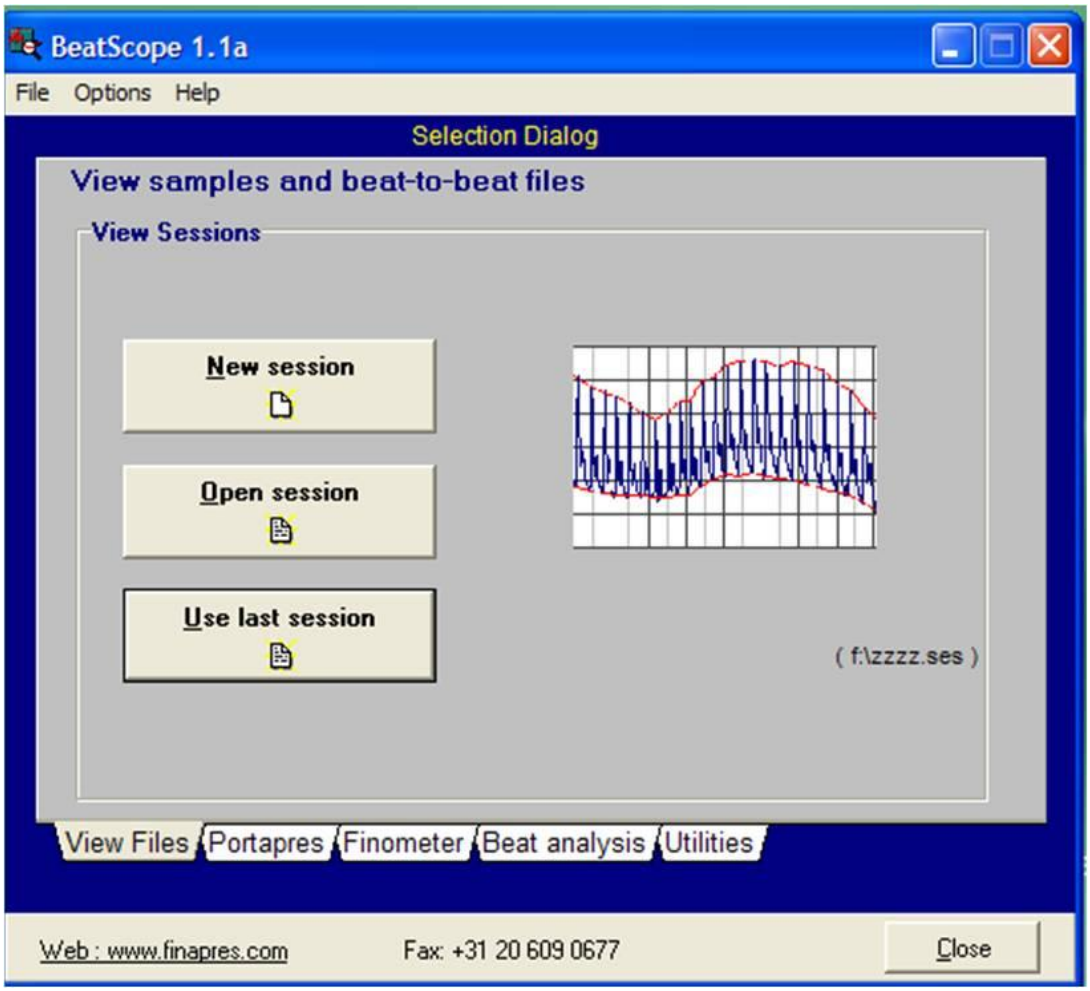


Figure 11. Third step in downloading data from the Finometer via BeatScope

After downloading was completed, we used the window to open the required file as a continuous waveform. We then chose the portion of the file that we needed to download by highlighting the needed portion of the file. We then exported data from file to the chosen file directory (figure 12).

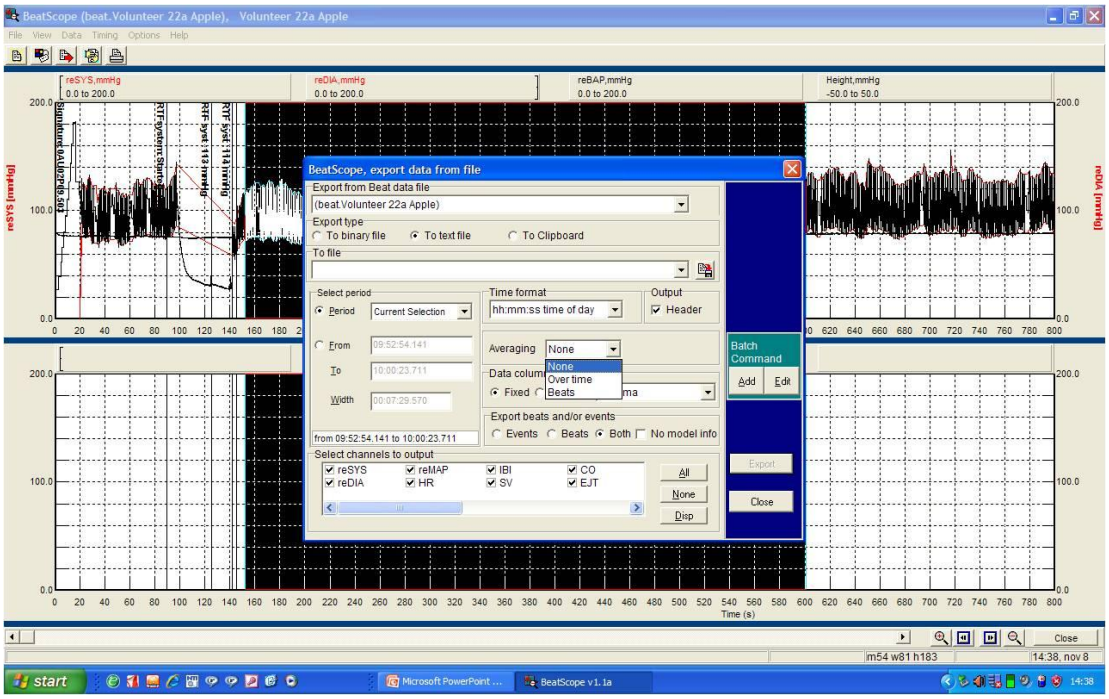


Figure 12. Fourth step in downloading data from the Finometer via BeatScope

The exported file was then transferred into Microsoft excel format, which was saved ready for analysis.

4.1.2 Pulse contour analysis

The finger pulse contour analysis was discussed in details in section 2.7.2, 2.7.3 and 2.7.4

We used the Pulse Trace device (Micro Medical, Gillingham, Kent, UK) for pulse contour analysis.

4.1.2.1 Procedure of operating the Pulse Trace device

The Pulse Trace device has a chargeable battery, but it can also work by direct connection to the electricity source. To collect data using Pulse Trace device, the finger probe was attached to the patient's index or middle finger of either arm, provided that the chosen finger was not the one used by the Finometer. The finger probe had to be clamped to the finger with its cable along the dorsal side of the finger. The patient's sex, age and weight were entered and a continuous pulse waveform was displayed on the screen. For measurements the device recorded pulse waveforms over a period of 20 seconds, and further analysed them to generate values for PPT, RI, SI and vascular age (VA). The Pulse Trace device has the option of storing data, but due to the limited amount of data required in our service evaluation, we manually noted the readings on a patient data sheet. The device was then switched off and the finger probe removed from the patient (Figure 13).

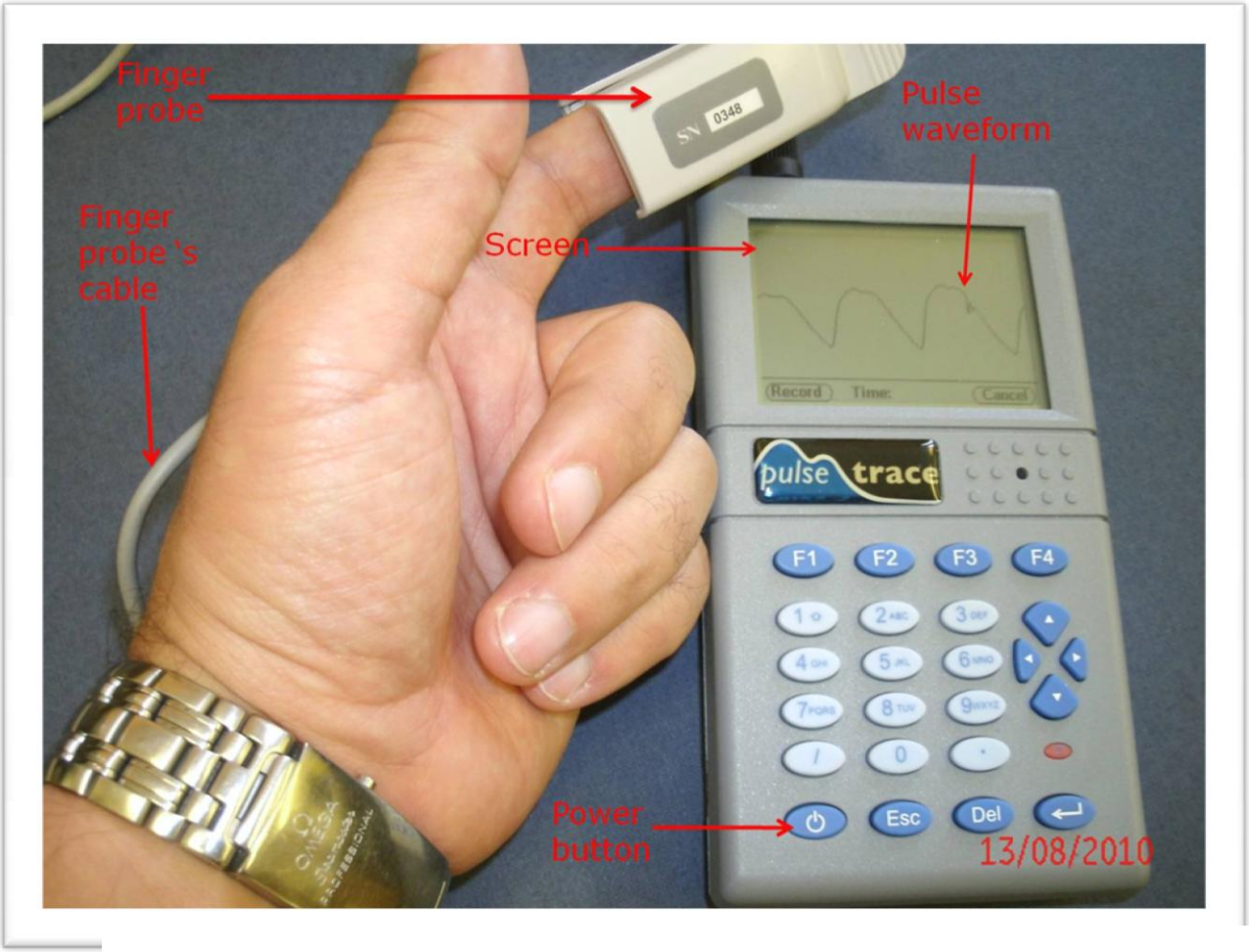


Figure 13. The Pulse Trace device (Micro Medical, Gillingham, Kent, UK)

4.1.3 Non-invasive blood pressure monitoring (NIBP)

Intermittent NIBP monitors are routinely used in operating theatres and haemodialysis units for the purpose of blood pressure monitoring. The NIBP monitors apply the oscillometric method, by which they provide SBP, DBP and MBP readings on intermittent basis, according to either a preset interval adjustment (automatic mode) or upon request (manual mode).

In both our service evaluations, the attending staff were the ones who set the frequency at which the NIBP measurements were to be taken according to their standard practice, and they personally operated the NIBP devices, we did not interfere in the routine care by any means.

It needs to be mentioned that the NIBP devices that were used in the operating theatres were built into the main anaesthesia monitors, and the frequency of measurements was set between 2 and 4 minutes.

During haemodialysis, NIBP monitoring was achieved by using portable NIBP devices, and only two readings were taken; a predialysis and a post dialysis reading.

4.2 Analysis

The haemodynamic data that was collected in both our service evaluations of routine induction of anaesthesia and maintenance haemodialysis was tested for normality, and was shown to be normally distributed. Moreover, continuous data are usually considered parametric.[181] Graphpad Prism software (Graphpad software, California, USA) was used for statistical analysis. Our results are expressed as mean (SD) unless otherwise mentioned.

This section describes the techniques that were used to analyse our data.

4.2.1 Student's t test

Student's t test of difference of means is used to assess if the means of 2 samples showed a significant difference. Two types of t tests can be performed depending on the source of data; an unpaired t test is used when the data is collected from 2 independent groups, whereas a paired t test is used when the data is collected from the same group with the measurements taken at 2 different time points. The null hypothesis would denote that there are no differences between the 2 groups that are to be compared. Results of the t test may show a significant difference between the means of the two groups when the p value is less than 0.05 (evidence to reject the null hypothesis), or may not show a significant difference between the means of the two groups when the p value is more than 0.05 (evidence to accept the null hypothesis).

4.2.2 Analysis of variance and Tukey's post hoc test

The use of a t test is limited to comparing the means of 2 groups. In order to compare the means of 3 or more measurements within same groups, testing with analysis of variance (ANOVA) for repeated measurements would be the appropriate choice. The null hypothesis in this case would be that there is no significant difference between the means that are to be compared.
Further analysis of the data by Tukey's post hoc test allows the testing of all possible 2-way comparisons for significant differences of means.[182]

4.2.3 Chi-squared test

Chi-squared test is used to test for the presence of a significant difference between the expected and the observed data in 1 or more categories of quantitative data with a sample size more than 10. The null hypothesis in this situation would be that there is no significant difference between the expected and the observed data. If the resultant p value is less than 0.05, the null hypothesis is rejected implying that a significant difference lies between the groups, whereas, if the p value was more than 0.05, the null hypothesis would be accepted meaning that there is no significant difference between the groups.

4.2.4 Bland and Altman technique

The Bland and Altman technique is considered the gold standard for the assessment of agreement between the same measurements obtained from a novel device and a validated device, thus, supplying grounds for the possibility of the former to replace the latter.[183] Two sets of simultaneous measurements from the novel device and the old device are taken. The data from both devices are plotted on a graph and the line of equality drawn (the line where all points of data would have lied upon if both devices delivered the same readings). The correlation coefficient (r) of the two devices is then calculated. It should be noted that the r assesses the strength of association, but not the agreement, and it is a value between -1 and +1, with -1 being the highest negative correlation and +1 being the highest positive correlation (Figure 14).

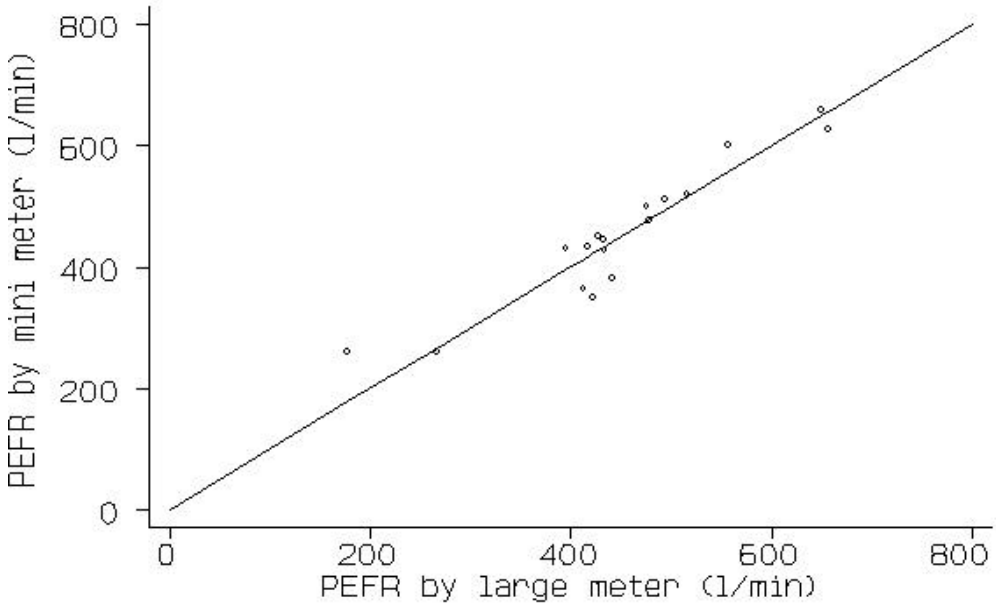


Figure 14. An example of plotted measurements obtained from two devices with the line of equality drawn (reproduced from Bland and Altman, 1986)[184]

It is well known that any two different devices cannot deliver identical measurements every time a measurement is taken simultaneously. This explains the need for assessing the degree of agreement between both devices, to ensure that the measurements obtained by the novel device lie within a clinically acceptable range of difference from the old device. A graph plot of the differences between each two simultaneous readings that are obtained from both devices against their average values is plotted. The 95% limit of agreement is then calculated from the mean difference (Bias) and the standard deviation (SD) of the differences (95% of the differences would occur between -1.96 SD and +1.96 SD, provided that the differences are normally distributed). The narrower the 95% limit of agreement, the better is the agreement between the two devices. The acceptable range of limits of agreement is decided according to the clinical impact of such range. Accordingly, reference ranges for BP measurements do not exist.

As an indicator of precision, the variability of the bias and the 95% limits of agreement are also calculated (95% confidence intervals). [184] Figure 15 displays an example of a Bland and Altman plot.

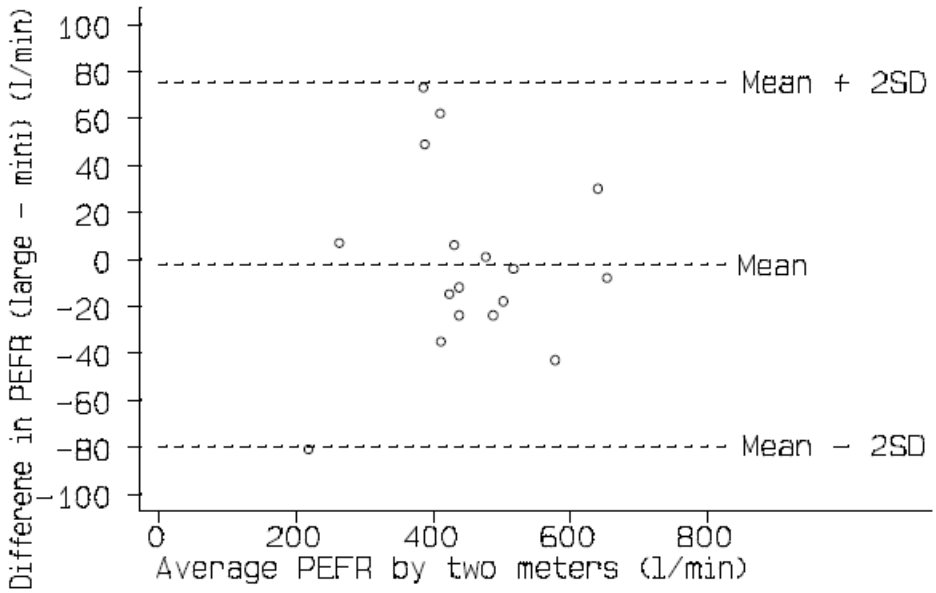


Figure 15. An example of a Bland and Altman plot of differences against averages (reproduced from Bland and Altman, 1986)[184]

4.2.5 Linear regression

Linear regression is used to model the relation between 2 variables, an outcome variable and a predictor variable. The data of the 2 variables are plotted on a graph. An assessment of the correlation coefficient should be done first, since there would be no point to fit a linear regression line if the correlation was not significant. If the 2 variables showed a significant correlation, the best straight line is drawn across the data (linear regression line). From the linear regression line, new values of one variable can be brought from the other. The square of the correlation coefficient (r^2) is calculated and it is used to assess the 'goodness of fit'. A higher value indicates a good fit [185] (Figure 16).

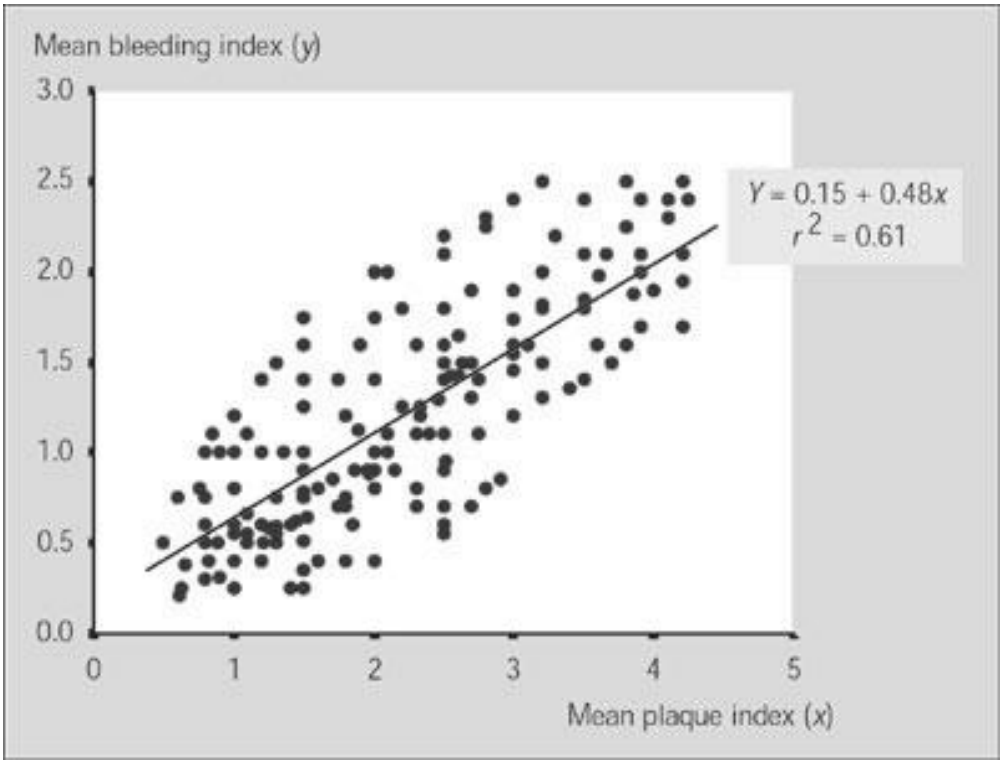


Figure 16. An example of a linear regression line (reproduced from Petrie et al, 2002)[185]

4.2.6 The British Hypertension Society (BHS) protocol for validation of BP devices

The BHS protocol for validation of BP measuring devices was published in 1990 and revised in 1993. According to the BHS protocol, the validation of a novel device is performed against the standard mercury sphygmomanometer technique. The minimum sample size required for the validation study is 85 subjects. Three observers, 2 mercury devices and the device to be tested are required for the study. The 2 mercury devices and the test device are all connected sequentially to the subject as shown in figure 17.

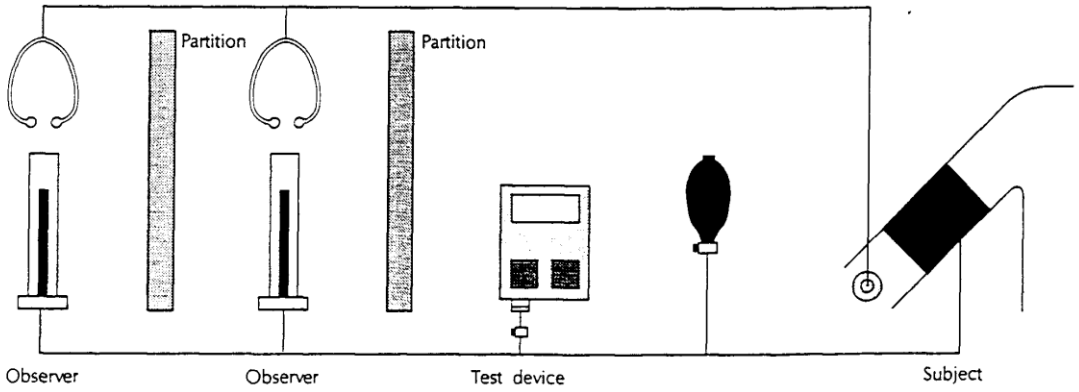


Figure 17. Procedure for sequential validation in the same arm (reproduced from Obrien 1993, et al)[150]

It is preferable to use the same arm rather than both arms to limit the inter-arm factor of error. Observers 1 and 2 are each assigned to one of the sphygmomanometer devices, while observer 3 is assigned to the test device. In each subject, 7 BP measurements are taken according to the sequence shown in figure 18.

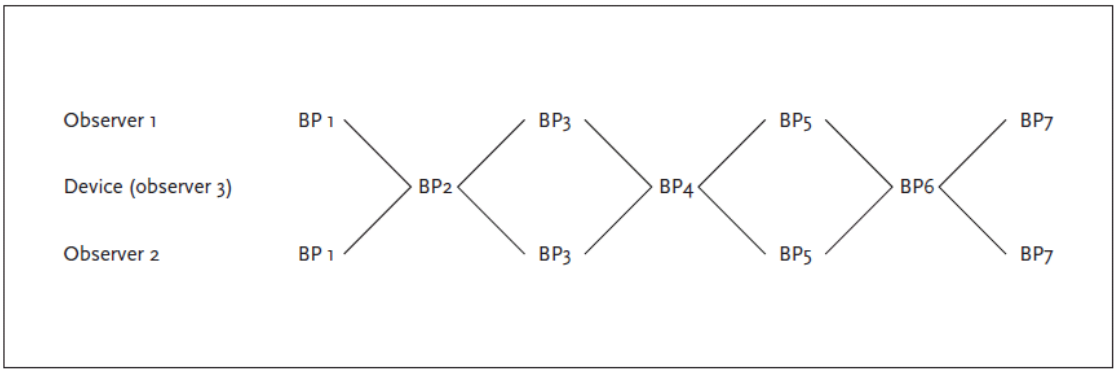


Figure 18. Sequential BP measurements according to the BHS protocol (reproduced from Braam 2003, et al)[186]

The time lag in between the 7 consecutive readings should be kept between 30 and 60 seconds. After the data has been collected, the differences in values between the mercury device and the test device are calculated. The BHS criteria are met when a BP machine achieves grade A or B for both SBP and DBP when compared to the sphygmomanometer method according to table 1. The grades correspond to the cumulative percentage of SBP and DBP measurements occurring within 5, 10 and 15 mmHg differences from the sphygmomanometer measurements. Only a device that has achieved a grade A or B for both SBP and DBP can be valid for use in healthcare.[150]

Table 1. BHS criteria for validation of a novel BP device

Absolute difference between standard and test device						
	≤ 5 mmHg		≤ 10 mmHg		≤ 15 mmHg	
Cumulative percentages	SBP %	DBP%	SBP %	DBP%	SBP %	DBP%
Grade A	60	60	85	85	95	95
Grade B	50	50	75	75	90	90
Grade C	40	40	65	65	85	85
Grade D	Lower than grade C					

4.2.7 The Association for the Advancement of Medical Instrumentation (AAMI) protocol for validation of BP devices

The AAMI protocol for validation of BP measuring devices was published in 1987 and revised in 1992. According to the AAMI protocol, the validation of a novel device is carried out against the mercury sphygmomanometer device in at least 85 subjects. For every subject, 3 sets of BP readings are taken by 2 trained observers (one assigned to the mercury device and the other to the study device). Simultaneous measurements are preferable to sequential measurements. The mean difference between the mercury device and the study device along with the standard deviation of the mean difference (SDD) are calculated for both the SBP and DBP. A device is considered valid for use in medical practice only if the absolute mean difference was ≤ 5 mmHg and the SDD was ≤ 8 mmHg for both the SBP and DBP.[149]

It needs to be mentioned that in both our service evaluations of induction of anaesthesia and maintenance haemodialysis, we have not abided completely to either of the protocols of the BHS and the AAMI, as we validated the Finometer against the conventionally used NIBP device rather than the standard mercury device, which are no more available in clinical settings.

5 A service evaluation of routine induction of anaesthesia involving an assessment of the adequacy of currently used intermittent noninvasive blood pressure (NIBP) devices in detecting episodes of transient hypotension

5.1 Introduction

Significant Intraoperative hypotension is associated with hazardous patient outcomes post surgery.[4, 5] Hence, tight regulation of the BP during anaesthesia has been an issue of major concern to anaesthetists for its impact on patient safety.

Perfusion of the vital organs is maintained by the process of autoregulation which strictly keeps the MBP between 60 and 120 mmHg.[187] A decrease in MBP to a value of less than 60 mmHg is known to cause a state of hypoperfusion.[188] Hypotension is commonly encountered during anaesthesia[1], it is usually mild and well tolerated. However, if significant episodes of hypotension are to be sustained, the perfusion and subsequently the integrity of the vital organs such as the brain, kidney, and liver will be affected.[189] In patients with low cardiac reserves the situation is even worse, as even the mild forms of hypotension can be intolerable. Recent evidence suggests that Intraoperative hypotension involving levels of MBP lower than 60 mmHg even for 1 min is associated with an increased risk of 1 year mortality after non-cardiac surgery.[4, 5] Adverse patient outcomes in response to Intraoperative hypotension explain the necessity for its effective identification and management.

The haemodynamic effects of individual drugs and techniques used in anaesthesia are well illustrated. However, relatively little is known about the gross haemodynamic effect of induction of anaesthesia in routine clinical practice, which involves the administration of different drugs and the employment of techniques simultaneously in a short period of time. The reason for this is that in the current clinical practice, continuous haemodynamic monitoring requires intra-arterial catheterisation; an invasive procedure that is not routinely employed. As discussed earlier, the Finometer is a continuous beat-by-beat noninvasive haemodynamic monitor that generates a continuous blood pressure waveform by applying a finger cuff. Important haemodynamic parameters such as the heart rate, systolic, diastolic and mean blood pressure, stroke volume, cardiac output and total peripheral resistance are derived on continuous basis from the generated blood pressure waveform. The Finometer is accurate in terms of blood pressure monitoring[8] and it accurately tracks the trend of change in cardiac output.[9] For this reason it is being widely used in the field of cardiovascular research; [10, 132-135] however its role as a haemodynamic monitor in routine clinical practice is not well recognised.

5.2 Aim

Considering the emerging evidence suggesting that Intraoperative hypotension is associated with an increased morbidity and mortality risk after non-cardiac surgery, we conducted a service evaluation and used continuous noninvasive haemodynamic monitoring brought by the Finometer, to assess the severity of hypotension encountered during routine induction of anaesthesia. We have specifically chosen the period of induction of anaesthesia, because it involves a variety of drugs and procedures that exert a direct effect on the cardiovascular system delivered to the patient in a short period of time. Routine induction of anaesthesia is conventionally monitored by the NIBP devices set at 2 – 4 minutes. We compared BP monitoring during induction of anaesthesia using Finometer with the NIBP devices that are being used conventionally. Then we assessed the adequacy of BP surveillance provided by the intermittent NIBP monitors in relation to the Finometer during the course of induction of anaesthesia.

Our core objective in this service evaluation was to assess the adequacy of the currently used NIBP monitoring in detecting BP changes and thus the level of patient safety they provide during routine induction of anaesthesia.

To evaluate this, we followed a 3 step analysis protocol:

- *Step 1*: We compared the blood pressure measurements simultaneously *obtained* by the Finometer and the NIBP during routine induction of anaesthesia
- *Step 2*: We characterised the haemodynamic changes occurring during routine induction of anaesthesia as assessed by the Finometer
- *Step 3*: We evaluated the ability of the conventional intermittent NIBP monitors to instantly detect maximum changes in BP as they occur in comparison with the Finometer

5.3 Patients and methods

5.3.1 Patients

This service evaluation was conducted in the operative theatres of the Queen's Medical Centre Campus, Nottingham University Hospital NHS Trust, over a period of 6 months from April to October 2009. One hundred patients undergoing induction of anaesthesia in routine clinical practice were involved in our service evaluation.

5.3.2 Methods

5.3.2.1 Patient recruitment

Operating theatres in Queen's Medical Centre delivering general anaesthesia were approached one hundred and ten times. Patients were recruited for evaluation if the attending anaesthetist agreed, and the evaluation could be carried out on the basis of availability of equipment and the timing of induction of anaesthesia.
Once the above criteria were met, the service evaluation was fully explained to the patients and the attending staff, in terms of the purpose behind conducting it, a brief description of the Finometer and the pulse plethysmograph. We also gave emphasis to the fact that the service evaluation would not interfere with the treatment received in any way and that they can opt out of the evaluation at any time without that affecting their standard care in any means. We also explained that their personal details would be kept confidential and that this service evaluation is a one off event that takes place only during the period of induction of anaesthesia.
There were no selection criteria in selecting patients, any patient undergoing induction of anaesthesia regardless of age, gender or type of surgery was recruited. A verbal approval from the patient for taking part in the service evaluation was ensured.

5.3.2.2 Data collection

Data was gathered from the patient, the patient's hospital file, NIBP monitor, Finometer and from the attending anaesthetist. It included the following:

- Demographic data (age, gender, height and weight)
- Co-morbidities
- Prescribed medications
- American Society of Anesthesiologists physical status classification (ASA)
- Type of surgery
- Anaesthetic drugs used during induction of anaesthesia
- Airway management procedures attempted during induction of anaesthesia
- Full record of the NIBP measurements before and during induction of anaesthesia
- Finometer data
- Pulse plethysmograph data (SI and RI)

All the data collected apart from the Finometer's data, was manually noted on pre-designed patient data sheets.

5.3.2.3 Methodology protocol

In anaesthesia practice, the NIBP arm cuff is usually not used on the arm where the intravenous (IV) line is inserted, in order for it to not interfere with the administration of medications and IV fluids every time an NIBP measurement is to be taken. We compared readings from contralateral arms rather than the same arm, due to the fact that simultaneous Finometer and NIBP measurements are not always successful from the same arm, as the NIBP measurements will completely block the arterial supply of the arm, and the Finometer might stop working. Therefore, we chose to apply the Finometer on the IV line arm (NIBP contralateral arm), as the Finometer only takes one brachial calibration measurement before the start of induction of anaesthesia, thus, it would not interfere with the drug and fluid administration.

On the arm that was chosen for the purpose of Finometer monitoring, an appropriately sized Finometer finger cuff was wrapped around the index or middle finger along with the Finometer's brachial cuff. The Finometer was switched on, and a brachial arterial measurement was taken for calibration. Once calibrated, the Finometer was kept operating throughout the whole period of induction of anaesthesia. The procedure of operating the Finometer is discussed in details in section 4.1.1.1.

For the purpose of standardisation, we used the Finometer's clock to note the timings of all actions taken during the procedure of induction of anaesthesia on the patient's data sheets. Those actions included the start and end of the procedure, and the NIBP measurements.

Every time an NIBP measurement was taken by the attending staff, we simultaneously pressed the Finometer's [mark] button, specifically at the moment when the NIBP measurement was displayed on the anaesthesia monitor. This enabled the labelling of the Finometer's reading that corresponded to this NIBP measurement upon retrieval of the haemodynamic data on the Finometer's raw data excel spreadsheets. We also noted the values of all the NIBP measurements that were taken during induction of anaesthesia along with their timing, on the patient data sheet. The procedure of data retrieval from the Finometer is discussed in details in section 4.1.1.2.

Using the Pulse Trace device, a pre induction of anaesthesia pulse wave analysis measurement of the SI and RI was taken and noted on the patient data sheet. The procedure of operating the Pulse Trace device is discussed in details in section 4.1.2.1. Induction of anaesthesia was then started.

This service evaluation did not interfere with the procedure of induction of anaesthesia including the frequency of NIBP measurements.
After completion of the process of induction of anaesthesia and when the anaesthetist was ready to move the patient from the anaesthetic room to the operating theatre, a post induction of anaesthesia pulse wave analysis SI and RI measurement was obtained and noted on the patient data sheet.
The Finometer and the Pulse Trace device were switched off, disconnected from the patient, and the patient was moved from the anaesthetic room to the operating theatre.

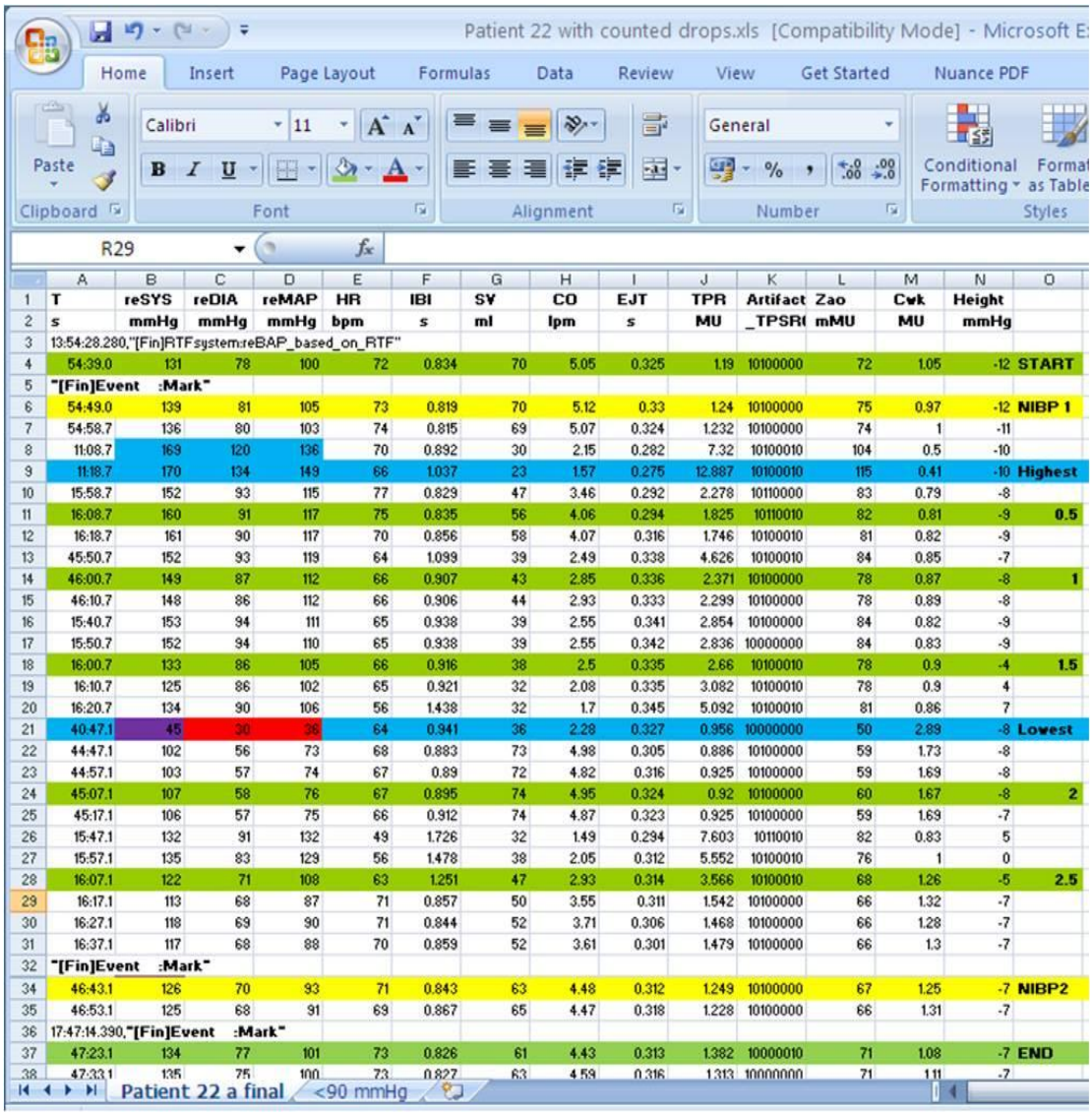
5.3.2.4 Data management

Using BeatScope version 1.1a software (product of Finapres Medical Systems BV, Arnhem), beat-by-beat non-averaged raw data from the Finometer was retrieved on a computer in Microsoft excel format. The procedure of data retrieval from the Finometer is discussed in details in section 4.1.1.2.
To be able to analyse the Finometer's data, we needed to identify the haemodynamic readings that corresponded to different time points in induction of anaesthesia on the Finometer's raw data excel spreadsheets, namely, the start and end of induction of anaesthesia, recordings at 0.5 minute intervals from the start to the end of induction of anaesthesia, measurements that correspond to the NIBP measurements that were taken during induction of anaesthesia, the highest and the lowest BP Finometer's readings, and a few conditional criteria involving times spent when BP values were at predetermined levels. An example of a patient's Finometer's raw data excel spreadsheet is shown in figure 19; however, data in between highlighted time points was compressed for the purpose of illustration.

Firstly, we were able to identify the Finometer's readings that corresponded to the NIBP measurements, by means of the "[Fin] Event: Mark" labels that were displayed on the Finometer's raw data excel spreadsheet. For the purpose of certainty, we double checked the exact timings from the manually noted timings on the patient's data sheets. We then highlighted the rows that displayed those readings on the Finometer's raw data excel spreadsheet and labeled them according to their sequence i.e. NIBP1, NIBP2, NIBP3 and NIBP4. The NIBP1 reading was strictly at the time of pre induction of anaesthesia, whereas, NIBP2, NIBP3 and NIBP4 occurred either during induction of anaesthesia or post induction of anaesthesia. That depended upon the duration of the procedure of induction of anaesthesia, which ranged between 2 and 4 minutes.

Secondly, we used a different colour to highlight the rows in the Finometer's raw data excel sheet that corresponded to both, the timing of the start and the timing of end of the procedure and labeled them "start" and "end" respectively.
Using the same colour, we then highlighted the rows in the Finometer's raw data excel spreadsheet that displayed the haemodynamic variables at 0.5 minute intervals from the start of induction of anaesthesia all the way to the end, and labeled them as 0.5 min, 1 min, 1.5 min, 2 min, 2.5 min, 3 min, 3.5 min and 4 min accordingly.
Thirdly, the highest and lowest BP readings along with their corresponding values of CO, SV, HR and TPR were identified by using conditional formatting. Conditional formatting is a tool in Microsoft excel that enables the identification of the maximum values per variable from the whole data set. Using this tool, we were able to identify the highest and lowest SBP, DBP and MBP values. We then chose the row in the spreadsheet that represented the highest and lowest BP readings on the basis of, if 2 out of the 3 variables (SBP, DBP and MBP) were shown to coincide in being the highest and lowest readings respectively. We then used a different colour to highlight both the highest and the lowest BP rows that were chosen, and labeled them as the "highest" and the "lowest" reading. It needs to be mentioned that on rare occasions, no 2 readings happened to coincide in being the highest or lowest readings. In this case we used the SBP as the indicator of the highest and lowest BP readings.

Fourthly, we identified the absolute values of each of the 20% increase, 20% decrease, 30% increase, 30% decrease, 40% increase and 40% decrease of the SBP, DBP and MBP from baseline values (NIBP1) per patient. These values along with their corresponding rules were entered on separate occasions to the conditional formatting tool per patient's raw data Finometer sheet. The conditional formatting tool automatically highlighted all the rows that contained rules involving each of these criteria. For example, if we wanted to highlight all the MBP readings that showed a more than 30% increase from baseline, and the baseline MBP was 100 mmHg. In this case, the absolute value of the 30% increase from baseline would be 130 mmHg. We entered the number 130 in the conditional formatting tool of excel, followed by entering a rule that asks it to highlight all the MBP cells that contain a number higher than 130. This has allowed us to calculate the time spent during each of the specified criteria. We also used conditional formatting to highlight the rows that contained measurements of the SBP that were less than 90 mmHg and rows that contained measurements of the MBP that were lower than 55 mmHg per patient and we calculated the total time spent in each.



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	T	reSYS	reDIA	reMAP	HR	IBI	SV	CO	EJT	TPR	Artifact	Zao	Cwk	Height	
2	s	mmHg	mmHg	mmHg	bpm	s	ml	lpm	s	MU	_TPSR(	mMU	MU	mmHg	
3	13:54:28.280,"[Fin]RTFsystem:reBAP_based_on_RTF"														
4	54:39.0	131	78	100	72	0.834	70	5.05	0.325	1.19	10100000	72	1.05	-12	START
5	"[Fin]Event	:Mark"													
6	54:49.0	139	81	105	73	0.819	70	5.12	0.33	1.24	10100000	75	0.97	-12	NIBP 1
7	54:58.7	136	80	103	74	0.815	69	5.07	0.324	1.232	10100000	74	1	-11	
8	11:08.7	169	120	136	70	0.892	30	2.15	0.282	7.32	10100010	104	0.5	-10	
9	11:18.7	170	134	149	66	1.037	23	1.57	0.275	12.887	10100010	115	0.41	-10	Highest
10	15:58.7	152	93	115	77	0.829	47	3.46	0.292	2.278	10110000	83	0.79	-8	
11	16:08.7	160	91	117	75	0.835	56	4.06	0.294	1.825	10110010	82	0.81	-9	0.5
12	16:18.7	161	90	117	70	0.856	58	4.07	0.316	1.746	10100010	81	0.82	-9	
13	45:50.7	152	93	119	64	1.099	39	2.49	0.338	4.626	10100010	84	0.85	-7	
14	46:00.7	149	87	112	66	0.907	43	2.85	0.336	2.371	10100000	78	0.87	-8	1
15	46:10.7	148	86	112	66	0.906	44	2.93	0.333	2.299	10100000	78	0.89	-8	
16	15:40.7	153	94	111	65	0.938	39	2.55	0.341	2.854	10100000	84	0.82	-9	
17	15:50.7	152	94	110	65	0.938	39	2.55	0.342	2.836	10000000	84	0.83	-9	
18	16:00.7	133	86	105	66	0.916	38	2.5	0.335	2.66	10100010	78	0.9	-4	1.5
19	16:10.7	125	86	102	65	0.921	32	2.08	0.335	3.082	10100010	78	0.9	4	
20	16:20.7	134	90	106	56	1.438	32	1.7	0.345	5.092	10100010	81	0.86	7	
21	40:47.1	45	30	36	64	0.941	36	2.28	0.327	0.956	10000000	50	2.89	-8	Lowest
22	44:47.1	102	56	73	68	0.883	73	4.98	0.305	0.886	10100000	59	1.73	-8	
23	44:57.1	103	57	74	67	0.89	72	4.82	0.316	0.925	10100000	59	1.69	-8	
24	45:07.1	107	58	76	67	0.895	74	4.95	0.324	0.92	10100000	60	1.67	-8	2
25	45:17.1	106	57	75	66	0.912	74	4.87	0.323	0.925	10100000	59	1.69	-7	
26	15:47.1	132	91	132	49	1.726	32	1.49	0.294	7.603	10110010	82	0.83	5	
27	15:57.1	135	83	129	56	1.478	38	2.05	0.312	5.552	10100010	76	1	0	
28	16:07.1	122	71	108	63	1.251	47	2.93	0.314	3.566	10100010	68	1.26	-5	2.5
29	16:17.1	113	68	87	71	0.857	50	3.55	0.311	1.542	10100000	66	1.32	-7	
30	16:27.1	118	69	90	71	0.844	52	3.71	0.306	1.468	10100000	66	1.28	-7	
31	16:37.1	117	68	88	70	0.859	52	3.61	0.301	1.479	10100000	66	1.3	-7	
32	"[Fin]Event	:Mark"													
34	46:43.1	126	70	93	71	0.843	63	4.48	0.312	1.249	10100000	67	1.25	-7	NIBP2
35	46:53.1	125	68	91	69	0.867	65	4.47	0.318	1.228	10100000	66	1.31	-7	
36	17:47:14.390,"[Fin]Event	:Mark"													
37	47:23.1	134	77	101	73	0.826	61	4.43	0.313	1.382	10000010	71	1.08	-7	END
38	47:33.1	135	75	100	73	0.827	63	4.59	0.316	1.313	10000000	71	1.11	-7	

Figure 19. An example of the Finometer's raw data sheets. Haemodynamic data in between the highlighted events were deleted to be able to compress the file for the purpose of demonstration.

Finally, all the highlighted data from the Finometer's raw data excel sheets were accordingly transferred into 4 master excel spreadsheets, each designed to tackle a different question:

5.3.2.4.1 Master spreadsheet 1 - Comparing blood pressure recordings obtained by the Finometer and the NIBP device

This master spreadsheet was divided into 4 groups of columns according to the sequence of the NIBP measurements that were taken (NIBP1, NIBP2, NIBP3 and NIBP4). Each group of columns was further divided into 8 sub-columns, which were labeled as NIBP's HR, SBP, DBP and MBP, and Finometer's HR, SBP, DBP and MBP.

Four sets of paired simultaneous Finometer and NIBP readings (NIBP1, NIBP2, NIBP3 and NIBP4), which were taken from the 100 patients at the times of pre, during and post induction of anaesthesia, were transferred from both the Finometer's raw data spreadsheet and the patient data sheets to master spreadsheet 1. This was accomplished by transferring the data sets that were labeled NIBP1, NIBP2, NIBP3 and NIBP4 from both the Finometer's raw data spreadsheet and the patient data sheets to their specific columns on master spreadsheet 1 that were also labeled as, NIBP1, NIBP2, NIBP3 and NIBP4. The sums of paired measurements per set were 100, 95, 91 and 25 for NIBP1, NIBP2, NIBP3 and NIBP4 respectively. A total of 311 paired BP readings were available.

This master spreadsheet was also designed to include other types of data, each in a designated column. The data included was the age, gender, diagnosis, surgical procedure, height, weight, smoking, ASA classification, diabetes (DM), hypertension (HTN), coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), and prescribed medications (steroids, statins and anti-hypertensive, anti-ischaemic heart disease and glycaemic control drugs). Also, anaesthetic drugs (thiopental, propofol, sevoflurane, isoflurane, nitrous oxide (N_2O), Opioids (morphine, fentanyl, alfentanil and remifentanil), muscle relaxants (Succinyl choline, atracrurium and rocuronium), benzodiazepines, and vasopressor drugs. The type of airway procedure was also included (oral and nasal endotracheal tube (ETT), laryngeal mask airway (LMA) and tracheostomy tube). It needs to be mentioned that all the categorical data included in this master spreadsheet were scored by either "0" or "1" according to the absence or the presence of the parameter respectively, for example,

if a patient was hypertensive, "1" was to be typed into the designated cell in the master spreadsheet, whereas, if not hypertensive, "0" was to be typed in the designated cell.

5.3.2.4.2 Master spreadsheet 2 – Gross haemodynamic changes that occurred during routine induction of anaesthesia as detected by the Finometer

Master spreadsheet 2 was divided into 2 main sections, the first section was designed to deal with the Finometer's data and the second section was designed to deal with the data obtained from the Pulse Trace device.

The first section was divided into 9 groups of columns according to their corresponding time intervals during the course of induction of anaesthesia (pre-induction (baseline) reading, 0.5 min, 1 min, 1.5 min, 2 min, 2.5 min, 3 min. 3.5 min and 4 min). Each group of columns was formed of 7 sub-columns that were labeled as SBP, DBP, MBP, HR, SV, CO and TPR.

From the Finometer's raw data spreadsheets, the highlighted rows of data that were labeled as baseline, 0.5 min, 1 min, 1.5 min, 2 min, 2.5 min, 3 min. 3.5 min and 4 min were transferred each to its designated position on master spreadsheet 2.

The Pulse wave analysis data was manually transferred from the patient data sheets to their corresponding positions in master spreadsheet 2. The differences between the pre and post induction of anaesthesia SI and RI readings along with the percentage change of the pre and post induction readings, were calculated using the formula tool in Microsoft excel.

5.3.2.4.3 Master spreadsheet 3 - Time and magnitude of haemodynamic changes as detected by the Finometer

Master spreadsheet 3 was divided into 2 main identically designed sections, the highest Finometer's BP reading (peaks) and the lowest Finometer's BP reading (troughs) sections. Each of these sections was composed of 3 groups of columns (baseline reading, peak / trough absolute value, and percentage change of peak / trough from baseline reading columns). Each of the columns was further divided into 7 columns, which displayed the values of SBP, DBP, MBP, HR, CO, SV and TPR. A separate column that showed the time lag between the peak / trough and the next available NIBP measurement was also included.

Data including the baseline readings, and the peak and trough values were transferred from the Finometer's raw data sheets to master spreadsheet 3. The percentage changes of peaks and troughs were calculated on master spreadsheet 3 using Microsoft excel's "formula" tool. The time lags between the peaks / troughs and the next available NIBP measurements were calculated from the Finometer's raw data sheets.

5.3.2.4.4 Master spreadsheet 4 - Time and magnitude of haemodynamic changes as detected by the NIBP

Master spreadsheet 4 was divided into 2 main identically designed sections, the highest NIBP reading (peaks) and the lowest NIBP reading (troughs) sections. Each of the sections was composed of 3 groups of columns (baseline reading, peak / trough absolute value, and percentage change of peak / trough from baseline reading columns). Each of the columns was further divided into 4 columns, which displayed the values of SBP, DBP, MBP, and HR. A separate column that showed the time lag between the peak / trough and the next available NIBP measurement was also included. Data including the baseline readings, and the peak and trough values were transferred from the 100 patients' data sheets to master spreadsheet 4. The percentage changes of peaks and troughs were calculated on master spreadsheet 4 using Microsoft excel's "formula" tool. The time lags between the peaks / troughs and the next available NIBP measurements were calculated from the patients' data sheets.

Having completed the 4 master spreadsheets, the data were ready for further analysis. Analysis of the data will be discussed in details later, each in its relevant section.

5.4 Results: Cohort analysis

In our service evaluation, the Finometer measurements were attempted in 104 patients in total, out of whom; measurements were not successful in 4 patients due to inability of the Finometer to detect a pulse waveform. Successful measurements were generated in 100 patients, equating to a 96% success rate. On the other hand NIBP devices failed to detect blood pressure measurements 5 times out of 316 attempts and that was due to substantial decreases in the blood pressure, which were detected by the Finometer at that time.

With regards to the Pulse trace device, only 52 complete sets of pre and post induction SI and RI recordings were successful out of 100 attempts.

The characteristics of our cohort of patients are displayed in table 2. The type of surgery, and the drugs and techniques used during induction of anaesthesia are displayed in tables 3 and 4 respectively.

Table 2. Cohort characteristics (n = 100)

	Mean (SD), n of patients or percentage
Age	53 (19) years
Gender	
○ Male	50%
○ Female	50%
Height (cm)	171 (8)
Weight (kg)	77 (16)
ASA	
○ ASA 1	22 patients
○ ASA 2	50 patients
○ ASA 3	24 patients
○ ASA 4	4 patients
Smokers	18%
DM	6%
HTN	33%
CAD	9%
COPD	6%
Prescribed medications	
○ Statins	9%
○ Steroids	5%

Table 3. Type of surgery (n = 100)

Procedure	Percentage
Emergency	20%
Hepato-pancreatico-biliary (HPB)	16%
Gastro-intestinal (GI)	17%
Orthopaedics	7%
Neuro-surgery	10%
Ear- nose - throat surgery (ENT)	22%
Dental	6%
Neuro-X-ray	2%

Table 4. Anaesthetic drugs and techniques used during induction of anaesthesia (n = 100)

	Percentage
Anaesthetic drug	
○ Propofol	96%
○ Thiopental	4%
○ Midazolam	7%
○ Sevoflurane	58%
○ Isoflurane	37%
○ N_2O	5%
Opioid	
○ Morphine	2%
○ Fentanyl	63%
○ Alfentanil	23%
○ Remifentanil	8%
Muscle relaxant	
○ Succinyl Choline	10%
○ Rocuronium	47%
○ Atracrurium	26%
Vasoactive drugs	3%
Airway management technique	
○ ETT (oral)	85%
○ ETT (nasal)	5%
○ LMA	6%
○ Tracheostomy tube	1%

Of the 100 patients, a vasoconstrictor agent was administered to 3 patients during the course of induction of anaesthesia due to major decreases in blood pressure according to measurements obtained by NIBP device. Endotracheal intubation was unsuccessful in 1 patient, and the surgery was postponed. Two patients underwent minor surgical procedures including manipulation under anaesthesia of total knee replacement and evacuation of retained products of conception to which neither endotracheal intubation nor laryngeal mask airway were attempted.

5.5 Results: Comparison of blood pressure measurements using NIBP and the Finometer during routine induction of anaesthesia

This section presents an evaluation of the accuracy of the Finometer during routine induction of anaesthesia, by comparing its BP readings to those simultaneously obtained by the NIBP device during routine induction of anaesthesia.

5.5.1 Data handling and statistics

The data that we needed for comparing the measurements of the Finometer with the NIBP's was obtained from master spreadsheet 1. Master spreadsheet 1 is discussed in details in section 5.3.2.4.1.

All the 311 pairs of simultaneous NIBP and Finometer SBP, DBP and MBP measurements were transferred collectively from master spreadsheet 1 to the Prism software for further statistical analysis. Using the Prism software, we performed an assessment of the correlation and linear regression to each set of 311 pairs of the SBP, DBP and MBP variables obtained from both the NIBP and the Finometer. The correlation and linear regression techniques are discussed in details in section 4.2.5.

We also assessed for the agreement between both the NIBP and the Finometer devices using the Bland and Altman analysis in the Prism software. This was carried out for each set of the 311 pairs of SBP, DBP, and MBP data. It needs to be mentioned that we have performed a naïve analysis and not corrected for repeated measurements as our sample size was big (100 patients) in relation to the small number of repeated measurements (3.1 measurements).[190] The Bland and Altman technique is discussed in details in section 4.2.4.

For further assessment of the accuracy of the Finometer in comparison to the NIBP, we applied the BHS and the AAMI criteria for accuracy of novel BP devices. We collectively gathered the 311 pairs of both, the SBP and DBP sets of data from master spreadsheet 1 and transferred the data to a new clear excel sheet for the purpose of working out the BHS criteria on the gathered SBP and DBP data. The BHS workout excel sheet consisted of 2 sets of columns, one for the SBP and the other for the DBP.

Each set of columns was further divided into 3 sub-columns, including an NIBP SBP/DBP column, a Finometer SBP/DBP column and a column for the difference between the values of both devices. We used the "countif" tool in excel, which counts the cells in a certain variable column that contain a pre set rule to calculate the number of readings present in the (difference between devices) column of each of the SBP and DBP, which contained values that are less than 5.1 mmHg, 10.1 mmHg and 15.1 mmHg. From these values we calculated the percentages of each of the numbers of readings that were ≤ 5 mmHg, ≤ 10 mmHg and ≤ 15 mmHg from the total 311 readings, and applied the BHS criteria for accuracy of BP devices as illustrated in table 1. The "countif" tool is discussed in more details in section 6.3.2.4.

The AAMI criteria for accuracy of BP devices were also applied to the same sets of SBP and DBP data. The BHS and the AAMI criteria are discussed in details in sections 4.2.6 and 4.2.7 respectively.

We also compared the NIBP and the Finometer in terms of the ability to track the changes in BP during induction of anaesthesia. Baseline NIBP (SBP, DBP and MBP) readings and Finometer (SBP, DBP and MBP) readings along with the second NIBP (SBP, DBP and MBP) readings and Finometer (SBP, DBP and MBP) readings were transferred from master spreadsheet 1 to a clear excel sheet.

On this excel sheet, the percentage changes of both, the second NIBP (SBP, DBP and MBP) readings and the second Finometer (SBP, DBP and MBP) readings from their corresponding baseline values were calculated. 95 simultaneous NIBP and Finometer (SBP, DBP and MBP) percentage change readings were available, which were then transferred to the Prism software for further analysis. The analysis included correlation and linear regression along with Bland and Altman techniques, which were described in details earlier.

5.5.2 Results

5.5.2.1 Correlation, and Bland and Altman analysis of the BP measurements of NIBP vs. Finometer

The averaged values of the 311 simultaneous pairs of NIBP and Finometer measurements obtained from our 100 patients, were 130 (27) vs. 131 (30) mmHg for SBP, 72 (17) vs. 76 (17) mmHg for DBP and 94 (20) vs. 97 (21) mmHg for MBP.

On applying correlation and linear regression analysis to each of the 311 simultaneous pairs of SBP, DBP and MBP measurements, a significant correlation was shown between the measurements of the NIBP and the Finometer. The r^2 and p values for the SBP, DBP and MBP were $r^2 = 0.75$ and $P<0.0001$, $r^2 = 0.51$ and $P<0.0001$, and $r^2 = 0.74$ and $P<0.0001$ respectively.

As mentioned earlier in section 4.2.4, the Bland and Altman technique assesses the limits of agreement of two devices, by plotting the differences against the averages of the readings simultaneously obtained from both devices on a graph. From this graph, the bias and the 95% limits of agreement are calculated. We applied the Bland and Altman technique and assessed the limits of agreements between the NIBP and the Finometer. The 311 pairs of simultaneous SBP, DBP and MBP measurements were plotted on 3 graphs. Our results showed that the bias and the 95% limits of agreement between the NIBP and the Finometer were within an acceptable range. The bias for SBP, DBP and MBP was -0.82, -3.83 and -3.12 mmHg respectively and the 95% limits of agreement (mean difference ± 1.96 SD) for the SBP, DBP and MBP were -31 to +29, -29 to +21 and -25 to +18 mmHg respectively. The line of goodness of fit showed that the Finometer under-read the SBP values in relation to the NIBP. It over-read the DBP at values lower than 70 mmHg and under-read it at values above 70mmHg. It showed that both devices were equal in terms of the MBP. See figures 20, 21 and 22.

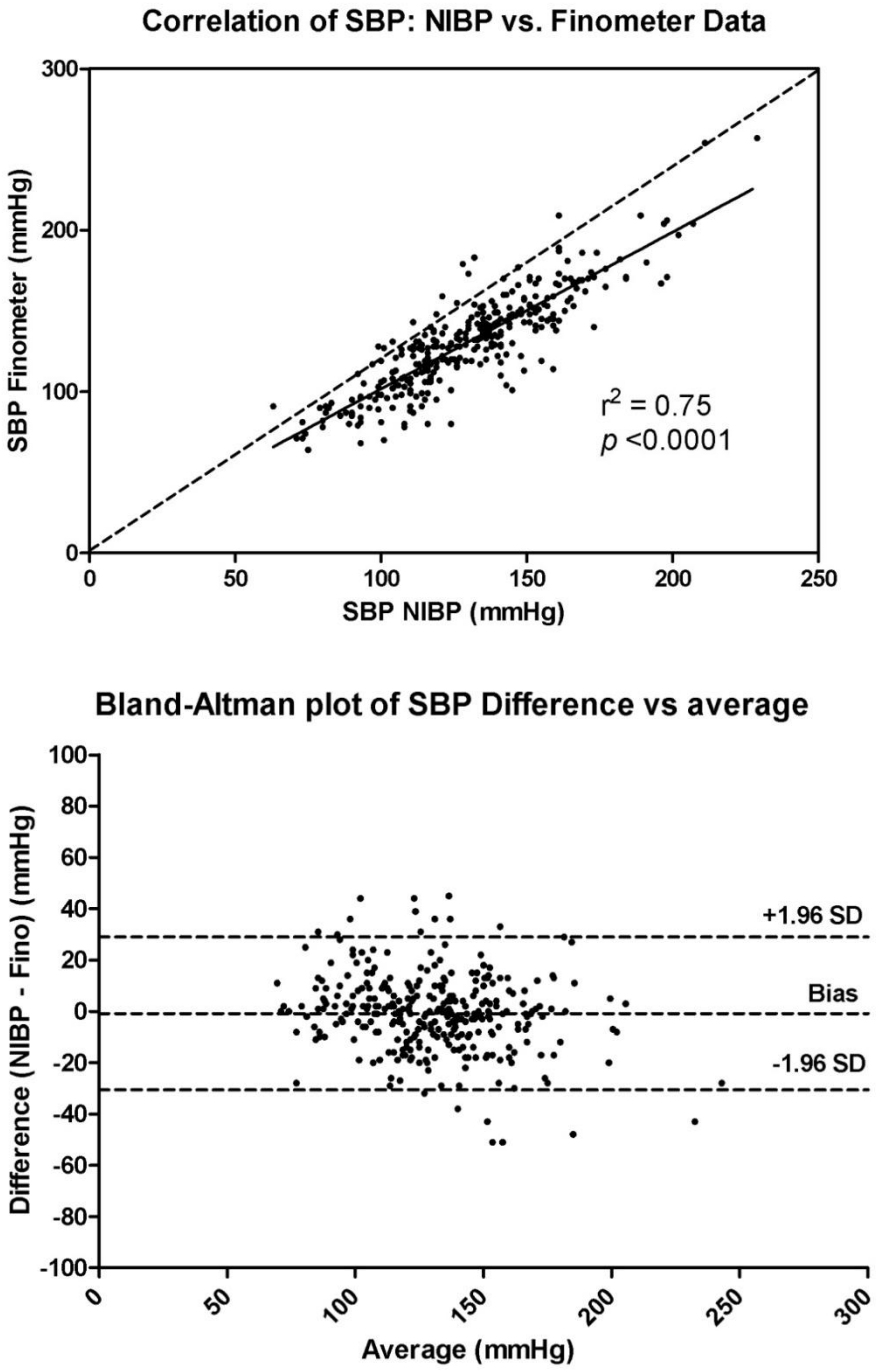


Figure 20. Pooled data for the SBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages.

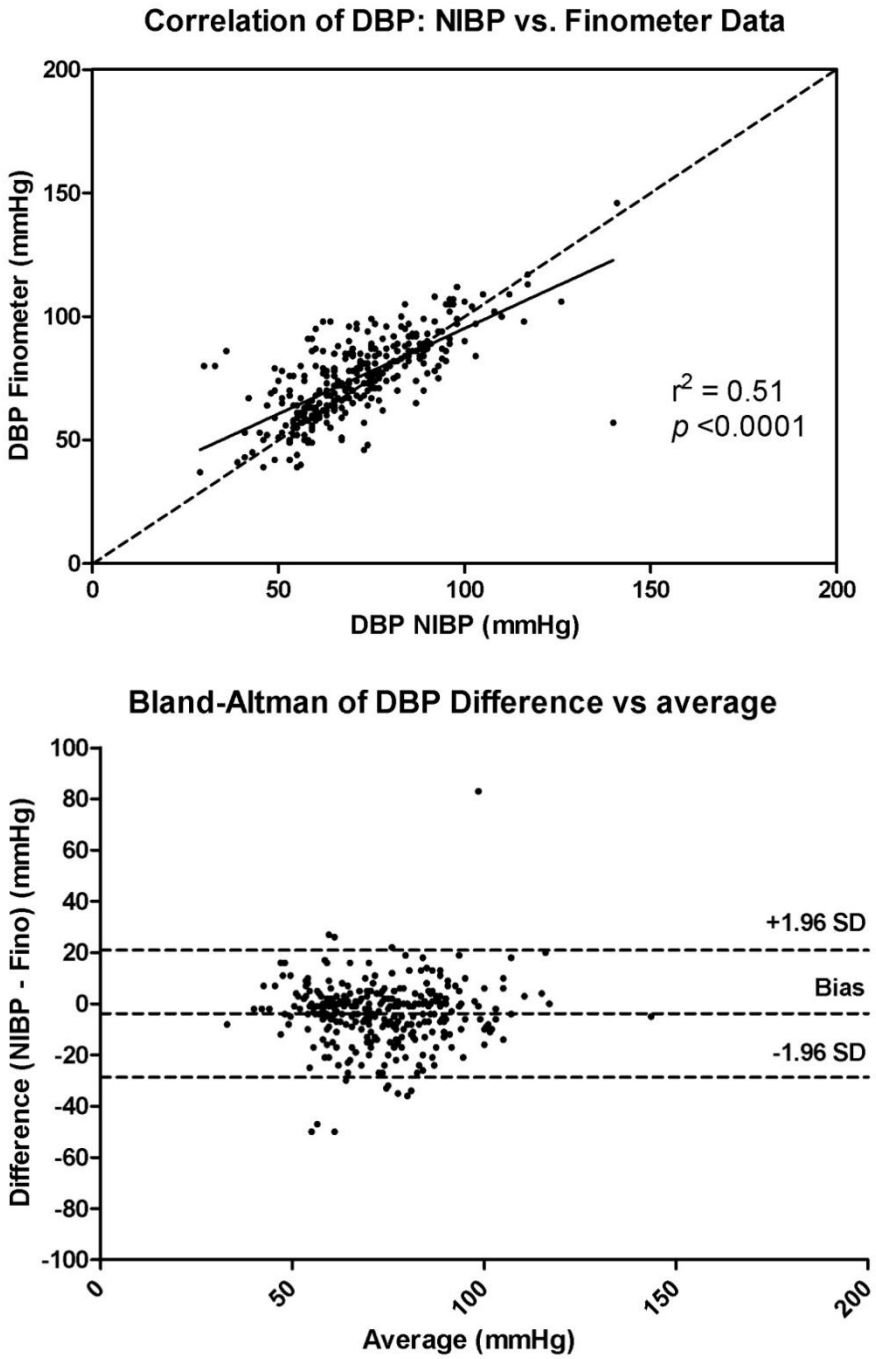


Figure 21. Pooled data for the DBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages.

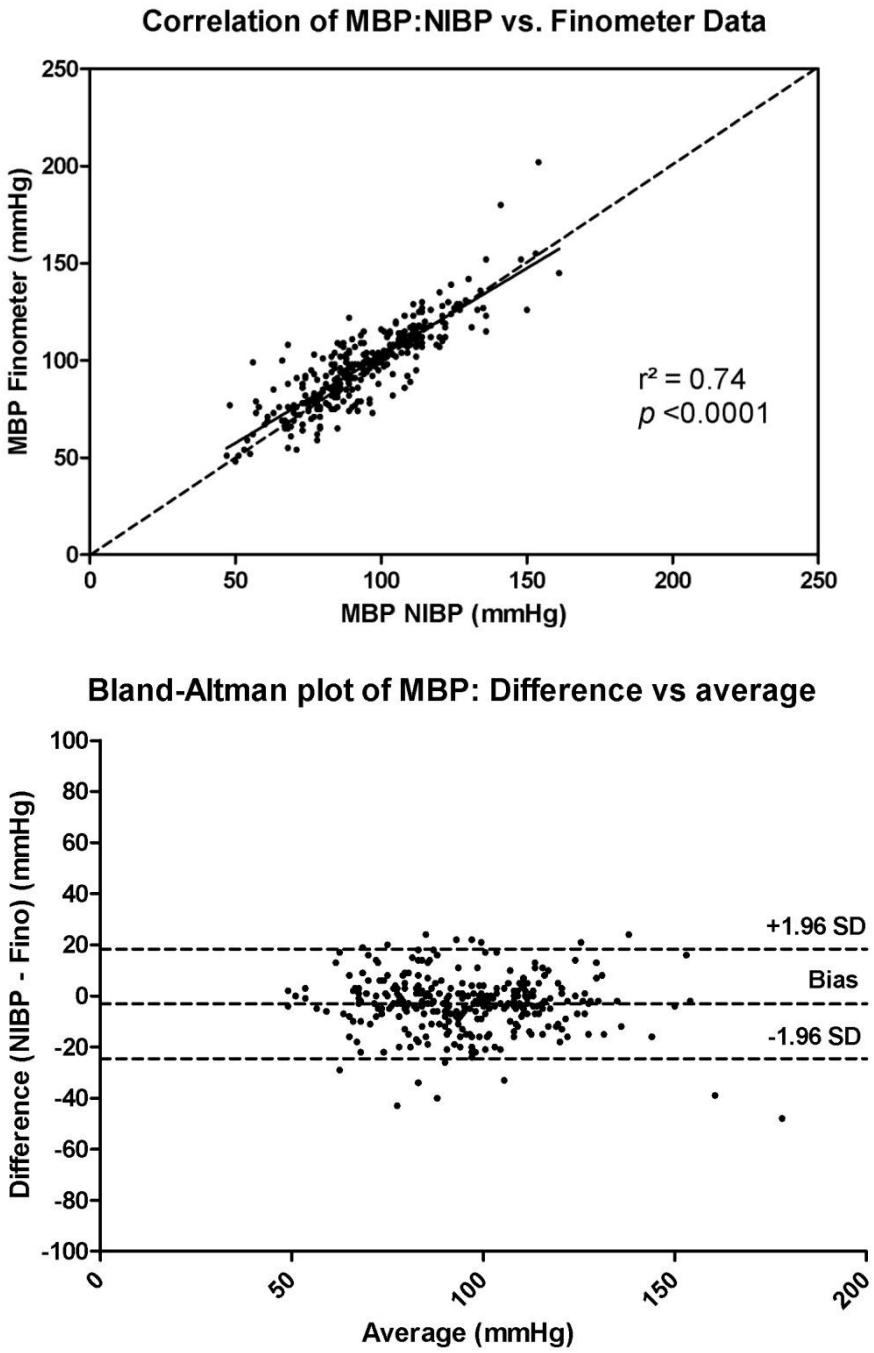


Figure 22. Pooled data for the MBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages.

5.5.2.2 The BHS validation

As mentioned earlier in section 4.2.6, the British Hypertension Society criteria for accuracy of BP machines are met when a BP machine achieves grade A/B when compared to the sphygmomanometer method according to the calculations displayed on table 1. On applying the BHS criteria to our 311 simultaneous pairs of SBP and DBP measurements, we found similar accuracy of the Finometer, but in comparison with the NIBP device (table 5).

Table 5. Assessment of the accuracy of the Finometer by applying the BHS criteria (n of readings = 311)

Absolute difference between NIBP and Finometer						
	≤ 5 mmHg		≤ 10 mmHg		≤ 15 mmHg	
Cumulative percentages	SBP %	DBP%	SBP %	DBP%	SBP %	DBP%
	71	85	81	92	90	95
Grade	A	A	B	A	B	A

5.5.2.3 The AAMI validation

As mentioned earlier in section 4.2.7, The AAMI criteria for accuracy of BP machines are met when the mean difference between the novel device and the mercury device is less than 5 mmHg, with a standard deviation of less than 8 mmHg for both the SBP and the DBP. We applied the AAMI criteria and used the NIBP as the standard device to validate against instead of the mercury device, to all our 311 pairs of NIBP and Finometer SBP and DBP sets of data. Our results showed that the Finometer failed to meet the AAMI criteria for accuracy of BP devices. The mean difference (standard deviation) between the Finometer and the NIBP was – 0.8 (15.2) mmHg for SBP, and – 3.8 (12.7) mmHg for DBP.

5.5.2.4 Comparison of NIBP and Finometer in terms of the ability to track relative changes in BP

As mentioned earlier in section 5.5.1, we compared 95 pairs of simultaneous NIBP and Finometer (SBP, DBP and MBP) percentage change from baseline readings, using correlation, linear regression, and Bland-Altman analysis.

A significant correlation was shown between the NIBP and the Finometer in terms of tracking BP changes from baseline. The r^2 and p values for the dSBP, dDBP and dMBP were $r^2 = 0.76$ and $P<0.0001$, $r^2 = 0.69$ and $P<0.0001$, and $r^2 = 0.82$ and $P<0.0001$ respectively.

Bland and Altman analysis showed that the bias for dSBP, dDBP and dMBP was -4.1, 2.29 and -1.03 % respectively, and the 95% limits of agreement (mean difference ± 1.96 SD) for the dSBP, dDBP and dMBP were -27 to +18, -24 to +27 and -20 to +18 % respectively. See figures 23, 24 and 25.

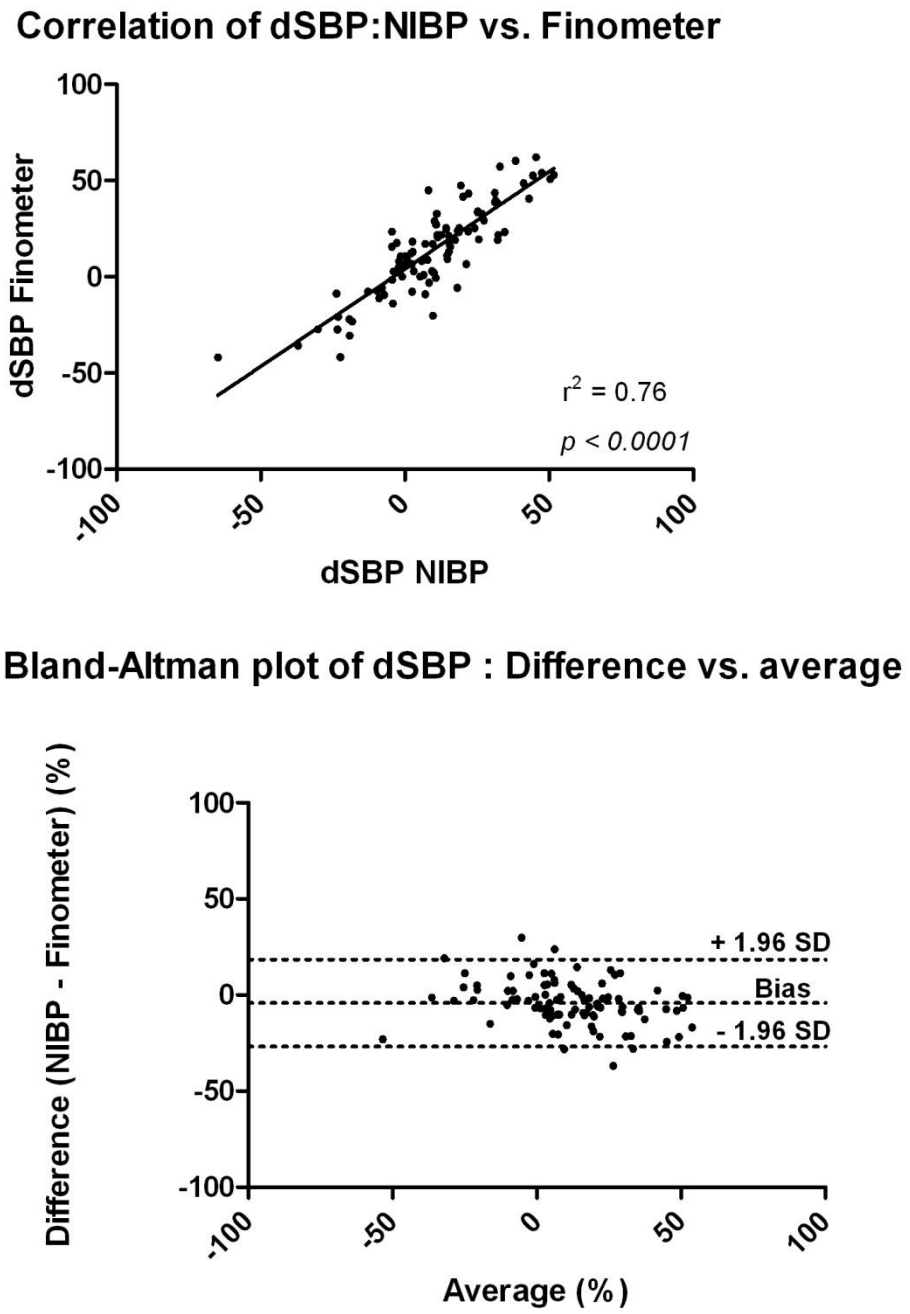


Figure 23. Pooled data for the dSBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages.

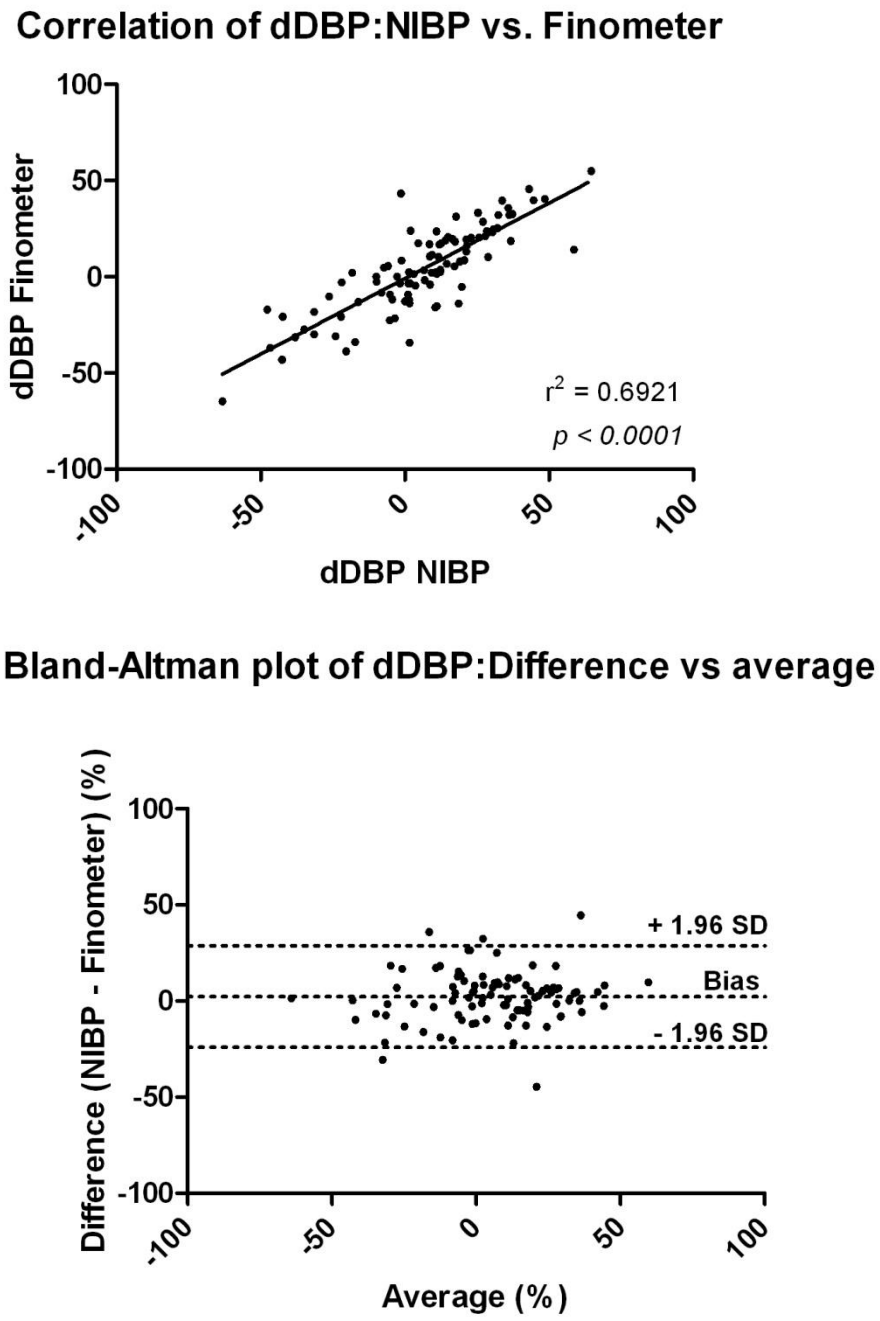


Figure 24. Pooled data for the dDBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages.

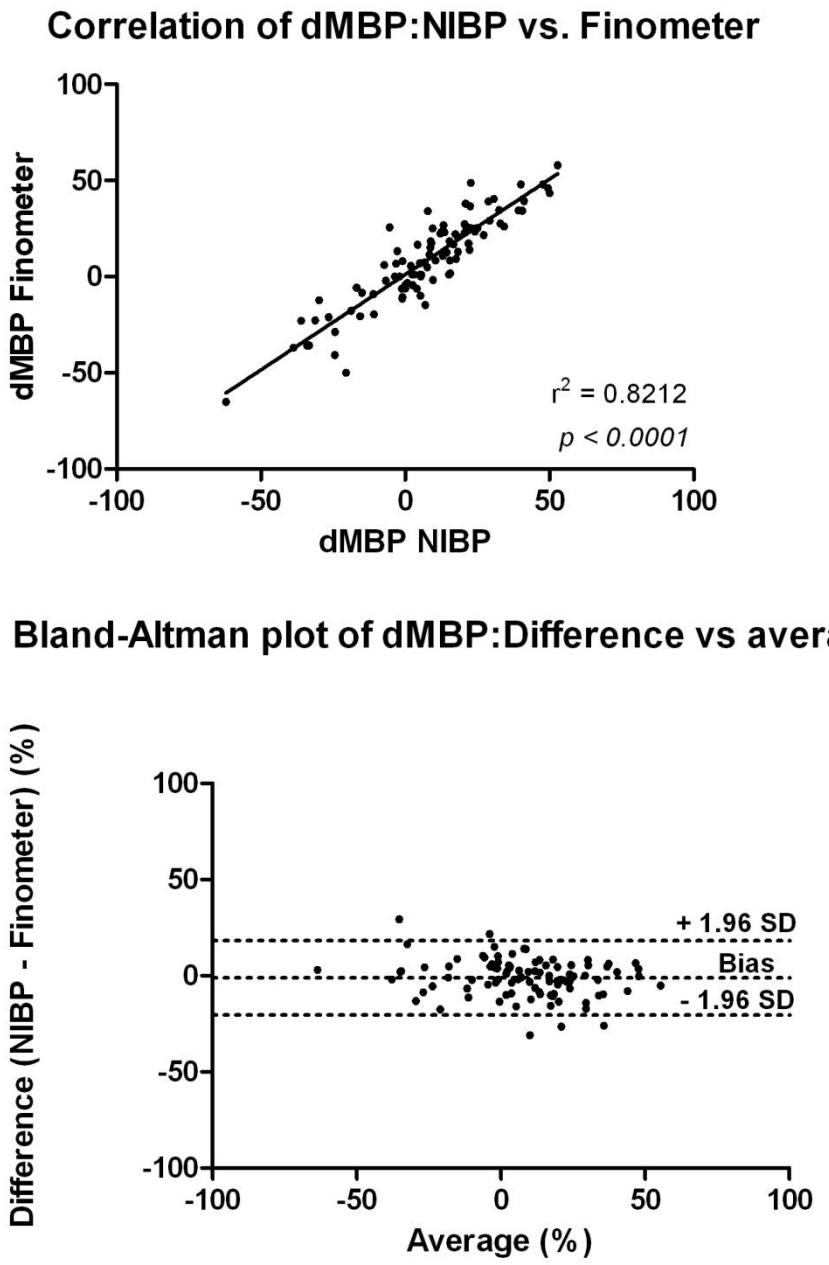


Figure 25. Pooled data for the dMBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages.

5.5.3 Discussion

Our aim in this section was to assess the accuracy of the Finometer in terms of BP monitoring, in comparison with the conventional NIBP device. Using correlation and linear regression techniques, a significant correlation was shown between the NIBP and the Finometer, the r^2 and p values for the SBP, DBP and MBP were $r^2 = 0.75$ and $P<0.0001$, $r^2 = 0.51$ and $P<0.0001$, and $r^2 = 0.74$ and $P<0.0001$ respectively. Bland and Altman analysis for assessment of the limit of agreement between the NIBP and the Finometer in our data, showed that the bias for SBP, DBP and MBP was -0.82, -3.83 and -3.12 mmHg respectively, and the 95% limits of agreement (mean difference ± 1.96 SD) for the SBP, DBP and MBP were -31 to +29, -29 to +21 and -25 to +18 mmHg respectively. The Finometer under-read the SBP values in relation to the NIBP. It over-read the DBP at values lower than 70 mmHg and under-read it at values above 70mmHg. Both devices were equal in terms of the MBP. As mentioned earlier, the AAMI criteria for validation of BP measuring devices considers a bias of ≤ 5 mmHg and a standard deviation of difference (SDD) of ≤ 8 mmHg as acceptable. According to these criteria, an acceptable range of 95% limits of agreement (1.96 SD) between two devices equates to 16 mmHg. Moreover, in a study by McCann and colleagues 5607 pairs of simultaneous noninvasive BP (Vasotrac) and intra-arterial BP readings were compared. Their results in terms of Bland-Altman analysis of the SBP showed that the bias was 1.7 mmHg and that the 95% limit of agreement was -15.7 to 19.1 mmHg, and these results were considered acceptable for accuracy.[191] Furthermore, Bruya and Demand stated that an acceptable range of difference between direct and indirect BP monitoring is 5 to 20 mmHg in critically ill patients, and that a range of up to 30 mmHg is considered acceptable in certain conditions such as post cardiac and vascular surgeries.[192] Accordingly, our results in terms of the limits of agreement can be considered clinically acceptable.

Furthermore, we applied both the BHS criteria and the AAMI criteria for validation of novel BP devices to our data. The Finometer met the BHS criteria. However, it failed to meet the AAMI criteria.

We also showed that the Finometer is comparable to the NIBP in terms of tracking the relative changes in BP during induction of anaesthesia. The r^2 and p values for the dSBP, dDBP and dMBP were $r^2 = 0.76$ and $P<0.0001$, $r^2 = 0.69$ and $P<0.0001$, and $r^2 = 0.82$ and $P<0.0001$ respectively. Bland and Altman analysis showed that the bias for dSBP, dDBP and dMBP was -4.1, 2.29 and -1.03 % respectively, and the 95% limits of agreement (mean difference ± 1.96 SD) for the dSBP, dDBP and dMBP were -27 to +18, -24 to +27 and -20 to +18 % respectively.

Our results indicate that the Finometer is a fairly accurate BP monitoring device for clinical use.

Similar accuracy of the Finometer in terms of BP monitoring was shown in several other studies. Hehenkamp and colleagues performed a study to validate Portapres, which is the portable version of the Finometer against the standard Riva-Rocci/Korotkoff (RRK) method, 30 normotensive pregnant ladies and 20 pre-eclamptic patients were enrolled in the study. Portapres met the AAMI criteria for accuracy of BP measuring devices. In regards to the BHS criteria, only DBP measurements met the criteria. A possible explanation for their failure to meet the BHS criteria could be the small number of subjects enrolled in their study, as it was clearly mentioned in the BHS protocol[150] that a minimum of 85 subjects are needed to validate a BP device.[143]

Another study by Guelen and colleagues assessed the accuracy of the Finometer against the brachial arterial pressure that is generated by the Finometer through applying the RRK method, on 37 post coronary angiography patients. Their results showed that the Finometer met the AAMI criteria[149] for accuracy of automated blood pressure devices.[144]

Schutte and colleagues also performed a validation study and subsequently compared the Finometer to the Riva-Rocci/Korotkoff sphygmomanometer method. 102 females; 24 were hypertensive, 25 obese normotensive and 35 lean normotensive were the subject of the study. Accuracy of the Finometer was assessed using the AAMI, and the BHS criteria of validation of BP devices in both, the total 102 patients and each of the subgroups. The Finometer met the validation criteria of the AAMI, and the BHS in all subgroups groups and in total.[8] It should be noted that a possible limitation to our work, is that we did not totally abide to the BHS and the AAMI protocols, in the sense that we compared the Finometer to the NIBP device rather than the standard mercury method. Also, according to these criteria, simultaneous readings from the same arm are preferable to simultaneous readings from contralateral arms. As mentioned earlier, we compared readings from contralateral arms rather than the same arm in our service evaluation, due to the fact that if both devices were applied to the same arm, the Finometer might have stopped working every time the NIBP device took a measurement. The fact that we did not totally abide to the AAMI protocol may explain the failure of our results to meet its criteria.

5.5.4 Conclusion

The Finometer has met the BHS criteria for accuracy of BP machines, and has shown reliability in terms of BP monitoring during induction of anaesthesia. Hence, it shows potential for use in operating theatres, in particular, whenever continuous BP monitoring is required.

5.6 Results: Haemodynamic changes during routine induction of anaesthesia

This section presents an assessment of the haemodynamic changes that occur during routine induction of anaesthesia, including the incidence of transient hypotension episodes as detected by the Finometer.

5.6.1 Data handling and statistics

The data required for the assessment of the gross haemodynamic changes that occur during induction of anaesthesia was retrieved from master spreadsheet 2. Master spreadsheet 2 is discussed in details in section 5.3.2.4.2.

In regards to the assessment of the incidence of transient hypotension episodes, we obtained the required data for each patient from the patient's corresponding Finometer's raw data sheet, as discussed in section 5.3.2.4.

The highest BP (peaks) and lowest BP (troughs) readings that occurred during induction of anaesthesia were obtained from master spreadsheet 3. Master spreadsheet 3 is discussed in details in section 5.3.2.4.3.

Firstly, to assess the gross haemodynamic changes that occurred during the period of induction of anaesthesia, we transferred the haemodynamic data of SBP, DBP, MBP, HR, SV, CO and TPR at baseline, 0.5 min, 1 min, 1.5 min, 2 min, 2.5 min, 3 min, 3.5 min and 4 min intervals from master spreadsheet 2 to the Prism software, and applied ANOVA with repeated measures and Tukey's post hoc test to the intervallic data of each variable. ANOVA and Tukey's post hoc test is discussed in details in section 4.2.2.

We then assessed the effect of induction of anaesthesia on arterial stiffness, by transferring the pre and post induction values of the SI and RI from master spreadsheet 2 to the Prism software. Using prism software, we used a paired Student's t test to compare each of the pre and post induction readings of SI, and the pre and post induction readings of RI.

Secondly, we used 4 definitions of transient hypotension episodes during induction of anaesthesia: SBP < 80 mmHg, MBP < 55 mmHg, and a more than 40% decrease in SBP and MBP from baseline values, all for more than 1 minute. We further defined a clinically significant change in BP as a 20% change from its baseline value.[193] We pinned out the number of patients who had a clinically significant decrease / increase in SBP, DBP and MBP. The data needed for these assessments of BP changes was gathered from the Finometer's raw data spreadsheets, as described in section 5.3.2.4.

Thirdly, we used master spreadsheet 3 to bring the values of the BP peaks and troughs during induction of anaesthesia, along with their corresponding HR, SV, CO and TPR values. The percentage changes of all those values from their baseline values were also brought from master spreadsheet 3. We then transferred all that data to the Prism software, and performed a paired t test to compare the peak / trough of each of the SBP, DBP and MBP variables with their baseline values. We also compared the peak's / trough's corresponding values of SV, CO, HR and TPR with their baseline values using a paired t test.

Finally, we classified our patients into 2 groups; a hypertensive group (33 patients) and a normotensive group (67 patients), and compared the hypertensive responses to induction of anaesthesia in both groups. Absolute and relative values of the SBP, DBP and MBP were obtained from master spreadsheet 3, and transferred to the Prism software. An un-paired t test was performed using the Prism software to compare both groups of patients in terms of the absolute and relative values of each of the SBP, DBP and MBP peaks and troughs.

5.6.2 Results

The most commonly used anaesthetic agents during induction of anaesthesia were propofol, an opioid, and isoflurane or sevoflurane.

5.6.2.1 Sample of Finometer traces recorded by BeatScope software from patients undergoing induction of anaesthesia

3 samples of Finometer traces showing the BP changes in response to induction of anaesthesia are displayed in figures

Figure 26, 27 and 28. A drop in BP is usually encountered shortly after the start of induction of anaesthesia. It is sustained till endotracheal intubation is carried out, which leads to a sudden rise in the BP.

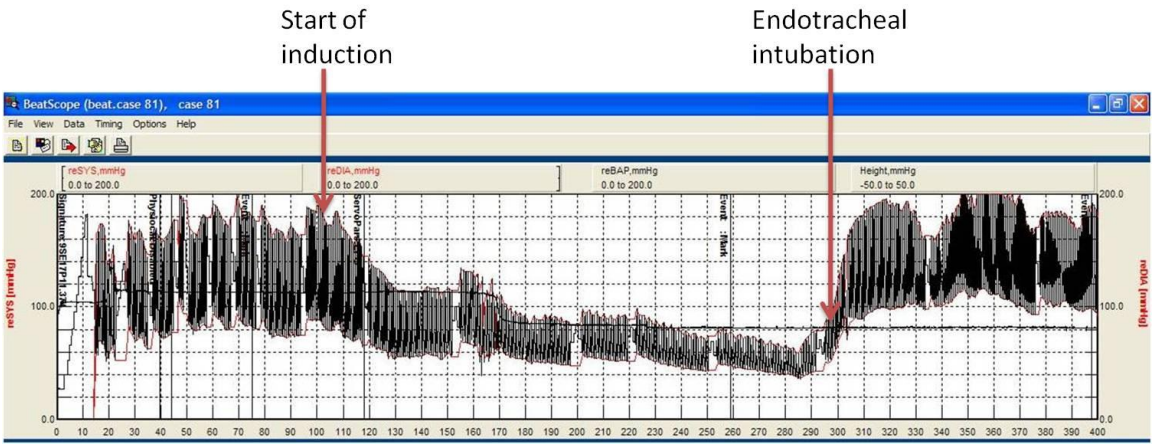


Figure 26. Finometer trace 1 (patient 81)

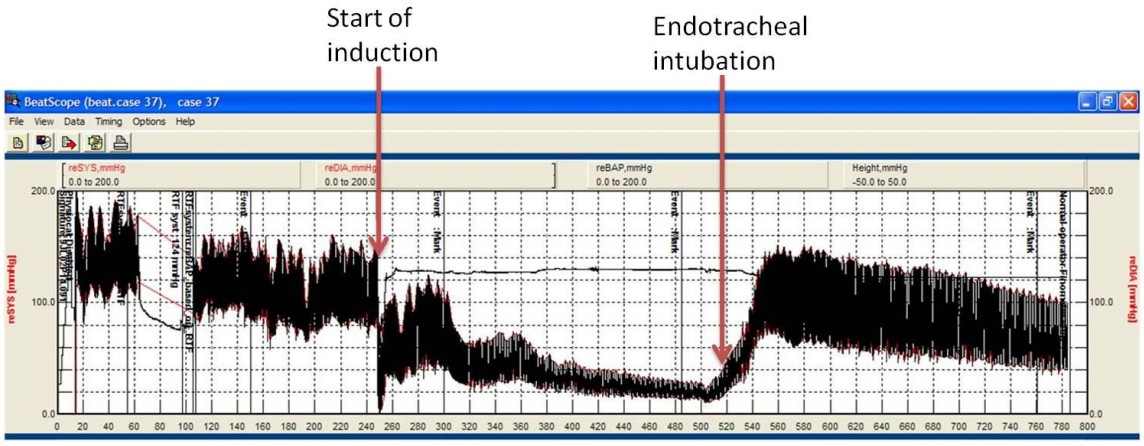


Figure 27. Finometer trace 2 (patient 37)

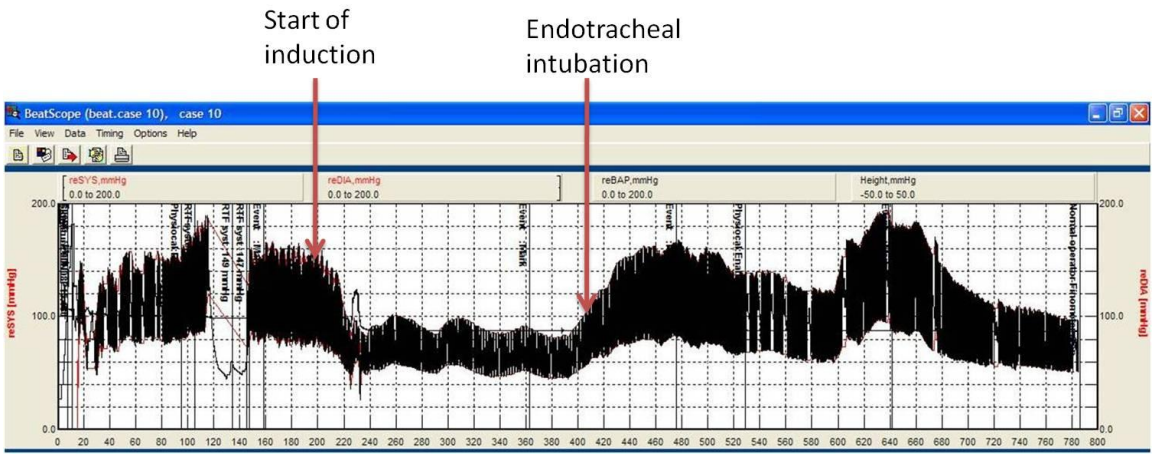


Figure 28. Finometer trace 3 (patient 10)

5.6.2.2 Haemodynamic changes during induction of Anaesthesia

The blood pressure decreased significantly as early as 30 seconds after induction of anaesthesia. There were corresponding significant decreases in the SV and CO. However, corresponding changes in heart rate (HR) and total peripheral resistance (TPR) were not significant (table 6).

Table 6. Mean (SD) of haemodynamic variables during induction of anaesthesia as assessed by the Finometer

Interval (min)	Baseline (n=100)	0.5 min (n=99)	1.5 min (n=98)	2.5 min (n=81)	3.5 min (n=32)	*P value*
HR (beats/m)	77 (15)	80 (17)	76 (18)	77 (17)	80 (22)	0.6767
SBP (mmHg)	145 (23)	125 (37)	119 (39)	116 (44)	127 (27)	<0.0001*
DBP (mmHg)	78 (14)	73 (20)	73 (22)	71 (25)	77 (27)	0.0272*
MBP (mmHg)	103 (16)	92 (24)	91 (28)	89 (32)	96 (33)	0.0008*
SV (ml)	77 (32)	67 (28)	59 (25)	59 (25)	61 (22)	<0.0001*
CO (l/m)	5.9 (2.6)	5.2 (2.3)	4.4 (2)	4.5 (2.2)	4.9 (2.1)	<0.0001*
TPR (MU)	1.35 (0.96)	1.47 (1.35)	1.74 (1.96)	1.49 (1.04)	1.53 (1.36)	0.6016

5.6.2.3 Incidence and magnitude of hypotension encountered during induction of anaesthesia

According to the definitions of hypotension used (SBP less than 80 mmHg, MBP less than 55 mmHg and a more than 40% decrease from baseline SBP and MBP readings for more than 1 minute), 9-30% of the patients had an episode of transient hypotension as detected by the Finometer during induction of anaesthesia. Of the 100 patients, 19 patients have sustained an episode of hypotension where the SBP was less than 80 mmHg for more than 1 minute (see tables 7 and 8).

Table 7. Number of patients with episodes of hypotension sustained for more than 1 minute during induction of anaesthesia as indicated by SBP less than 80 mmHg, MBP less than 55 mmHg and a more than 40% decrease from baseline SBP and MBP readings.

Finometer	SBP <80	MBP <55	SBP >40% ↓	MBP >40% ↓
n of patients (n = 100)	19	9	30	19

Table 8. Number of patients sustaining the episode of SBP < 80 mmHg

Interval	>1 min	>2 min	>3 min	>4min
n of patients (n = 100)	19	6	6	1

5.6.2.4 Clinically significant drops in BP

Clinically significant drops in BP, defined as a more than 20% decrease from the baseline values of the SBP, DBP and MBP were encountered in 83%, 64% and 73% of our patients respectively at some stage during induction of anaesthesia and more than 30% of those sustained it for more than 2.5 minutes.

5.6.2.5 Maximum decrease in BP encountered during induction of anaesthesia

The percentage changes of the SBP, MBP and DBP values during the lowest blood pressure readings (troughs) from their baseline values were 38%, 32% and 28% respectively.

Using a paired t test to compare the SBP, DBP and MBP values during the BP trough with their baseline values, a statistically significant decrease in the SBP, MBP and DBP was shown. See table 9.

The corresponding changes in HR, CO, SV and TPR from their baseline values are displayed in table 10; the changes in HR, CO, SV and TPR were 3%, 24%, 23% and 8% respectively.

Using a paired t test to compare the HR, CO, SV and TPR during the BP trough with their baseline values, a statistically significant decrease in the CO and SV was shown. The HR and TPR remained stable.

Table 9. Percentage change of lowest BP readings (troughs) from baseline as detected by the Finometer (n = 100)

	Baseline	Trough	% change of trough from baseline	*P* value
SBP (mmHg)	145 (23)	89 (26)	38 %	<0.0001*
MBP (mmHg)	103 (16)	70 (16)	32 %	<0.0001*
DBP (mmHg)	78 (14)	56 (16)	28 %	<0.0001*

Table 10. The changes in HR, CO, SV &TPR during the BP trough (n = 100)

	Baseline	Reading during BP trough	% change from baseline	*P* value
HR (beats/min)	77 (15)	75 (18)	3 %	0.1024
CO (l/min)	5.9 (2.6)	4.2 (2.1)	24 %	<0.0001*
SV (ml)	77.1 (32)	56.0 (25)	23 %	<0.0001*
TPR (MU)	1.4 (1)	1.3 (1)	8 %	0.79

5.6.2.6 Clinically significant rises in BP

Clinically significant elevations in BP, defined as a more than 20% increase from the baseline values of the SBP, DBP and MBP were encountered in 53%, 74% and 67% of our patients respectively at some stage during induction of anaesthesia.

5.6.2.7 Maximum increase in BP encountered during induction of anaesthesia

The percentage changes of the SBP, MBP and DBP values during the highest blood pressure readings (peaks) from their baseline values were 24%, 29% and 33% respectively.

Using a paired t test to compare the SBP, DBP and MBP values during the BP peaks with their baseline values, a statistically significant increase in the SBP, MBP and DBP was shown. See table 11.

The corresponding changes in HR, CO, SV and TPR from their baseline values are displayed in table 12; the changes in HR, CO, SV and TPR were 19%, 4%, 18% and 64% respectively.

Using a paired t test to compare the HR, CO, SV and TPR during the BP peaks with their baseline values, a statistically significant decrease in the CO and SV and a statistically significant increase in the HR and TPR was shown.

Table 11. Percentage change of highest BP readings (peaks) from baseline as detected by the Finometer (n = 100)

	Baseline	peak	% change of peak from baseline	*P* value
SBP (mmHg)	145 (23)	180 (34)	24 %	<0.0001*
MBP (mmHg)	103 (16)	133 (26)	29 %	<0.0001*
DBP (mmHg)	78 (14)	104 (23)	33 %	<0.0001*

Table 12. The changes in HR, CO, SV &TPR during the BP peak (n = 100)

	Baseline	Reading during BP peak	% change from baseline	*P* value
HR (beats/min)	77 (15)	89 (20)	19 %	<0.0001*
CO (l/min)	5.9 (2.6)	5.3 (2.9)	4 %	0.0107*
SV (ml)	77.1 (32)	61 (32)	18 %	<0.0001*
TPR (MU)	1.4 (1)	1.96 (1.3)	64 %	<0.0001*

5.6.2.8 Comparison of hypertensive vs. normotensive patients in terms of magnitude and percentage change of BP peaks from baseline during induction of anaesthesia

As mentioned earlier in section 5.6.1, we assigned our patients into 2 groups according to the incidence of hypertension amongst them, into a hypertensive group and a normotensive group.

Using an unpaired t test, we then compared the two groups' SBP, DBP and MBP absolute values during the highest BP readings (peaks). We also compared the percentage changes of these SBP, DBP and MBP values from their baseline values in both groups. No significant difference between the 2 groups in either of the comparisons was shown (table 13).

Table 13. Hypertensive vs. normotensive hypertensive response to induction of anaesthesia

	Hypertensive (33/100)	Normotensive (67/100)	*P value*
Peak SBP	187 (36)	177 (33)	0.1592
Peak MBP	133 (30)	133 (24)	0.99
Peak DBP	102 (27)	106 (21)	0.497
dSBP	24%	26%	0.7448
dMBP	27%	33%	0.259
dDBP	32%	38%	0.281

5.6.2.9 Effect of induction of anaesthesia on arterial stiffness

Table 14 shows a comparison between the pre induction and post induction of anaesthesia readings of the SI and RI. A statistically significant difference is shown between pre and post induction of anaesthesia readings of both, SI and RI.

Table 14. Effect of induction of anaesthesia on stiffness index (SI) and reflection index RI (n of readings = 52)

	Pre induction of anaesthesia	Post induction of anaesthesia	% change	*p* value
SI (m/s)	10.15 (3.38)	8.56 (2.86)	16 %	0.0039*
RI (%)	70 (14)	61 (17)	13 %	0.0006*

5.6.3 Discussion

We used continuous noninvasive haemodynamic monitoring by the Finometer as part of this service evaluation to characterise the haemodynamic changes that occur during routine induction of anaesthesia.

Collective analysis of our individual patient's haemodynamic data showed that there was a significant decrease in BP as early as 0.5 minutes from the start of induction of anaesthesia. There were corresponding significant decreases in the SV and CO, HR and TPR remained stable however.

The incidence of transient hypotension episodes that lasted for more than 1 minute in our patients ranged between 9 and 30%. That depended upon the definition of hypotension that we used. As discussed later in this section, previous studies reported that episodes of hypotension of SBP less than 80 mmHg are associated with poor patient outcomes. Of the 100 patients, 19 patients had such an episode of SBP less than 80 mmHg for more than 1 minute.

We defined a clinically significant change in BP as a more than 20% change from its baseline value. Clinically significant transient decreases in BP were encountered in more than 60% of our patients at some stage during induction of anaesthesia. On the other hand, clinically significant transient increases in BP were encountered in more than 50% of our patients at some stage during induction of anaesthesia.

During induction of anaesthesia, both the lowest BP readings (troughs) and the highest BP readings (peaks) that were recorded by the Finometer showed a statistically significant change from their baseline values. CO and SV values during both the troughs and peaks in BP were significantly lower than their baseline readings. Moreover, during the BP trough the HR and TPR remained stable, but during the BP peak, the HR and TPR were significantly higher than their baseline values.

We also showed that in our cohort of patients, there was no significant difference between the hypertensive patients and the normotensive patients in terms of both, the magnitude of the BP peaks and their relative change from baseline.
In terms of the assessment of the effects of induction of anaesthesia on arterial stiffness, we found a statistically significant difference between the pre and post induction of anaesthesia values of both the SI and the RI.
Confirming our finding of the high prevalence of hypotension during induction of anaesthesia, Bijker and colleagues applied the 25 most frequently used definitions of Intraoperative hypotension (IOH) in literature, on 15,509 patients undergoing non-cardiac surgery. Their results showed an incidence of IOH that ranged between 5% and 99% according to the IOH definition implied.[55] Possible explanations for their wider range of incidence of IOH compared to our findings; is that they used 25 definitions of IOH in contrast to only the 4 definitions that were used in our service evaluation, also, the fact that our observations were only during induction of anaesthesia, compared to the entire operative procedure BP surveillance in their study.
Another study that was published in 2009 by Bijker and colleagues focused on the association of IOH with 1 year mortality after non-cardiac surgery. The most frequently used 16 IOH definitions in previous literature were applied on 1705 patients undergoing non-cardiac surgery. Their results showed that the following definitions showed a trend of a higher 1 year mortality rate in elderly patients: SBP lower than 80 mmHg, MBP lower than 60 mmHg and a 40-45% decrease in both SBP and MBP from baseline values, all definitions for a duration of at least 1 minute.[4] Furthermore, Monk and colleagues showed a 3.6% increase in 1 year mortality risk for every 1 min the SBP was lower than 80 mmHg during non-cardiac surgery.[5] These results may serve as an explanation to the reason for specifically choosing those 4 definitions of hypotension in our service evaluation.

O'Reilly and colleagues retrospectively identified the incidence of hypotension episodes in 2383 patients who have been anaesthetised for surgery. They defined hypotension episodes as SBP values between 90 and 70 mmHg for more than 5 minutes in case of continuous BP monitoring, and for 3 consecutive readings in case of NIBP monitoring. Their results showed that SBP levels that were equal to or lower than 85 mmHg were independent predictors of mortality. They also showed a linear relationship between mortality and SBP values lower than 90 mmHg.[56]

Sympathetic stimulation encountered during surgery at times like induction of anaesthesia, can elevate the blood pressure by 20 – 30 mmHg in normotensive patients. This response is exaggerated even more in hypertensive patients.[194] Reich and colleagues studied the effect of Intraoperative hypertension on the negative surgical outcome (NSO), which was defined as: a more than 10 days stay in hospital with a postoperative morbid state, or in-hospital mortality. 797 patients were the subject of their study, who were further divided into 2 groups; 388 patients with long operation durations (more than 220 min operation duration) and 409 patients with short operation durations (less than 220 min operation duration). The BP and HR raw data was available at 15 second intervals from computerised anaesthesia information systems (CompuRecord; Philips, Andover, MA), from which the median values of the SBP, DBP MBP and HR were calculated per 5 minute epoch. Their results showed, no significant association between the incidence of epochs of SBP > 160 mmHg and NSO in the short operation duration group. However, in the long operation duration group, 48% of the patients had an epoch of SBP above 160 mmHg during the course of the operation, and that was associated with a NSO.[179] A possible limitation to Reich's study is that only one definition of hypertension based on an absolute value was used rather than the relative change from baseline.

It needs to be mentioned that we have not assessed for the incidence of episodes of hypertension, as we were just studying the effects of anaesthesia during the short period of induction, where hypertension is likely to occur only momentarily in response to intubation. Thus, we only assessed for the acute BP elevations in response to induction of anaesthesia.

Owing to the fact that this was a service evaluation where we did not make any changes to the standard of care that was delivered to our patients, we were only able to assess the crude changes in arterial stiffness rather than the endothelial function changes in response to induction of anaesthesia. Measurement of the endothelial function is a procedure involving a relative assessment of the effects of two drugs on the arterial stiffness; salbutamol, which is a $ß_2$-adrenoreceptor agonist that initiates an endothelial dependent vasodilatory response via stimulating endothelial nitric oxide synthase, and glyceryl trinitrate, which initiates an endothelial independent vasodilatory response mediated by nitric oxide (NO)[178, 195] Then the effects of induction of anaesthesia on arterial stiffness were to be assessed and compared to the measured endothelial function.

Our results indicate that the Finometer shows potential for routine use in operating theatres via providing comprehensive noninvasive continuous haemodynamic monitoring especially during the period of induction of anaesthesia, where substantial fluctuations in the BP are likely to occur, along with the high incidence of transient hypotension episodes that are known to be associated with deleterious patient outcomes.

Further studies are warranted to assess for perioperative morbidity and mortality in association with haemodynamic aberrations that occur during anaesthesia. Other studies to assess the effect of anaesthetic drugs used during induction of anaesthesia on the endothelial function are also encouraged. Finally, studies to evaluate whether extra information about haemodynamic changes, as assessed by the Finometer, have an impact on clinical management of haemodynamics during induction of anaesthesia.

5.6.4 Conclusion

BP instability is commonly encountered during routine induction of anaesthesia.

Decreases in BP at the start of induction of anaesthesia are associated with a stable HR and TPR, and a decreased SV and CO, whereas, increases in the BP at airway management are associated with a rise in HR and TPR, and a fall in SV and CO.

Transient significant hypotension episodes are commonly encountered during induction of anaesthesia.

The hypertensive response to intubation was similar in hypertensive and normotensive patients.

A decline in the arterial stiffness in response to induction of anaesthesia occurs.

5.7 Results: Conventional intermittent blood pressure monitoring or continuous noninvasive haemodynamic monitoring in detecting maximum changes in BP that occur during routine induction of anaesthesia

In this section, we have compared the ability of the conventional NIBP monitoring and the continuous noninvasive haemodynamic monitoring (Finometer) in detecting BP aberrations that occur during induction of anaesthesia.

5.7.1 Data handling and statistics

We obtained the percentage change from baseline values of the lowest BP readings (troughs) and the highest BP readings (peaks), of the Finometer and the NIBP from master spreadsheets 3 and 4 respectively. We then transferred these readings to the Prism software, and using a paired t-test, we compared the NIBP's and the Finometer's percentage changes from baseline values of the SBP, DBP and MBP readings during the BP trough / peak. Master spreadsheets 3 and 4 are discussed in details in sections 5.3.2.4.3 and 5.3.2.4.4 respectively.

We also compared the Finometer and the NIBP devices in terms of the number of patients detected, who had either a 30% increase or a 30% decrease in BP from baseline values, by using a Chi squared test in Prism software. The data that was used for this comparison was obtained from the patients' Finometer's raw data spreadsheets, which are discussed in details in section 5.3.2.4.

The time lag between both the highest and the lowest blood pressure values recorded by the Finometer and their next available NIBP measurement, were obtained from master spreadsheet 3.

5.7.2 Results

5.7.2.1 Comparison between the Finometer and the NIBP for the ability to detect BP troughs

On comparing the NIBP and the Finometer devices in terms of the ability to detect the maximum decreases in BP (troughs) from their baseline values, we found that the intermittent measurements by NIBP underestimated the magnitude of the BP troughs in comparison to the Finometer, as shown in table 15.

We then compared the ability of both devices to detect the number of patients who had a significant decrease in BP during induction of anaesthesia, defined as more than 30% decrease in SBP, DBP and MBP from baseline values regardless of the duration. The number of patients who had significant hypotension was underestimated by the NIBP in comparison to the Finometer (Table 16); this was mainly because the intermittent recordings often missed the maximum changes seen on continuous monitoring due to the time lag between the drop in BP and the next available NIBP reading, as shown in table 17. The mean time lag between lowest BP readings detected by the Finometer and the next available NIBP readings was 1 m 29 s.

Table 15. Comparison between percentage changes of lowest blood pressure readings from baseline (NIBP vs. Finometer) (n = 100)

	% change of trough from baseline (NIBP)	% change of trough from baseline (Finometer)	Difference	*P* value
SBP	24 %	38 %	14 %	<0.0001*
DBP	22 %	28 %	6 %	<0.0001*
MBP	22 %	32 %	11 %	<0.0001*

Table 16. n of readings >30% decrease from baseline as detected by NIBP vs. Finometer

	n of readings>30% decrease from base (NIBP) n=100	n of readings>30% decrease from base (Finometer) n=100	*p* value (Chi squared test)
SBP	27	63	<0.0001*
DBP	25	33	0.2745
MBP	25	52	0.002*

Table 17. Time lag between lowest blood pressure readings detected by the Finometer and next available NIBP readings

Time lag	< 1 min	1-2 min	> 2 min
n of patients (n = 100)	37	35	28

5.7.2.2 Comparison between Finometer and NIBP for the ability to detect BP peaks

We compared the NIBP and the Finometer devices in terms of the ability to detect the maximum increases in BP (peaks) from their baseline values. Our results showed that the intermittent measurements by NIBP underestimated the magnitude of the BP peaks in comparison to the Finometer as illustrated in table 18.

We then compared the ability of both devices to detect the number of patients who had a significant hypertension during induction of anaesthesia, defined as more than 30% increase in SBP, DBP and MBP from baseline values regardless of the duration. The number of patients who had significant hypertension was underestimated by the NIBP in comparison to the Finometer (Table 19); as the case with hypotension, this was mainly because the intermittent recordings often missed the maximum changes seen on continuous monitoring due to the time lag between the BP peak and the next available NIBP reading, as shown in table 20. The mean time lag between highest BP readings detected by the Finometer and the next available NIBP readings was 1 m 54 s.

Table 18. Comparison between percentage changes of highest BP readings from baseline (NIBP vs. Finometer) (n = 100)

	% change of peak from baseline (NIBP)	% change of peak from baseline (Finometer)	Difference	*P* value
SBP	12 %	25 %	13 %	<0.0001*
DBP	16 %	36 %	20 %	<0.0001*
MBP	22 %	31 %	9 %	<0.0001*

Table 19. n of readings >30% increase from baseline as detected by NIBP vs. Finometer

	n of readings>30% increase from base (NIBP) n=100	n of readings>30% increase from base (Finometer) n=100	*p* value (Chi squared test)
SBP	5	41	<0.0001*
DBP	14	55	<0.0001*
MBP	13	48	<0.0001*

Table 20. Time lag between highest BP readings detected by the Finometer and next available NIBP readings

Time lag	< 1 min	1-2 min	> 2 min
n of patients (n = 100)	20	36	44

5.7.3 Discussion

In this section, we assessed the ability of the NIBP to provide sufficient BP surveillance during routine induction of anaesthesia by comparing it with continuous noninvsive BP monitoring using the Finometer. It was shown in section 5.6 that routine induction of anaesthesia is associated with substantial BP changes.

Firstly, we compared the NIBP's and the Finometer's ability to detect the magnitude of both BP peaks and BP troughs. Our results showed that the NIBP underestimated the magnitude of both the BP peaks and the BP troughs in comparison to the Finometer.

Secondly, we compared both devices' ability to identify the number of patients who had significant hypotension and the number of patients who had significant hypertension during induction of anaesthesia. The NIBP underestimated both, the number of patients who had significant hypotension and the number of patients who had significant hypertension in comparison with the Finometer.

Thirdly, we indicated the time lag between each of the BP peaks and the BP troughs that were detected by the Finometer and their next available NIBP measurements. The average time spent between each of the Finometer's BP troughs and BP peaks, and their next available NIBP measurements was 1 m 29 s and 1 m 54 s respectively.

In support of our findings, Dueck and Jameson compared the ability of NIBP and continuous noninvasive BP monitoring brought by the Tensys T-line® device, in detecting episodes of hypotension, defined as SBP <85 mmHg for more than 5 min, in 25 patients during the whole period of anaesthesia. The NIBP missed 22% of the hypotension episodes and there was a delayed detection in a further 22% in comparison with continuous noninvasive BP monitoring.[196]

Furthermore, Siebig and colleagues assessed the advantage of using continuous noninvasive BP monitoring by means of a CNAP® device (CN Systems, Graz) in 40 sedated patients undergoing endoscopic procedures. A total of 103117 CNAP measurements and 333 NIBP measurements were recorded and analysed. They calculated the variance of the CNAP readings during the time between each two consecutive NIBP readings (NIBP interval). Mean (SD) of the NIBP intervals was 7.5 (4.6) minutes. Results of variance in relation to baseline NIBP values showed a 30.85% decrease and a 22.43% increase of the CNAP MBP readings for every NIBP interval. Moreover, they noticed that 15.8% of the readings that were obtained by the CNAP showed a clinically significant (more than 20%) change from baseline NIBP values. They also showed that 3.6% of their CNAP SBP values were below 100 mmHg and that none of those were detected by the NIBP. A possible limitation to their study is that the ethics committee did not accept blinding of the CNAP BP measurements to the attending endoscopists, which explains the long NIBP intervals and the possibility of overestimating the inaccuracy of the NIBP in detecting BP changes in their results.[193]

Our results show that during induction of anaesthesia, continuous noninvasive BP monitoring using the Finometer provides better surveillance of the BP in comparison to the conventional intermittent NIBP devices, which would allow the attending anaesthetist to promptly intervene in response to potentially harmful BP aberrations and achieve a tighter BP control. Extra safety to the patient may be added in doing that. Further studies are warranted to explore this potential.

5.7.4 Conclusion

Significant changes in BP are encountered during routine induction of anaesthesia. Their magnitude is underestimated, and detection delayed or missed by NIBP monitors. Continuous noninvasive BP monitoring by the Finometer provides more comprehensive BP surveillance during induction of anaesthesia, which may enhance patient safety.

5.8 Results: An example of the haemodynamic changes during the whole period of anaesthesia as detected by the Finometer

We approached one of the neuro-surgery operating theatres in Queen's Medical Centre NHS Trust, as part of our service evaluation. The same procedure of patient and anaesthetist consent that was discussed earlier was followed.
We recruited a 77 year old male patient, known hypertensive on a beta blocker, and his ASA was 2. He was diagnosed with a chronic subdural haematoma and scheduled for burr-hole evacuation.
The Finometer was applied to the patient and was kept running all the way from the pre induction period till the patient was moved from the operating theatre to recovery. Finometer's data was retrieved on a Finometer's raw data excel sheet. We used the Finometer's raw data excel sheet to plot two graphs, both showing the haemodynamic variables at 10 second intervals. One graph displayed the SBP, DBP, MBP, HR, SV (figure 29), and the other displayed the CO and TPR (figure 30). We used two graphs rather than one, to accommodate the range differences between different haemodynamic variables. In both graphs we used blue longitudinal lines to mark the time points corresponding to NIBP measurements that were taken during the procedure, and red longitudinal labeled lines to mark the time points corresponding to actions taken during the whole period of anaesthesia.
The NIBP data was manually noted on a patient data sheet. We transferred the NIBP'S SBP, DBP and MBP data from the patient data sheet into a new clear excel sheet, and plotted a third graph that displayed the NIBP'S SBP, DBP and MBP values over time (figure 31). Once again, we used red longitudinal labeled lines to mark the time points corresponding to actions taken during the whole period of anaesthesia.

The red longitudinal labeled lines in the 3 graphs (figures 29, 30, and 31) represented the following actions:
Line A: One litre intravenous fast drip administered.
Line B**:** Start of induction of anaesthesia.
Line C: Endo-tracheal intubation.
Line D, G and H: Metaraminol (alpha adrenergic agonist that causes vasoconstriction) administered.
Line E: Knife to skin.
Line F: One litre intravenous slow drip administered.
Line I: Skin stitches.
Line J: Anaesthetics reduced.
Line K: Suctioning.
Line L: Extubation and airway placement.

Anaesthesia was induced by propofol and rocuronium, and maintained by sevoflurane.

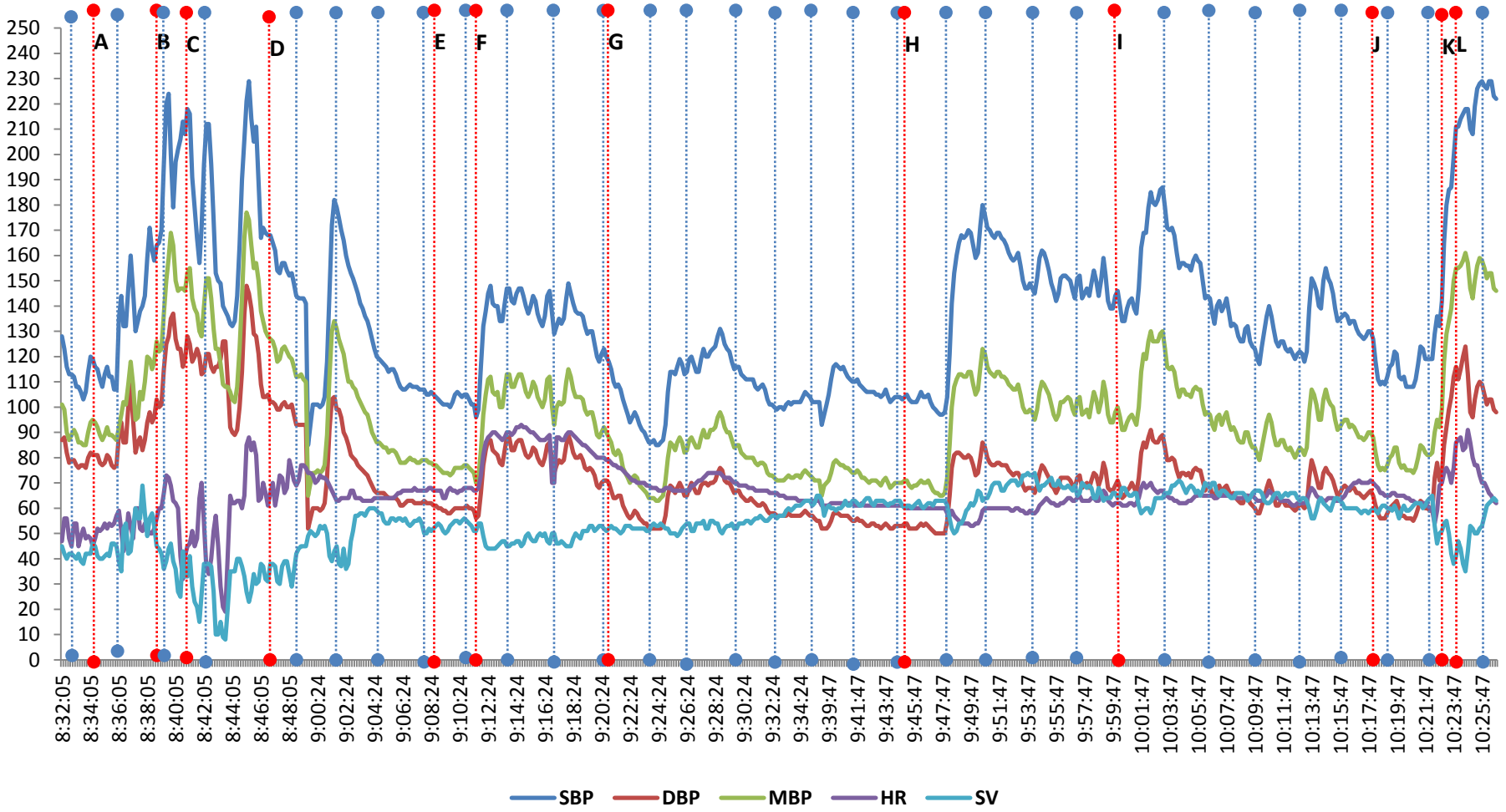


Figure 29. Graph showing the changes in SBP, DBP, MBP, HR and SV as detected by the Finometer during a whole surgical procedure. Blue lines correspond to NIBP measurements and red lines correspond to actions taken during the procedure

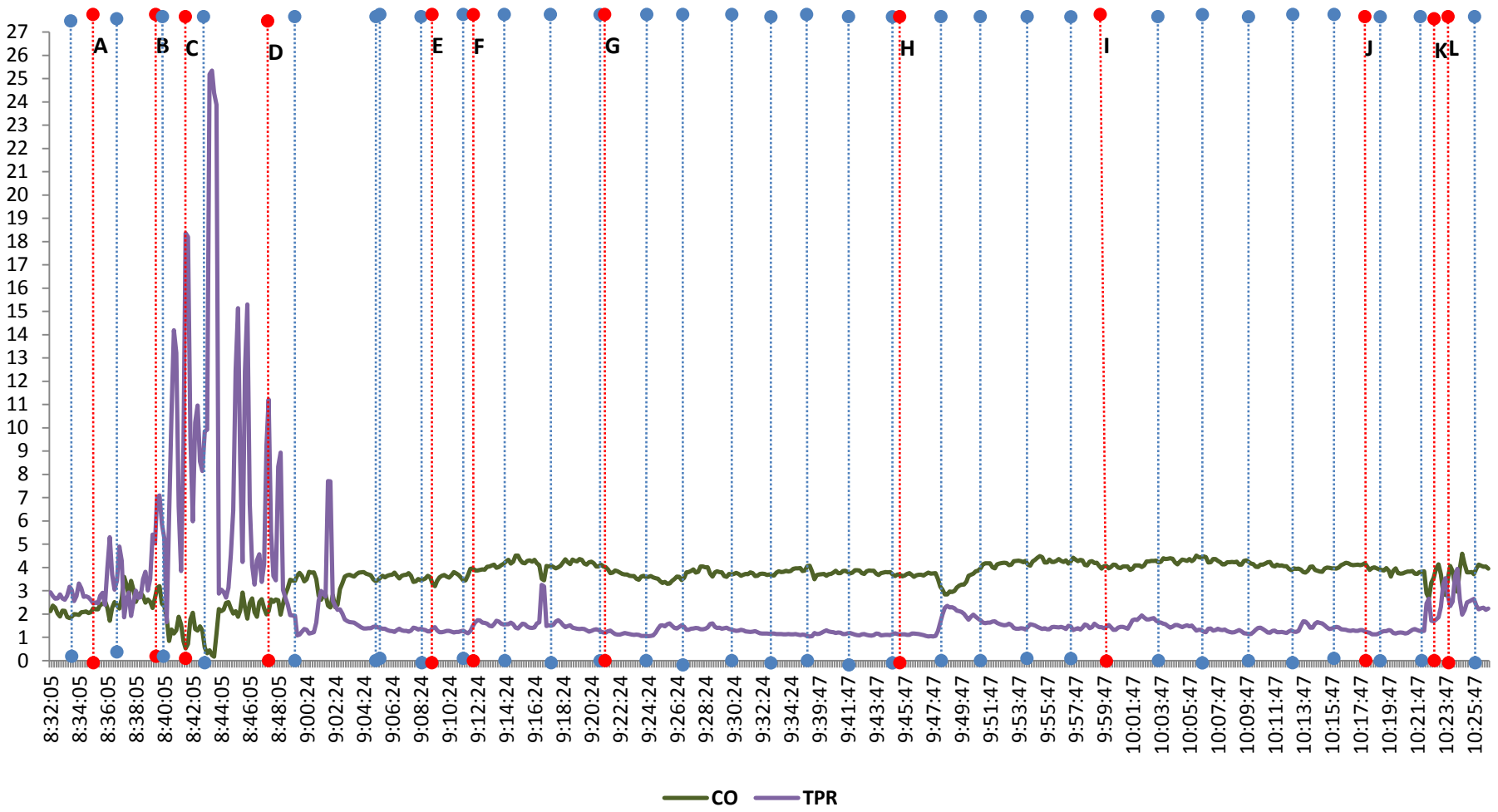


Figure 30. Graph showing the changes in CO and TPR as detected by the Finometer during a whole surgical procedure. Blue lines correspond to NIBP measurements and red lines correspond to actions taken during the procedure

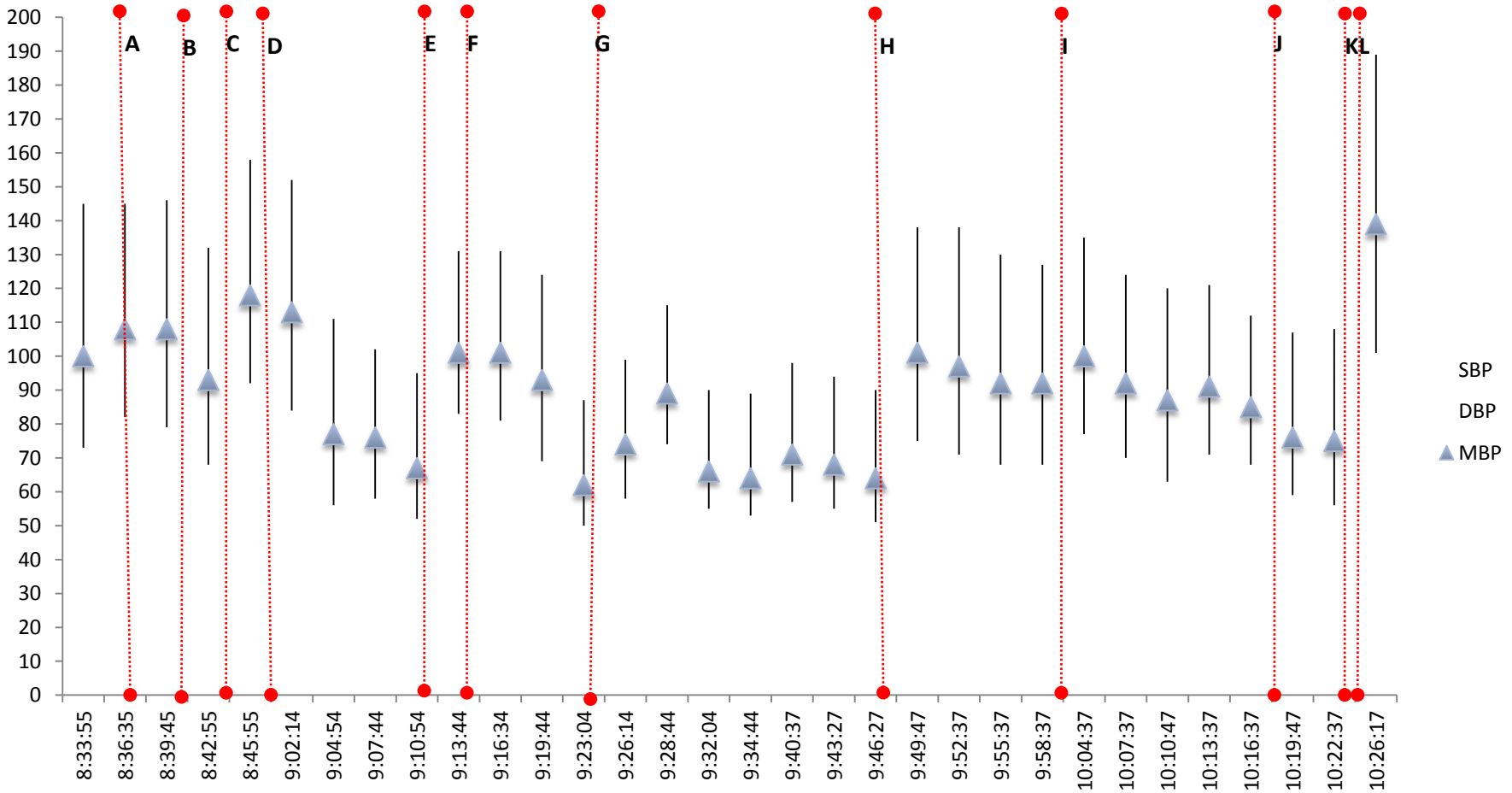


Figure 31. Graph showing the changes in SBP, DBP and MBP as detected by the NIBP during a whole surgical procedure. Red lines correspond to actions taken during the procedure

This shows how a number of peaks and troughs in BP can be detected by continuous Finometry, and that the associated changes in CO and TPR can guide the anaesthetist to undertake appropriate corrective measures.

On the other hand, haemodynamic information generated by the NIBP during the whole period of general anaesthesia was limited to the detection of few points when the BP dropped to an SBP level ≤ 90 mmHg.

In the pre-induction of anaesthesia period, both the SV and the CO were low; their values were 42 ml and 1.99 L / min respectively. The BP was maintained by an elevated TPR of 2.771 MU (normal TPR range is 0.6-1.4 MU (mmHg/ml/sec)), indicating that the patient was dehydrated. Over the course of anaesthesia and surgery, administration of IV fluids seems to have increased the CO and decrease TPR and stabilise patient's overall condition. Such information is not possible from NIBP alone.

In summary, conventional NIBP monitoring indicated that our patient was haemodynamically stable prior to surgery. However, the extra haemodynamic information that was generated by the Finometer revealed that the patient was dehydrated. On the basis of the Finometer's extra information, Intravenous fluids were administered, and the patient's volume status was shown to normalise approximately 1 hour after induction. This extra knowledge that was offered by the Finometer raises the question of whether the quality of care provided to the patient in terms of better haemodynamic stability would have further improved, if we had used the Finometer a few hours before the operation to noninvasively detect the patient's volume status at an earlier stage, hence, giving the chance to optimise the patient's volume status prior to surgery.

5.9 Summary

Our results have clearly demonstrated that continuous noninvasive haemodynamic monitoring using the Finometer provides better surveillance of blood pressure changes than the conventional NIBP during induction of anaesthesia. In order to demonstrate that, we carried out a 3 step analysis protocol of our beat-by-beat data:

First, we assessed the feasibility of using the Finometer during induction of anaesthesia, and it has shown both accuracy and reliability in terms of BP monitoring in comparison with the conventional NIBP device.

Second, we characterised the haemodynamic response to routine induction of anaesthesia. Significant decreases in the BP were shown that were associated with falls in the SV and CO. Also, significant increases in the BP were shown, which were associated with rises in the HR and TPR, and falls in the SV and CO. We also demonstrated that the BP reached unsafely low levels which were sustained for more than 1 min in 9-30% of our patients depending on the definition of hypotension used.

Third, we showed that continuous noninvasive BP monitoring using the Finometer is more reliable in instant detection of the commonly occurring BP aberrations than the conventional intermittent NIBP monitors, which not only underestimated, but even missed more than 50% of those aberrations Also, extensive time lags between the BP aberrations that were detected by the Finometer and their next available NIBP measurements were encountered.

Monitoring of induction of anaesthesia by NIBP devices has long been considered standard practice. However, based on our findings of the high incidence of significant changes in the BP, we believe that noninvasive continuous haemodynamic monitoring of routine induction of anaesthesia may provide better patient safety. Furthermore, additional data generated by the Finometer such as SV, CO and TPR may serve as guidance for prompt and proper management of haemodynamics.

A possible limitation to our service evaluation is that when we applied the BHS and AAMI criteria for accuracy of BP devices, we compared the Finometer with the NIBP, rather than the standard sphygmomanometer method, which is not used currently in clinical practice. Also we compared Finometer and NIBP readings taken from contralateral arms, which is not preferable by the BHS and AAMI protocols. Lastly, the Finometer readings were not blinded to the anaesthetists.

In our service evaluation, we showed an association between hypotension during induction of anaesthesia and a significant decrease in SV, which validates the question whether preoperative fluid optimisation can provide better haemodynamic stability during anaesthesia. We also believe that the Finometer can be used to characterise the haemodynamic responses to different anaesthetic agents and procedures during the whole course of anaesthesia.

We also showed the potential benefits of using the Finometer during the whole period of anaesthesia in comparison with the current NIBP measurement protocols.

In conclusion, continuous noninvasive BP monitoring using the Finometer is acceptable in terms of BP monitoring. Potentially, it provides higher levels of patient safety during routine induction of anaesthesia than the conventional intermittent NIBP monitors, through better detection of BP aberrations. Further studies are encouraged to assess the feasibility of using continuous noninvasive BP monitoring during the entire surgical procedure.

6 A service evaluation of maintenance haemodialysis involving an assessment of the adequacy of the currently used intermittent noninvasive blood pressure (NIBP) devices in detecting BP aberrations

6.1 Introduction

Patient safety has been an area of major concern to health care providers during the last 3 decades. Major advancements in quality assessment tools and protocols have been accomplished. Many health care areas have been successfully assessed, and subsequently, measures to enhance the level of patient safety have been adopted.[197] During maintenance haemodialysis, where a large volume of fluids (2-4 litres) is removed from the circulation over a period of 3-4 hours, putting into consideration that the blood volume of a patient on haemodialysis is approximately 4.5 litres, of which the plasma volume contributes to almost 3 litres. Therefore, it would not be surprising if haemodynamic instability occurred during haemodialysis, especially that patients on chronic haemodialysis are known to have a variety of co-morbid conditions that may affect the integrity of their regulating cardiovascular responses to haemodialysis induced hypovolaemia. However, traditional intermittent monitoring of blood pressure in dialysis units does not reflect the need for enhanced haemodynamic monitoring which these patients would require.

Ideally, maintenance haemodialysis would be best monitored haemodynamically on continuous basis using an intra-arterial catheter, but due to its invasive nature and the risk of complications, its routine use in chronic haemodialysis patients is not justified. Maintenance haemodialysis is conventionally monitored by the intermittent NIBP devices; a predialysis and a post-dialysis reading are usually taken. Extra NIBP readings are taken whenever the patient experiences symptoms suggestive of hypotension, such as unexplained anxiety, headache, nausea, vomiting and muscular cramps.

6.2 Aim

Considering recent evidence suggesting that Intradialytic BP aberrations are associated with a poor patient outcome, we conducted this service evaluation and used continuous noninvasive haemodynamic monitoring by the Finometer, to assess the severity of both, intradialytic hypotension and intradialytic hypertension during maintenance haemodialysis. We have specifically chosen the procedure of maintenance haemodialysis as we anticipated major haemodynamic changes to occur during its course. Explanations for these anticipated haemodynamic changes are discussed in the previous section.

We assessed the Finometer's feasibility in terms of BP monitoring during maintenance haemodialysis, by comparing its accuracy and success rate with the NIBP devices that are being used conventionally.

Our main objective in this service evaluation was to assess the adequacy of the currently employed NIBP monitoring protocols in detecting BP aberrations and thus the level of patient safety they provide during maintenance haemodialysis.

To evaluate this, we followed a 3 step analysis protocol:

- *Step 1:* We compared the blood pressure measurements simultaneously obtained by the Finometer and the NIBP during maintenance haemodialysis
- *Step 2:* We characterised the haemodynamic changes occurring during maintenance haemodialysis as assessed by the Finometer
- *Step 3:* We evaluated the ability of the intermittent NIBP monitors to instantly detect maximum changes in BP as they occur in comparison with the Finometer

6.3 Patients and methods

6.3.1 Patients

This service evaluation was conducted in the Haemodialysis Unit of the Nottingham City Hospital NHS Trust, over a period of 4 months from September to December 2009. Twenty five patients undergoing maintenance haemodialysis were the subject of our service evaluation.

6.3.2 Methods

6.3.2.1 Patient recruitment

The Renal Unit at Nottingham City Hospital is composed of two haemodialysis units for stable patients. The Main Dialysis Unit and the Centenary Unit which can accommodate up to 26 and up to 14 patients per dialysis session respectively, with a total capacity of 40 patients per session.

Each of the haemodialysis units delivers 3 haemodialysis sessions per day, six days a week. The first session starts at 7:00 am and ends at 11:00 am, the second session starts at 12:00 pm and ends at 4:00 pm and the third session starts at 6:00 pm and ends at 10:00 pm. Chronic haemodialysis patients typically attend 3 evenly spaced haemodialysis sessions per week, for example on Monday, Wednesday and Friday. We did not approach unstable patients, who were dialysed in a third unit called the Lamley unit.

A total of 33 stable patients undergoing maintenance haemodialysis were approached. Patient information leaflets were handed out to patients 2-3 days prior to the haemodialysis session that was to be evaluated. The service evaluation was fully explained in terms of the purpose behind conducting it. We briefly described the Finometer and how it works. We also gave emphasis to the fact that there was no obligation to taking part and that the service evaluation would not interfere with the treatment received in any way and that they can opt out of the evaluation at any time without that affecting their standard care in any means.

We also explained that their personal details will be kept confidential and that this service evaluation is a one off event that takes place during one haemodialysis session only. There was no bias in selecting patients; any patient undergoing maintenance haemodialysis regardless of age or gender was recruited. A verbal approval from the patient for taking part in the service evaluation was ensured. The patient was monitored with Finometer if he / she agreed.

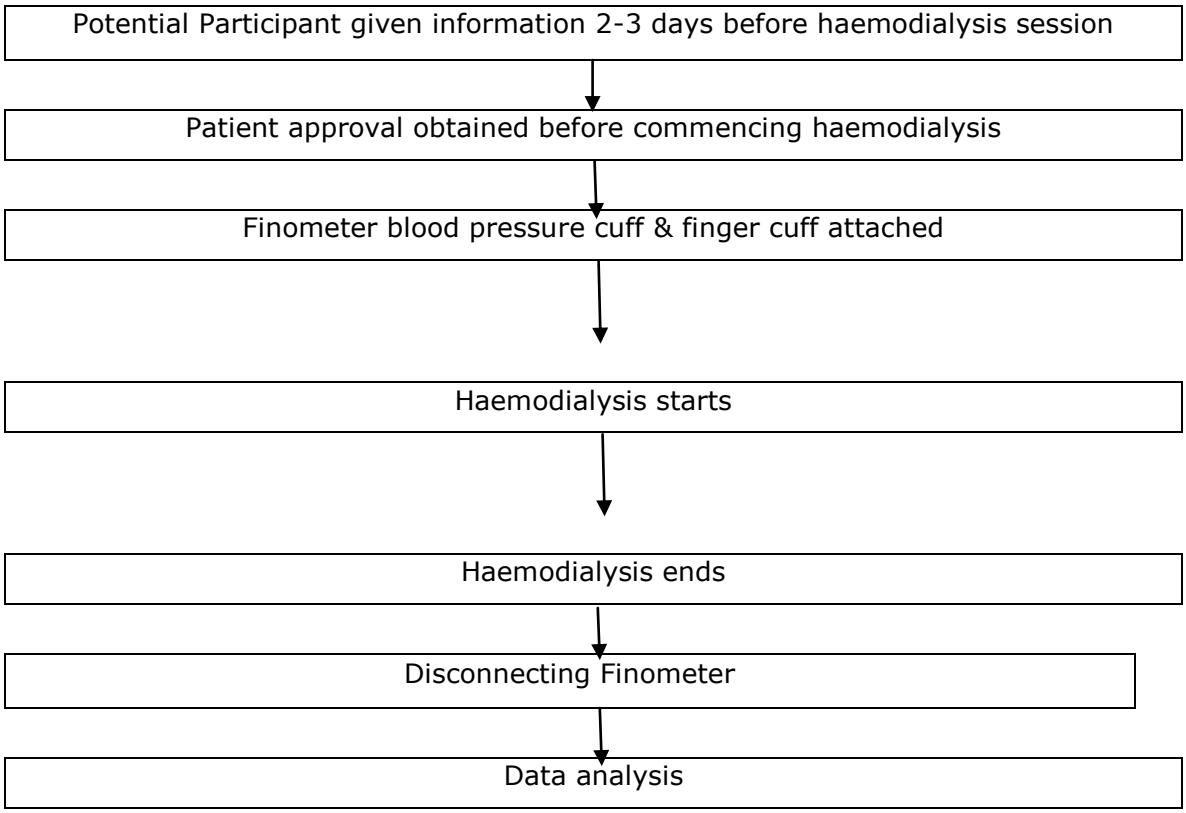
6.3.2.2 Data collection

Data was gathered from the patient, the patient's hospital file, the renal unit computer record system (RS 6000 and NOTIS systems), the NIBP monitor, the Finometer and from the attending staff. The data collected included the following:

- Demographic data (age, gender, height, weight and vintage)
- Co-morbidities
- Prescribed medications
- Dialysis related technical information (Interdialytic weight gain, residual urine, fluid to be removed, pump speed and type of vascular access)
- Renal related medical history (duration on haemodialysis and duration on renal replacement therapy)
- Full record of the NIBP measurements predialysis and post-dialysis
- Finometer data

6.3.2.3 Methodology protocol

Flow chart



Haemodialysis was delivered either through an arterio-venous (AV) Fistula or a central line. In patients with AV fistulae, the Finometer was applied to the non-access arm, to not interfere with the dialysis procedure and also due to the fact that the normal haemodynamic properties of the fistula arm would have been altered. In patients with central lines, the use of either arm was considered acceptable, thus, we applied the Finometer to the arm opposite to that which was chosen by the attending staff for NIBP measurements.

It needs to be mentioned that simultaneous Finometer and NIBP measurements from the same arm are not always successful, as the NIBP measurements will completely block the arterial supply of the arm, so the Finometer may stop working. An appropriately sized finger cuff was applied to the index or middle finger and the Finometer was started. Cross over between the 2 fingers during haemodialysis was done whenever the patient felt uncomfortable because of the finger cuff. The procedure of operating the Finometer is discussed in details in section 4.1.1.1. Concerning patients with AV fistulae, NIBP measurements were strictly taken by the attending staff from the non-access arm, which is the same arm used by the Finometer. Therefore, we had to stop the Finometer after it has taken initial measurements to let the attending staff obtain a predialysis NIBP reading, then we re-applied the Finometer once the NIBP reading was taken. This has caused a delay of approximately 5 minutes between the predialysis Finometer reading and its corresponding predialysis NIBP reading. However in patients with central line access, we were able to obtain an NIBP reading from one arm and a simultaneous reading from the other arm. Finometer was then kept running throughout the entire haemodialysis session. Also, at the end of the dialysis session, the Finometer had to be stopped in patients with AV fistulae as they were requested to apply pressure on the site of haemodialysis using the arm that was used by the Finometer to control any bleeding. As soon as the bleeding was controlled the Finometer was re-attached and kept operating for 5 minutes to bring a post dialysis reading. Once the post dialysis Finometer reading was obtained, the Finometer was stopped and a post dialysis NIBP measurement was obtained from the Finometer's arm.
On the other hand, in patients with central line access the Finometer was kept operating throughout the entire haemodialysis session, including the time when a post dialysis NIBP measurement was taken by the attending staff from the other arm.

All actions taken during the procedure of maintenance haemodialysis were noted in the patient's data sheets along with their times, which were obtained strictly from the Finometer's clock for the purpose of standardisation. These actions included the start and the end of the procedure, and the NIBP measurements. In patients with central line vascular access, we pressed the Finometer's [mark] button whenever an NIBP measurement was taken simultaneously whilst the Finometer was operating. The mark option of the Finometer is discussed in section 5.3.2.3.

6.3.2.4 Data management

Using BeatScope version 1.1a software (product of Finapres Medical Systems BV, Arnhem) data from the Finometer was retrieved on a computer in Microsoft excel format, and beat-by-beat haemodynamic data obtained from the Finometer was further averaged over 10 second intervals. The procedure of data retrieval from the Finometer is discussed in details in section 4.1.1.2.

We applied fairly similar methods to those previously used in the service evaluation of induction of anaesthesia to analyse the Finometer's data, but with a few alterations in both the figures and the techniques (section 5.3.2.4).

In brief, we identified the haemodynamic readings that corresponded to different time points during the procedure of haemodialysis on the Finometer's raw data excel spreadsheets. These were the haemodynamic readings at the times of the start and readings at 0.5 hours intervals from the start till the end of haemodialysis, readings that correspond to the NIBP measurements taken, the highest and the lowest BP readings, and a few conditional criteria involving time durations when BP values were at predetermined levels (figure 19).

In patients with central line vascular access, we were able to identify and highlight the Finometer's readings that simultaneously corresponded to the NIBP readings by using the "[Fin] Event: Mark" labels that were displayed on the Finometer's raw data excel spreadsheet. However, in patients with AV fistulae, we simply highlighted the readings that were closest in timing to the NIBP's. These highlighted readings were accordingly labeled as NIBP1 (pre dialysis reading) and NIBP2 (post dialysis reading).

Using a different colour, we then highlighted the start and the end of the procedure, and rows of haemodynamic variables corresponding to 0.5 hour, 1 hour, 1.5 hours, 2 hours, 2.5 hours, 3 hours, 3.5 hours and 4 hours from the start to the end of the haemodialysis procedure.

We then used the "conditional formatting" tool that is available in Microsoft excel to identify the highest and lowest SBP, DBP and MBP values. Both, the row that represented the highest BP value and the row that represented the lowest BP readings were chosen on the basis of, if two out of the three readings of SBP, DBP and MBP coincided in being the highest and the lowest readings respectively. On a few occasions when those criteria were not met, we simply chose the row that involved the highest BP and the lowest BP reading according to the highest SBP and the lowest SBP values respectively. The chosen highest and lowest BP rows were then highlighted using a third colour.

Lastly, we averaged the haemodynamic data in this service evaluation over 10 seconds rather than on beat-by-beat basis, which enabled us to make use of the "countif" tool of Microsoft excel. The "countif" tool counts the cells in a certain variable column that contain a pre set rule, and since each cell in our Finometer's raw data sheet represented 10 seconds, all we had to do was multiply the number of cells that were calculated by the "countif" tool by 10 which gave the total duration spent according to the pre set rule in seconds, and by dividing this number by 60 it was converted into minutes.

The procedure we followed to identify the amount of time spent during each preset definition of hypertension and hypotension using the "countif" tool was as follows: We identified the absolute values of the 30% increase and the 30% decrease of the SBP, DBP and MBP from their baseline values per patient. These values along with their corresponding rules (e.g. countif the cells that contain readings higher than 180) were entered separately to the "countif" tool per patient's raw data Finometer excel sheet. The "countif" tool then counted all the cells that met the entered rule. This has allowed us to calculate the time spent during each of the specified hypotension and hypertension definitions. We also used the "countif" tool to calculate the duration of time spent when the SBP readings were lower than 90 mmHg, and higher than both, 160 mmHg and 180 mmHg.
All the collected data including the data that was highlighted on the Finometer's data spreadsheets were transferred to 3 master excel spreadsheets, each designed to tackle a different question. These 3 spreadsheets were quite similar to those that were used in the service evaluation of induction of anaesthesia (sections 5.3.2.4.1, 5.3.2.4.2 and 5.3.2.4.3).

The following 3 sections include descriptions of the 3 master spreadsheets that were used in this service evaluation:

6.3.2.4.1 Master spreadsheet 1 - Comparing blood pressure recordings obtained by the Finometer and the NIBP device

Master spreadsheet 1 was divided into 2 sections: The first section included 2 groups of columns (NIBP1 and NIBP2). Each group of columns was further divided into 8 sub-columns, which were labeled as NIBP's HR, SBP, DBP and MBP, and Finometer's HR, SBP, DBP and MBP. Two sets of paired Finometer and NIBP readings that were taken from the 25 patients at the times of pre dialysis and post dialysis were transferred from both the patient's data sheets and the Finometer's raw data spreadsheets to their corresponding sites in master spreadsheet 1.

The second section was designed to include other sets of data, each in a designated column. These data included the age, gender, height, weight, smoking, Haemoglobin (Hb) level, DM, HTN, CAD, COPD, and prescribed medications (statins, angiotensin converting enzyme inhibitors (ACEi) / angiotensin receptor blockers (ARB), beta blockers, calcium channel blockers, diuretics, insulin, oral hypoglycaemic drugs, anti-ischaemic heart disease drugs, steroids, midodrine (vasoconstrictor) and others). We also included columns for haemodialysis related issues including, autonomic neuropathy, vascular calcification, hyperparathyroidism, Interdialytic weight gain, residual urine, amount of fluid to be removed, vascular access (AV fistula and central line), pump speed, duration on renal replacement therapy (RRT) and duration on haemodialysis.

Categorical data was scored by either "0" or "1" according to the absence or the presence of the parameter respectively. An illustrative example is given in section 5.3.2.4.1.

6.3.2.4.2 Master spreadsheet 2 - Gross haemodynamic effects of maintenance haemodialysis as detected by the Finometer

Master spreadsheet 2 was divided into 10 groups of columns according to their corresponding time intervals during the course of haemodialysis, a pre dialysis reading, readings at 0.5 hour, 1 hour, 1.5 hours, 2 hours, 2.5 hours, 3 hours, 3.5 hours and 4 hours, and a post dialysis reading. As discussed earlier in section 5.3.2.4.2, each group of columns was formed of 7 sub-columns for SBP, DBP, MBP, HR, SV, CO and TPR and the corresponding data was transferred to these columns from the Finometer's raw data spreadsheets.

6.3.2.4.3 Master spreadsheet 3 - Time and magnitude of haemodynamic changes as detected by the Finometer

The haemodialysis service evaluation master spreadsheet 3 was identical to master spreadsheet 3 of the service evaluation of induction of anaesthesia. Master spreadsheet 3 is discussed in details in section 5.3.2.4.3.

Having completed the 3 master spreadsheets, our data were ready for further analysis. Analysis of the data will be discussed in details later, each in its relevant section.

6.4 Results: Cohort analysis

We approached 33 patients undergoing maintenance haemodialysis; 3 patients refused to take part in the evaluation due to inconvenience of extra monitoring; 1 patient was unable to give informed consent; measurements were not successful in 4 patients due to inability of the Finometer to detect a finger pulse waveform; successful Finometer measurements were obtained in 25 patients.

The characteristics of our patients are displayed in table 21.

Table 21. Cohort characteristics (n =25)

	Mean (SD) or percentage
Age (years)	61 (18.6)
Gender	
○ Male	48%
○ Female	52%
Height (cm)	168 (12)
Weight (kg)	80 (28)
Hb (g/dL)	11 (1.6)
Smokers	16%
DM	24%
HTN	48%
CAD	36%
COPD	8%
Autonomic neuropathy	8%
Hyperparathyroidism	68%
Dialysis related information	
○ Interdialytic weight gain (kg)	1.9 (1.1)
○ Residual urine (ml)	519 (725)
○ Duration on RRT (years)	5.5 (7.8)
○ Duration on HD (years)	2.4 (3.6)
Vascular access	
○ AV fistula	76%
○ Central line	24%
Prescribed medications	
○ Statins	68%
○ Steroids	16%
○ Anti-ischaemic drugs	60%
○ ACEi / ARB	44%
○ Calcium channel blockers	36%
○ Beta blockers	32%
○ Insulin	12%
○ Oral hypoglycaemic drugs	16%

6.5 Results: Comparison of blood pressure measurements using NIBP and the Finometer during maintenance haemodialysis

This section presents an evaluation of the feasibility of using the Finometer for BP monitoring during maintenance haemodialysis, by assessing its success rate in providing BP monitoring, and by comparing its BP readings to those obtained by the NIBP device during maintenance haemodialysis sessions for accuracy.

6.5.1 Data handling and statistics

The haemodynamic data that we needed for comparing the NIBP and the Finometer was obtained from master spreadsheet 1, which was discussed in details in section 6.3.2.4.1. Statistical analysis of the data was then carried out using the Prism software.

Firstly, we used paired t test to compare the corresponding measurements of both the NIBP and the Finometer in each of the 25 predialysis measurements and the 25 post dialysis measurements, which were labeled as NIBP1 and NIBP2 respectively in master spreadsheet 1.

Then we collectively transferred all the 50 pre and post dialysis paired sets of NIBP's and Finometer's SBP, DBP and MBP readings from master spreadsheet 1 to the Prism software. Using the Prism software, we applied the correlation and linear regression methods to each of the 50 pairs of NIBP's and Finometer's SBP, DBP and MBP. The correlation and linear regression methods are discussed in details in section 4.2.5.

We then used the Bland and Altman technique to assess for the agreement between each of the NIBP's and the Finometer's 50 paired sets of SBP, DBP and MBP readings. As explained earlier, a naive assessment was done. The Bland and Altman technique is discussed in details in section 4.2.4.

Finally, we applied both, the BHS and the AAMI criteria for accuracy of novel BP devices to our 50 paired sets of NIBP's and Finometer's SBP and DBP readings that were obtained from master spreadsheet 1, as shown in table 1. The BHS and the AAMI criteria are discussed in details in sections 4.2.6 and 4.2.7 respectively, and the procedure we followed to apply the BHS criteria is discussed in section 5.5.1.

6.5.2 Results

Out of the 29 Finometer monitoring attempts, 25 were successful, equating to an 86% success rate.

6.5.2.1 Table comparing the pre and post dialysis BP as measured by the NIBP vs. Finometer

Using paired t test, we compared each of the NIBP's and Finometer's 25 pre dialysis SBP, DBP and MBP measurements, and 25 post-dialysis SBP, DBP and MBP measurements, as shown in table 22 . No statistical significant differences were shown between any of the SBP, DBP and MBP measurements taken by the two devices, neither in the predialysis nor in the post dialysis period.

Table 22. Comparison between the NIBP's and the Finometer's pre dialysis and post dialysis BP readings

	Pre-dialysis			Post-dialysis		
	NIBP	Finometer	*P value*	NIBP	Finometer	*P value*
SBP (mmHg)	141 (25)	142 (24)	ns	130 (24)	128 (24)	ns
DBP (mmHg)	77 (13)	76 (15)	ns	74 (11)	71 (12)	ns
MBP (mmHg)	97 (15)	99 (15)	ns	93 (14)	92 (14)	ns

6.5.2.2 Correlation, and Bland and Altman analysis of the BP measurements of NIBP vs. Finometer

The total 50 pairs of pre and post dialysis NIBP's and Finometer's SBP, DBP and MBP measurements that were obtained from the 25 patients were compared using correlation and linear regression, along with the Bland and Altman method. Our results showed a significant correlation between the measurements of the NIBP and the Finometer. The r^2 and p values for the SBP, DBP and MBP were $r^2 = 0.64$ and $P<0.0001$, $r^2 = 0.35$ and $P<0.0001$, and $r^2 = 0.5$ and $P<0.0001$ respectively.
As mentioned earlier in section 4.2.4, the Bland and Altman technique assesses the limits of agreement of two devices, by plotting the differences against the averages of the readings simultaneously obtained from both devices on a graph. From this graph, the bias and the 95% limits of agreement are calculated. We applied the Bland and Altman technique and assessed the limits of agreements between the NIBP and the Finometer. The results showed that the bias for SBP, DBP and MBP was 0.6, 1.44 and -1.12 mmHg respectively and the 95% limits of agreement (mean difference ± 1.96 SD) for the SBP, DBP and MBP were 31 to -30, 24 to -22 mmHg and 21 to -23 respectively. The line of goodness of fit showed that the Finometer and the NIBP were equal in terms of the SBP, DBP and MBP. See figures 32, 33 and 34.

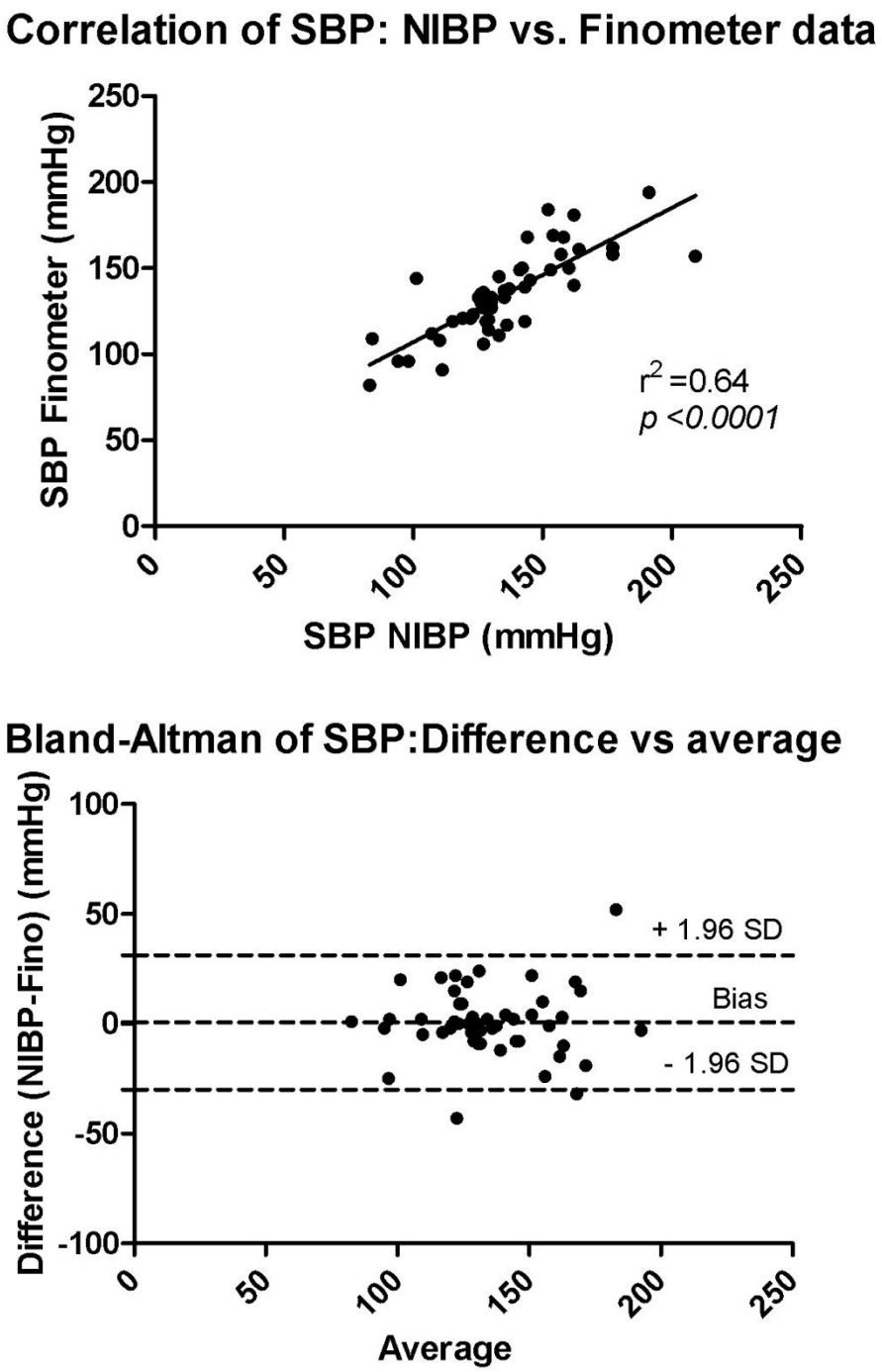


Figure 32. Pooled data for the SBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages.

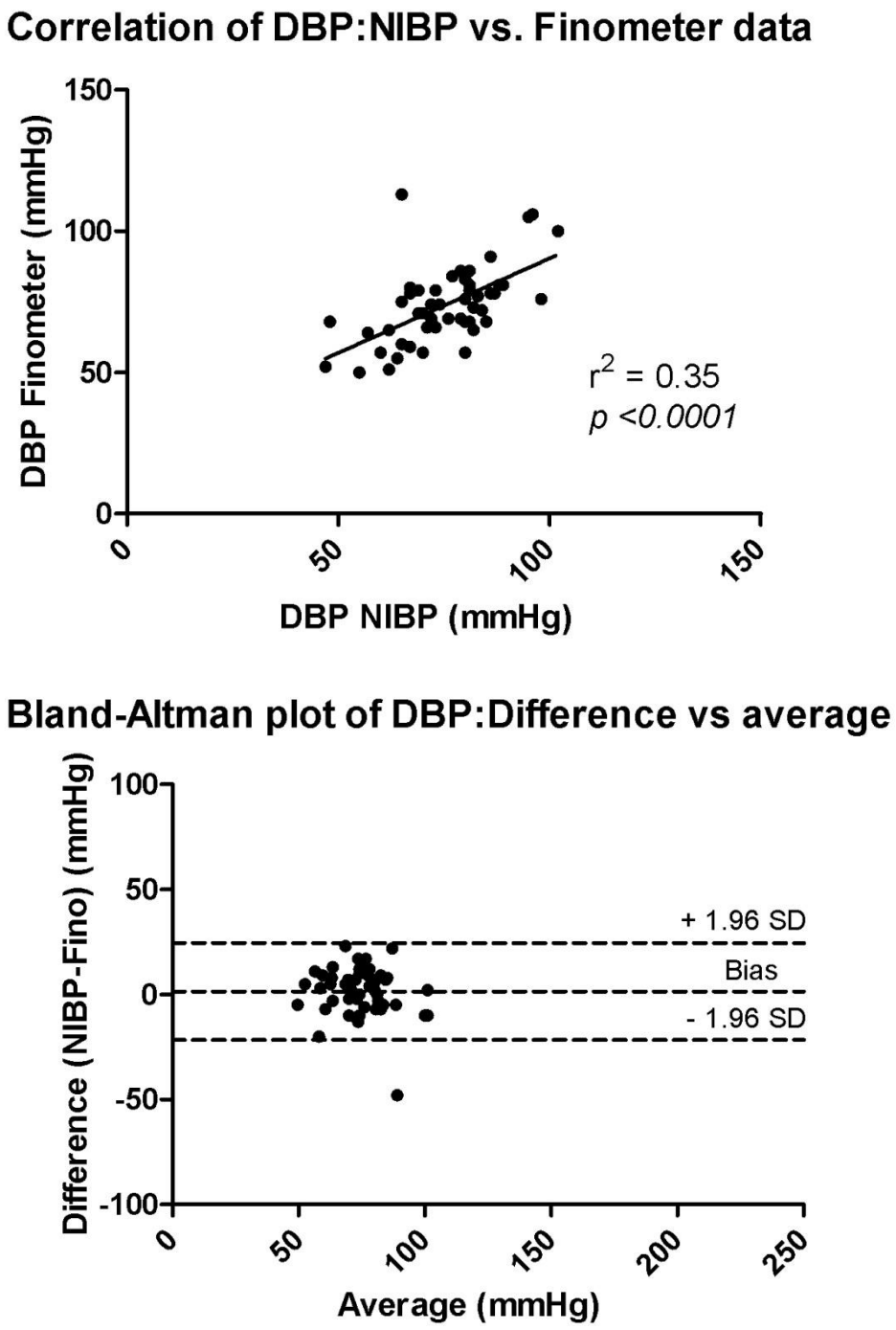


Figure 33. Pooled data for the DBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages.

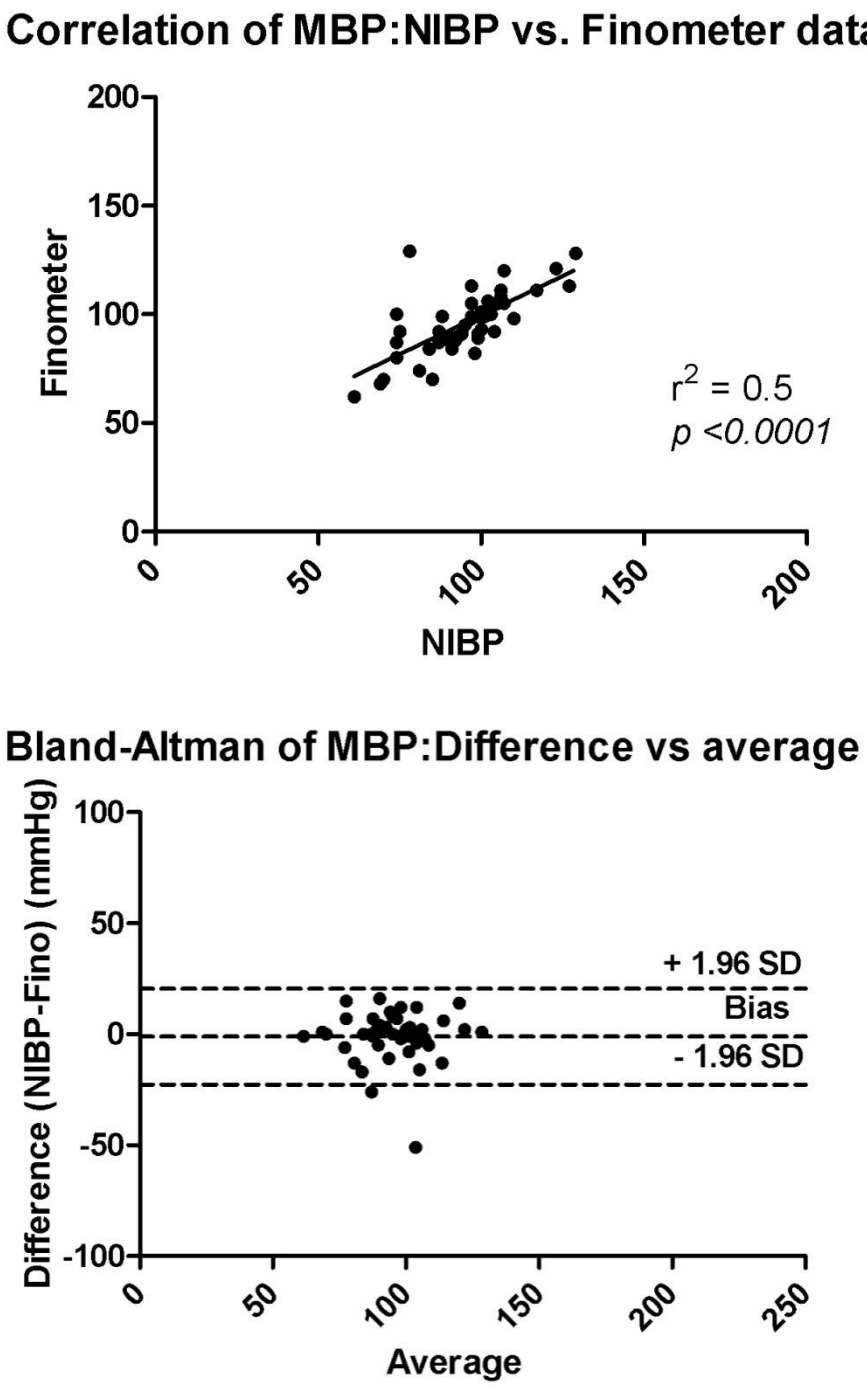


Figure 34. Pooled data for the MBP measurements of NIBP vs. Finometer. Upper panel: Correlation and linear regression of pooled data for NIBP against Finometer. Lower panel: Bland-Altman plot of the differences between NIBP & Finometer against their averages.

6.5.2.3 The BHS validation

As mentioned earlier in section 4.2.6, the British Hypertension Society criteria for accuracy of BP machines are met when a BP machine achieves grade A/B when compared to the mercury device according to the calculations displayed in table 1. We applied the BHS criteria to compare each of the 50 SBP and DBP readings obtained from the Finometer with the NIBP device rather than the mercury device. Our results showed that the Finometer failed to meet the BHS criteria of accuracy of BP devices as illustrated in table 23.

Table 23. Assessment of the accuracy of the Finometer by applying the BHS criteria

Absolute difference between NIBP and Finometer						
	≤ 5 mmHg		≤ 10 mmHg		≤ 15 mmHg	
Cumulative	SBP %	DBP%	SBP %	DBP%	SBP %	DBP%
percentages	48	36	66	74	74	88
Grade	C	D	C	C	D	D

6.5.2.4 The AAMI validation

As mentioned earlier in section 4.2.7, The AAMI criteria for accuracy of BP machines are met when the mean difference between the novel device to be assessed for accuracy and the mercury device is less than 5 mmHg, with a standard deviation of less than 8 mmHg for both the SBP and the DBP.

We applied the AAMI criteria and used the NIBP as the standard device to validate against instead of the mercury device, to all the 50 pairs of NIBP and Finometer SBP and DBP sets of data. Our results showed that the Finometer failed to meet the AAMI criteria for accuracy of BP devices. The mean difference (standard deviation) between the Finometer and the NIBP was 0.62 (15.6) mmHg for SBP, and 1.44 (11.74) mmHg for DBP.

6.5.3 Discussion

In our service evaluation we have assessed the feasibility of using the Finometer in a cohort of patients on chronic haemodialysis, who are known to have a variety of co-morbid conditions.

Firstly, knowing that patients undergoing chronic haemodialysis have a high incidence of vascular abnormalities, which are known to impede the ability of the Finometer to detect a pulse waveform from the finger, we evaluated the success rate of the Finometer in providing haemodynamic monitoring. The Finometer delivered successful haemodynamic monitoring in 86% of the total number of patients that the Finometer was attempted upon.

Secondly, we assessed for the accuracy of the Finometer in terms of BP monitoring by comparing its readings to those obtained by the conventional NIBP devices, and it has shown an acceptable degree of accuracy. No significant differences between the two devices in terms of both, the pre dialysis and post dialysis SBP, DBP and MBP readings have been shown. Also, using correlation and linear regression techniques, a significant correlation was shown between the NIBP and the Finometer, the r^2 and p values for the SBP, DBP and MBP were $r^2 = 0.64$ and $P<0.0001$, $r^2 = 0.35$ and $P<0.0001$, and $r^2 = 0.5$ and $P<0.0001$ respectively. Bland and Altman analysis for assessment of the limit of agreement between the NIBP and the Finometer in our data, showed that the bias for SBP, DBP and MBP was -0.82, -3.83 and -3.12 mmHg respectively, and the 95% limits of agreement (mean difference ± 1.96 SD) for the SBP, DBP and MBP were 31 to -30, 24 to -22 and 21 to -23 mmHg respectively, as described earlier in section 5.5.3, these results indicate an acceptable agreement between both devices. Also, the line of goodness of fit showed that the Finometer and the NIBP were equal in terms of the SBP, DBP and MBP

However, the Finometer failed to meet both, the BHS and the AAMI criteria for accuracy of BP devices in our evaluation. A possible explanation for this is that we performed the validation on a much lesser number of patients than that recommended by the AAMI and BHS criteria (85 patients). Another explanation which was mentioned earlier in section 6.3.2.3 is that there was a time lag between both the predialysis and post dialysis Finometer readings and their corresponding NIBP readings in the 19 patients with AV fistulae, as we were not able to use the vascular access arm in these patients for BP monitoring by either device.
There were agreements with our findings of accuracy of the Finometer in a number of studies, as discussed earlier in section 5.5.3.[8, 143, 144]
We have started collecting further data after being granted ethics approval for resuming our work and running an observational study on a bigger scale.

6.5.4 Conclusion

The Finometer is a feasible option for BP monitoring in a cohort of patients on regular haemodialysis. Further studies are warranted to explore this potential.

6.6 Results: Gross haemodynamic changes in response to maintenance haemodialysis as detected by the Finometer

This section presents an assessment of the gross haemodynamic changes that occur in response to maintenance haemodialysis.

6.6.1 Data handling and statistics

Statistical analysis was carried out using the Prism software, and all the data we needed for analysis in this section was obtained from master spreadsheet 2, which is discussed in details in section 6.3.2.4.2.

We firstly performed 7 comparisons between the pre dialysis and post dialysis SBP, DBP, MBP, HR, SV, CO and TPR variables that were retrieved from master spreadsheet 2 using a paired t test.

Then, to collectively assess the gross haemodynamic changes that occurred in our patients during haemodialysis, we transferred the collective haemodynamic data of SBP, DBP, MBP, HR, SV, CO and TPR at baseline, 0.5 hr, 1 hr, 1.5 hr, 2 hr, 2.5 hr, 3 hr, 3.5 hr, 4 hr and post dialysis from master spreadsheet 2 to the Prism software, and applied ANOVA and Tukey's post hoc test to the intervallic data of each variable. ANOVA and Tukey's post hoc test is discussed in details in section 4.2.2.

Furthermore, we assessed for inter-patient variability in terms of haemodynamic responses to haemodialysis. In order to do that, we obtained the intervallic SBP, DBP, MBP, HR, SV, CO and TPR data at baseline, 0.5 hr, 1 hr, 1.5 hr, 2 hr, 2.5 hr, 3 hr, 3.5 hr, 4 hr and post dialysis for each patient separately from master spreadsheet 2, and we plotted 7 graphs for each of the haemodynamic variables (SBP, DBP, MBP, HR, SV, CO and TPR). In each of the 7 graphs, 25 lines of intervallic data representing the 25 patients were plotted at baseline, 0.5 hr, 1 hr, 1.5 hr, 2 hr, 2.5 hr, 3 hr, 3.5 hr, 4 hr and post dialysis.

6.6.2 Results

6.6.2.1 Comparison between the Finometer's predialysis and post dialysis readings (n = 25)

Using a t test we compared the Finometer's 25 predialysis and 25 post dialysis values of each of the haemodynamic variables (SBP, DBP, MBP, SV, CO and TPR). A significant drop in the SBP, MBP, SV and CO along with a significant rise in the HR was shown upon completion of haemodialysis. TPR remained stable however (Table 24).

Table 24. Paired t test for all Finometer's haemodynamic variables pre and post dialysis (n = 25)

	Pre-dialysis	Post-dialysis	*P value*
SBP (mmHg)	142 (24)	128 (24)	0.0038*
DBP (mmHg)	76 (15)	71 (12)	0.1315
MBP (mmHg)	99 (15)	92 (14)	0.0390*
HR (bpm)	74 (11)	80 (13)	0.0033*
SV (ml)	91 (37)	76 (31)	0.0148*
CO (l/m)	6.6 (2.6)	6 (2.6)	< 0.0001*
TPR (MU)	1.303 (1.06)	1.178 (0.712)	0.6136

6.6.2.2 ANOVA and Tukey's post hoc test

ANOVA and Tukey's post hoc test was used to compare the values of each of the haemodynamic variables obtained by the Finometer (HR, SBP, DBP, MBP, SV, CO and TPR) at 0.5 hour time intervals, from the start till the end of the haemodialysis sessions. None of the variables has shown a significant change during the course of haemodialysis, as illustrated in table 25.

Table 25. Mean (SD) of haemodynamic variables during routine haemodialysis

Interval (min)	Baseline (n=25)	0.5 hr (n=24)	1.5 hr (n=24)	2.5 hr (n=23)	3.5 hr (n=21)	Post dialysis (n=25)	*P value*
HR (beats/m)	74 (11)	76 (11)	73 (11)	76 (12)	79 (14)	80 (13)	0.4567
SBP (mmHg)	142 (24)	140 (32)	130 (26)	125 (31)	128 (34)	128 (24)	0.2293
DBP (mmHg)	76 (15)	77 (17)	72 (15)	70 (15)	70 (14)	71 (12)	0.4238
MBP (mmHg)	99 (15)	99 (23)	93 (18)	91 (20)	91 (19)	92 (14)	0.3861
SV (ml)	91 (37)	81 (30)	77 (30)	76 (34)	72 (27)	76 (31)	0.714
CO (l/m)	6.6 (2.6)	6.0 (2.3)	5.6 (2.2)	5.6 (2.3)	5.5 (1.8)	6.0 (2.6)	0.8984
TPR (MU)	1.3 (1.06)	1.29 (0.81)	1.27 (0.64)	1.28 (0.74)	1.13 (0.33)	1.18 (0.71)	0.8804

6.6.2.3 Individual patient analysis of the haemodynamic response to haemodialysis

We further compared each of the haemodynamic variables (HR, SBP, DBP, MBP, SV, CO and TPR) in relation to time on individual patient basis by plotting a graph for each variable. Each graph was a plot of the values of one of the haemodynamic variables against the 0.5 hourly time intervals for the 25 patients.
Considerable inter-patient variability in terms of the magnitude and timing of all the haemodynamic variables' responses to haemodialysis was shown (figures 35 – 41).

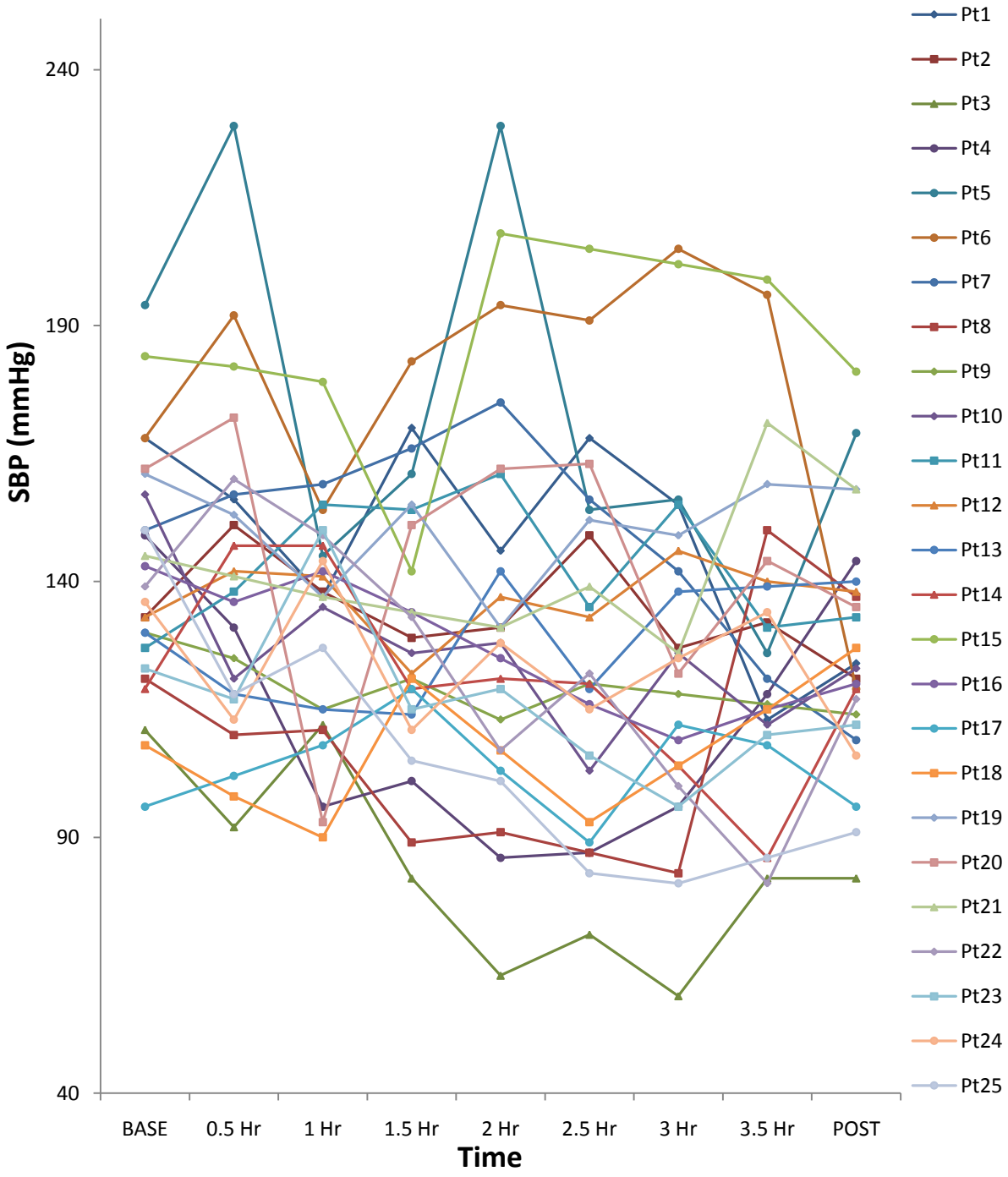


Figure 35. Graph showing the SBP values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer

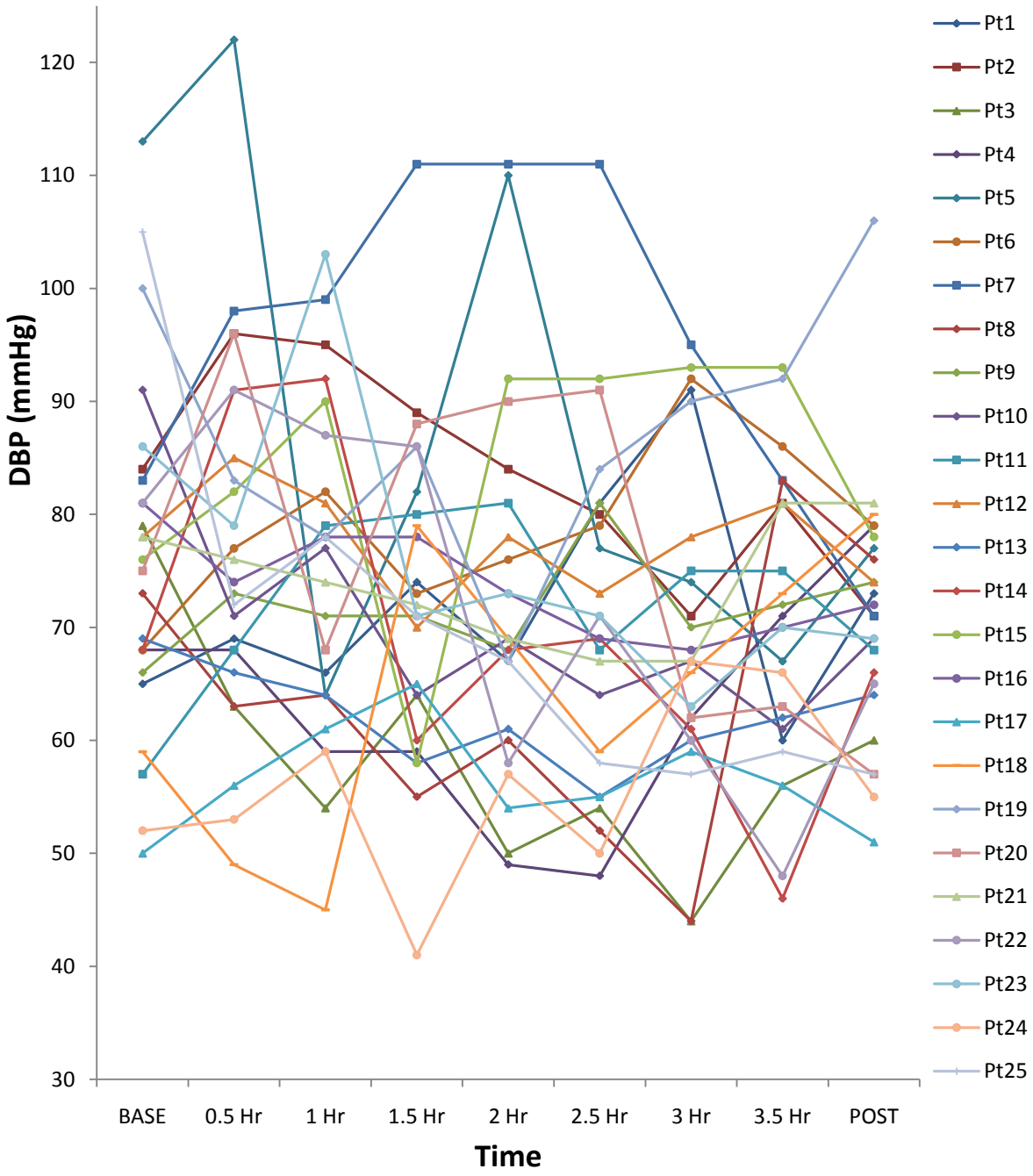


Figure 36. Graph showing the DBP values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer

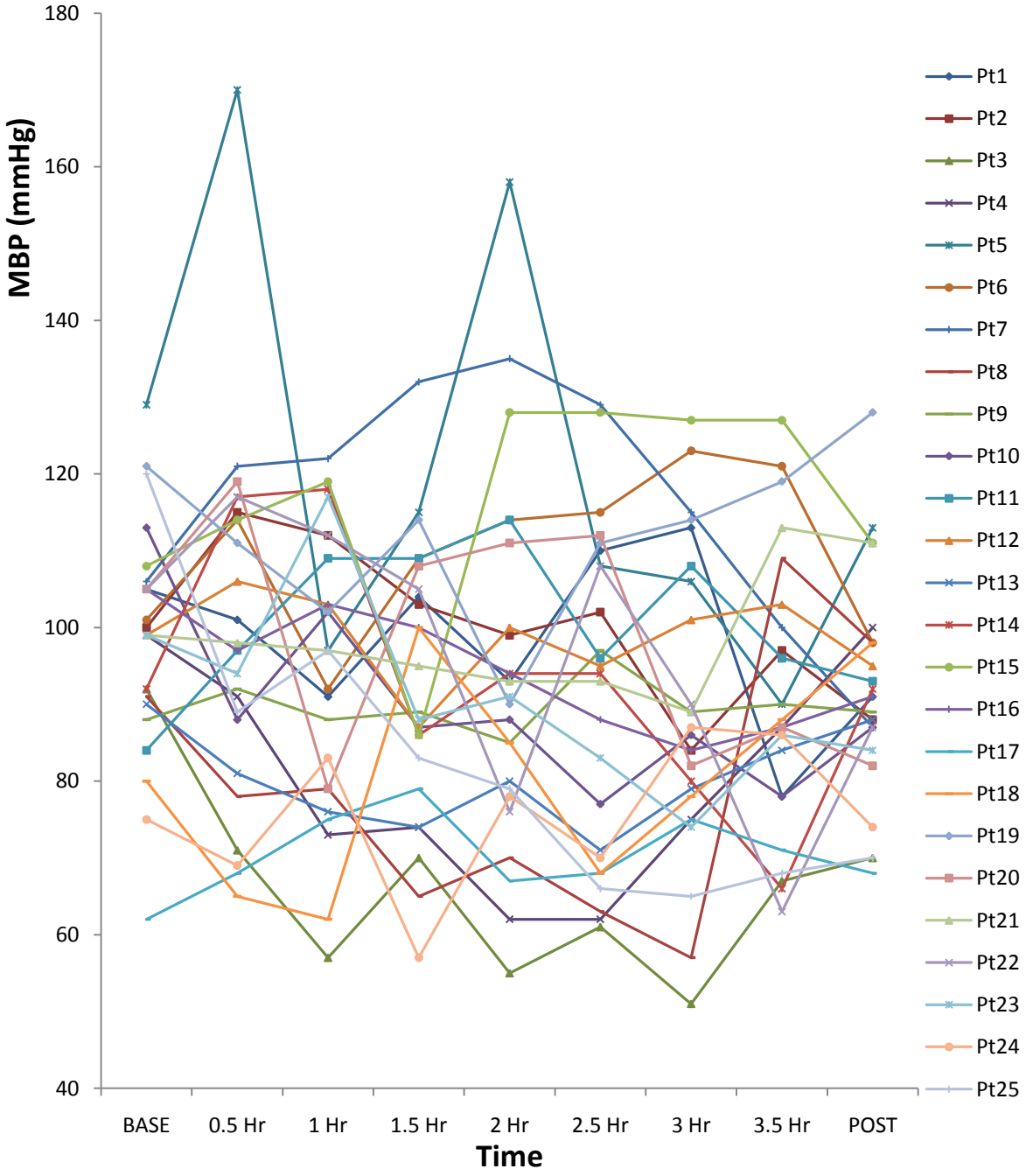


Figure 37. Graph showing the MBP values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer

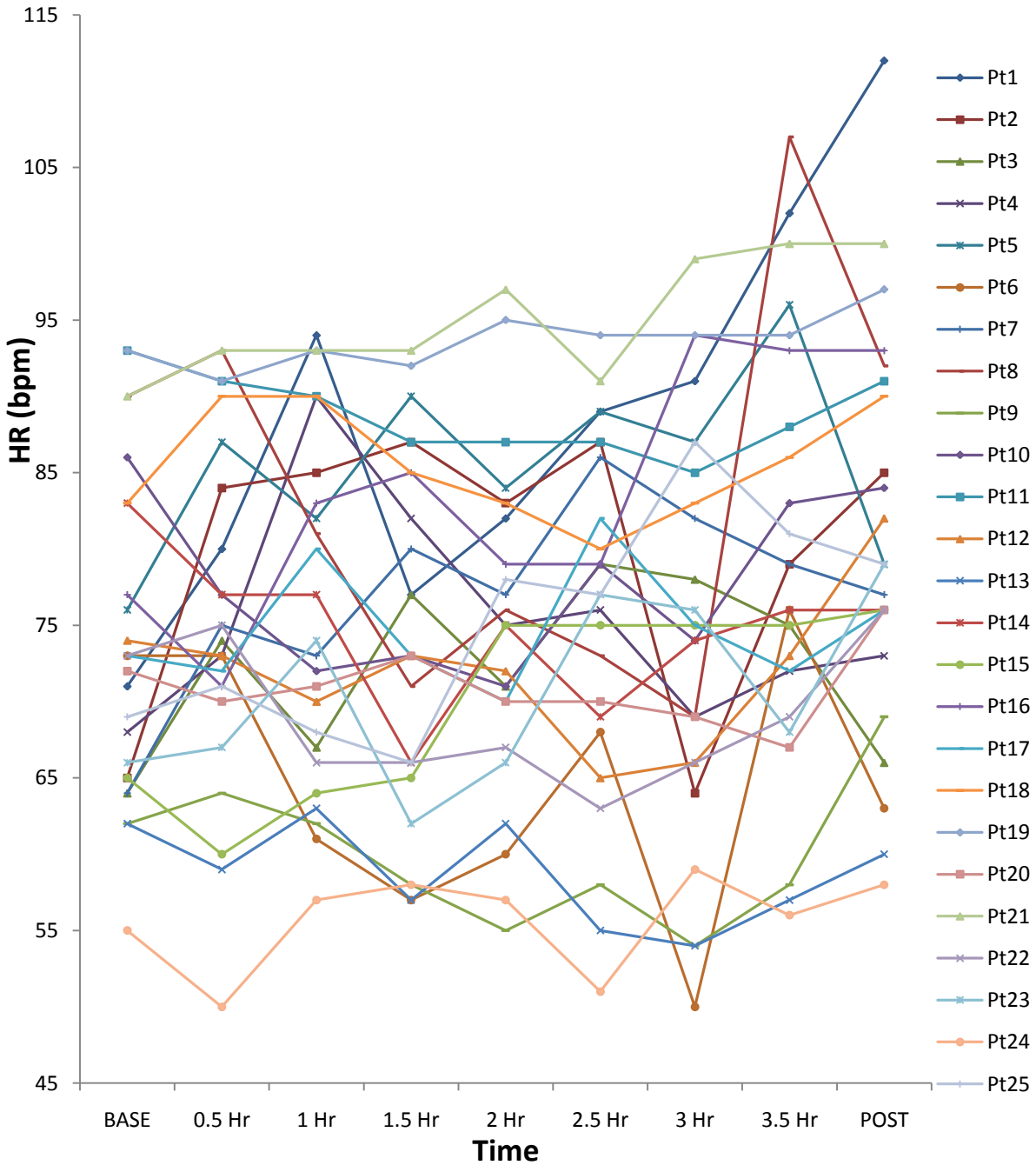


Figure 38. Graph showing the HR values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer

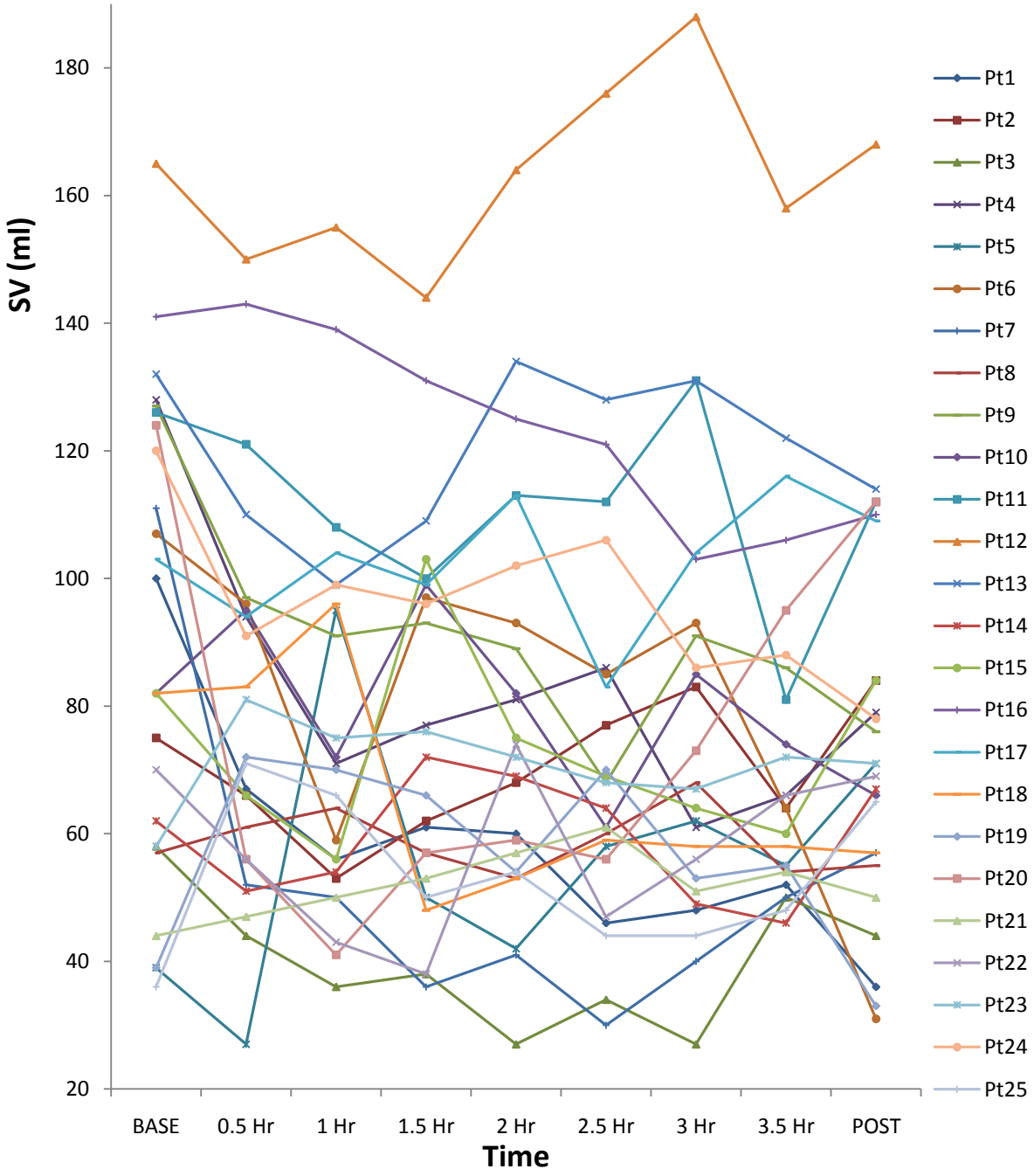


Figure 39. Graph showing the SV values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer

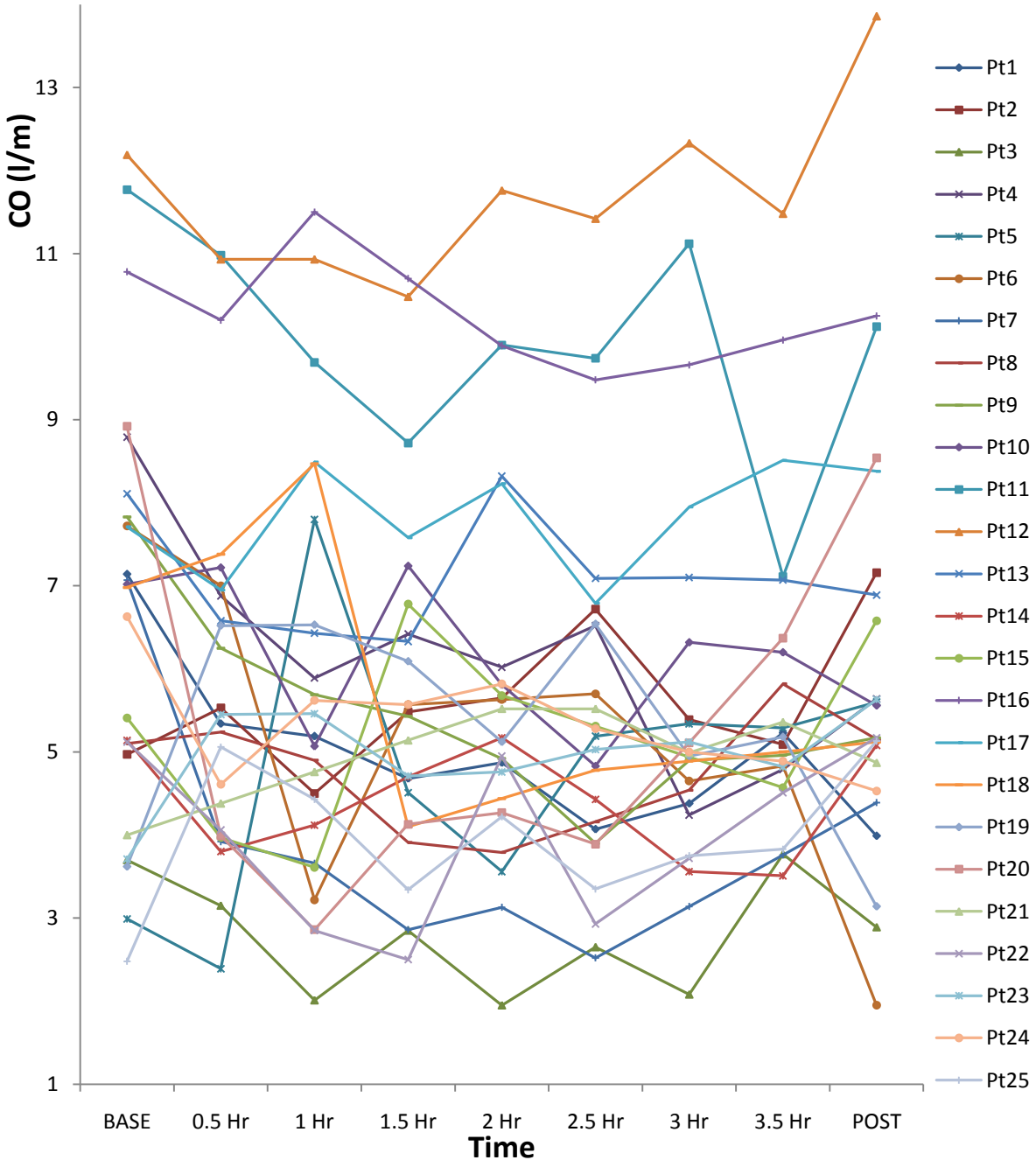


Figure 40. Graph showing the CO values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer

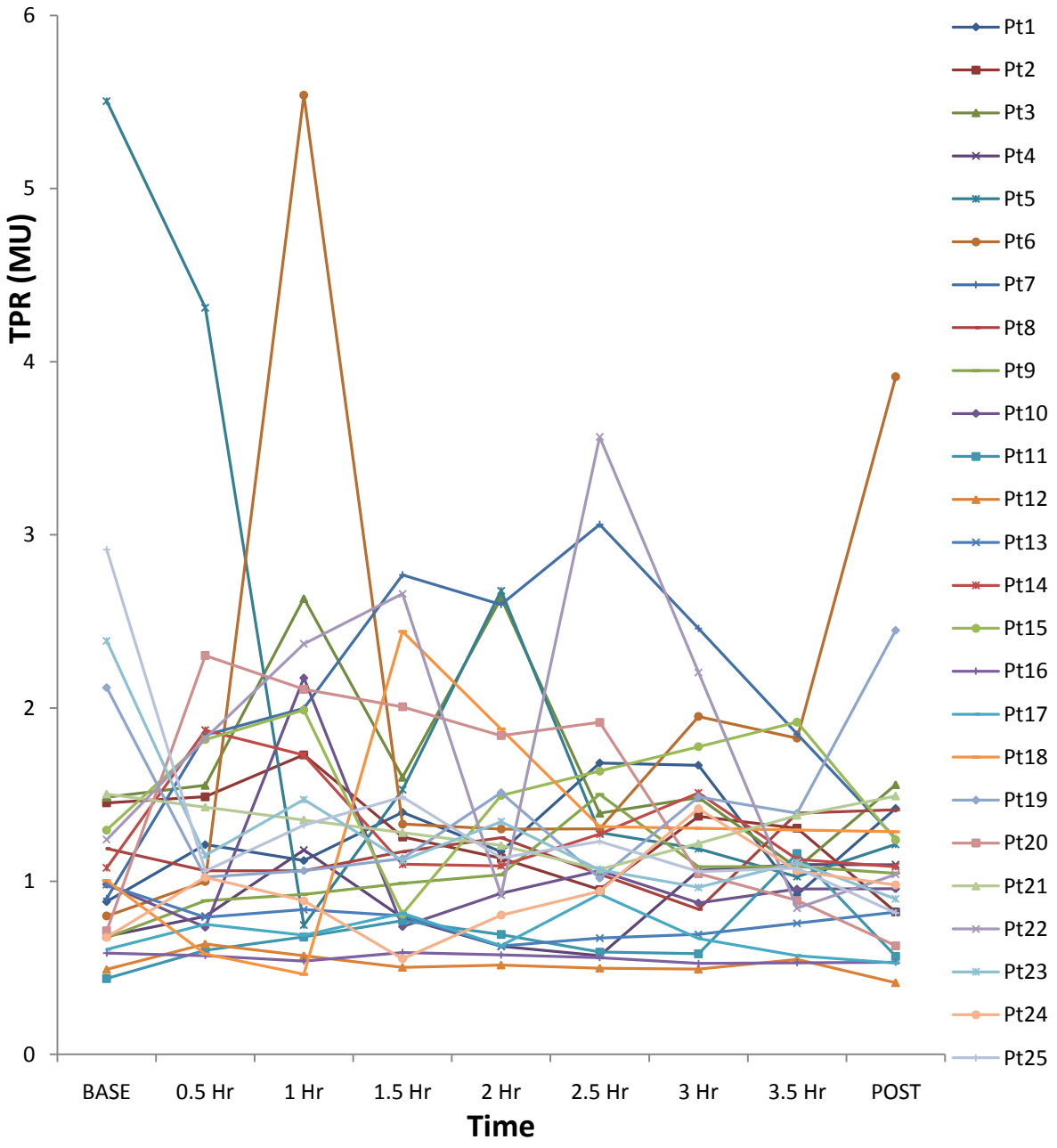


Figure 41. Graph showing the TPR values at 0.5 hourly intervals during the whole period of haemodialysis for the 25 patients as detected by the Finometer

6.6.3 Discussion

As mentioned earlier in section 2.2, haemodialysis involves the removal of large volumes of fluids from the circulation in a relatively short period of time. Normally, the compensatory cardiovascular response of the body to the haemodialysis induced hypovolaemia involves an increased plasma refilling rate (PRR) that occurs at capillary level in opposition to the ultrafiltration rate (UFR)[40], which keeps the blood volume constant. Also, in response to haemodialysis induced hypovolaemia, an increase in the venous tone and peripheral vascular resistance is encountered[38, 44], along with the activation of the sympathetic nervous system, which causes an initial increase followed by a decrease in the HR, and an increase in myocardial contractility.[49, 50] Patients on chronic haemodialysis are known to have an impaired capacity of the normal cardiovascular response to haemodialysis induced hypovolaemia.[39] This may be explained by the high incidence of co-morbid conditions amongst those patients. Also, they are usually prescribed medications, which may further limit the capacity of their compensatory haemodynamic responses to haemodialysis induced hypovolaemia.

Little is known about the gross haemodynamic response to routine haemodialysis, as this needs continuous haemodynamic monitoring on beat-by-beat basis which would have involved intra-arterial catheterisation. The routine use of intra-arterial BP monitoring is not justified due to its invasive nature and risk of complications. We utilised the Finometer, a continuous beat-by-beat noninvasive haemodynamic monitor that works by applying a finger cuff to monitor entire sessions of maintenance haemodialysis. The haemodynamic data that was generated by the Finometer on continuous basis was further analysed to identify the gross haemodynamic changes that occur in response to maintenance haemodialysis. The Finometer is discussed in details in section 2.6.4.

Initially, we compared the pre and post dialysis values of haemodynamic variables. A significant drop in the SBP, MBP, SV and CO along with a significant rise in the HR was shown upon completion of the haemodialysis sessions. TPR remained stable however.

We further analysed the 25 patients' haemodynamic data collectively in terms of changes in each of the haemodynamic variables (SBP, MBP, DBP, SV, CO, HR and TPR) that was encountered during haemodialysis at 30 minutes time intervals. No significant change was shown in any of the haemodynamic variables in response to routine haemodialysis. This may be explained by the cancelling out effect of the collective data analysis, as when we further analysed the same data on individual patient basis, extensive inter-patient variability in terms of timing and magnitude of haemodynamic responses of different variables to haemodialysis was shown.

As previously mentioned, the normal cardiovascular response to volume loss would be an increase in the PRR, venous tone and peripheral vascular resistance, and a cardiac compensatory sympathetic stimulation that involves tachycardia initially followed by bradycardia, and an increase in the myocardial contractility. The resultant effect of this response would be an increased CO and TPR, thus keeping blood pressure stable in reaction to haemodialysis induced hypovolaemia. Our results suggest that failure of the normal compensatory cardiovascular response to haemodialysis may be due to failed TPR and CO responses. A possible explanation to our finding of a failed TPR (vasoconstrictor) response is that patients on chronic haemodialysis have a wide range of co-morbidities and are also on medications that may affect the integrity of their peripheral vascular responses such as, angiotensin converting enzyme inhibitors and calcium channel blockers. Another explanation could be the high incidence of autonomic neuropathy seen in patients on chronic haemodialysis, which is known to hinder their vasoconstrictor response.[198]

Also, it has been reported that an imbalance between the vaso-active substances, such as the vasodilator agents nitric oxide (NO) and calcitonin gene related peptide (CGRP), and the vasoconstrictor agents nor-adrenaline and angiotensin ll exists in patients on chronic haemodialysis.[199] Moreover, emerging evidence suggests that NO plays an important role in the pathogenesis of intradialytic hypotension.[200, 201]
Further studies to confirm our findings and to identify the cause of the failed vasoconstrictor response to chronic haemodialysis are warranted.

6.6.4 Conclusion

In a cohort of patients on chronic haemodialysis a significant drop in the BP, SV and CO along with a significant rise in the HR is shown in response to haemodialysis, whereas TPR remains stable. An inter-patient variability is observed in terms of the magnitude and timing of the haemodynamic responses to haemodialysis.
A failed vasoconstrictor response to haemodialysis induced hypovolaemia is seen in patients on chronic haemodialysis, which may serve as an explanation for intradialytic hypotension.
Continuous noninvasive haemodynamic monitoring using the Finometer provides a broad insight of the haemodynamics during haemodialysis, thus, the potential for identifying haemodynamic mishaps in individual patients undergoing chronic haemodialysis and subsequently prompting effective intervention.

6.7 Results: Assessment of the Incidence of significant hypotension during maintenance haemodialysis

This section presents an assessment of the incidence of transient hypotension episodes during maintenance haemodialysis as detected by the Finometer.

6.7.1 Data handling and statistics

The haemodynamic data required for the assessment of the incidence of intradialytic hypotension was retrieved from both, the 25 patients' Finometer raw data sheets and master spreadsheet 3, which were discussed in details in sections 6.3.2.4 and 6.3.2.4.3 respectively.

Data involving age, inter dialytic weight gain and vintage on haemodialysis were gathered from master spreadsheet 1, which was discussed in details in section 6.3.2.4.1.

The Prism software was used for statistical analysis of our data.

Firstly, we used master spreadsheet 3 to bring the values of the SBP, DBP, MBP, HR, SV, CO and TPR during the BP troughs, their baseline values and their percentage changes from baseline values. We then transferred all the gathered haemodynamic data to the Prism software, and carried out a paired t test to compare the values of each of the SBP, DBP, MBP, HR, SV, CO and TPR during the BP troughs with their baseline values.

We then used three definitions of hypotension episodes that were based upon changes from baseline values, namely, a more than 30% decrease in each of the SBP, DBP and MBP for more than 10 minutes.

Recent evidence suggests that the frequent occurrence of episodes of hypotension of SBP less than 90 mmHg is associated with an increased risk of mortality.[202] Based on this evidence, we used a fourth definition of intradialytic hypotension that implies this absolute figure of SBP less than 90 mmHg, for duration of more than 10 min. As mentioned earlier, we gathered the data needed for these assessments of BP reductions from the Finometer's raw data spreadsheets.

We further assigned our patients into 2 groups according to the occurrence of SBP of less than 90 mmHg for 10 min episodes; hypotension episode group (group 1) and no hypotension episode group (group 2).

In group 1, we used ANOVA and Tukey's post hoc test to compare the pre-dialysis, post-dialysis and mean values of all variables recorded during the hypotension episode. The mean values of all the variables during the hypotension episode were

calculated as follows: We used the "conditional formatting" tool to highlight all the cells in the SBP column that contained values lower than 90 in each of the 25 patients' Finometer's raw data sheets, then we transferred the whole rows of all variables which contained a highlighted SBP lower than 90 into a new clear excel sheet, and we calculated the mean and standard deviations of each of the variables. ANOVA and Tukey's post hoc test is discussed in section 4.2.2, and conditional formatting is discussed in sections 5.3.2.4 and 6.3.2.4.

We also calculated the total duration of time spent during each of the defined hypotension episodes (30% decreases in SBP, DBP and MBP, and SBP lower than 90 mmHg) from the Finometer's raw data sheets, as described in section 6.3.2.4.

In group 2, we compared pre and post dialysis SBP, DBP, MBP, HR, SV, CO and TPR using a paired t test.

We then compared both groups 1 and 2 in terms of, predialysis SBP, DBP, MBP, HR, SV, CO and TPR, and post dialysis SBP, DBP, MBP, HR, SV, CO and TPR using an unpaired t test. We also compared the 2 groups in terms of age, Interdialytic weight gain and vintage (number of years) on haemodialysis using an unpaired t test.

6.7.2 Results

6.7.2.1 Maximum decreases in the BP encountered during haemodialysis

The percentage change of the lowest blood pressure reading from baseline values is shown in table 26; the changes in SBP, DBP and MBP were all statistically significant. The corresponding changes in HR, CO, SV and TPR are displayed in table 27, CO and SV showed a statistically significant decrease in comparison to baseline values, whereas HR and TPR remained stable.

Table 26. Percentage change of lowest BP readings (troughs) from baseline as detected by the Finometer (n = 25)

	Baseline	Trough	% change from baseline	*P value*
SBP (mmHg)	141 (24)	86 (27)	39%	< 0.0001*
DBP (mmHg)	76 (15)	47 (11)	38%	< 0.0001*
MBP (mmHg)	99 (15)	61 (16)	38%	< 0.0001*

Table 27. The change in HR, CO, SV &TPR during the BP trough (n = 25)

	Baseline	Reading during BP trough	% change from baseline	*P* value
HR (beats/min)	74 (11)	75 (13)	1.4%	0.6776
CO (l/min)	6.6 (2.6)	5.4 (2.7)	18%	0.0286*
SV (ml)	91 (37)	72 (35)	21%	0.0063*
TPR (MU)	1.3 (1.06)	1.01 (0.69)	22%	0.2365

6.7.2.2 Hypotension episodes of more than 30% decrease from baseline values of the SBP, DBP and MBP for more than 10 minutes

Of the 25 patients, 8, 7 and 7 patients had an episode of more than 30% decrease from baseline values of the SBP, DBP and MBP respectively for more than 10 minutes.
The mean (SD) duration when the BP was less than 30% of the baseline value was 21 (39), 21 (43) and 18 (36) minutes for the SBP, DBP and MBP respectively.

6.7.2.3 Hypotension episodes of SBP less than 90mmHg for more than 10 minutes (group 1)

Of the 25 patients, 7 had a cumulative episode of SBP less than 90 mmHg for more than 10 minutes. The mean (SD) duration when the BP was less than 90 mmHg in group 1 was 55 (56) minutes. The shortest and the longest continuous durations when the SBP was less than 90 mmHg were 4.3 min and 150 min respectively. Table 29 displays the durations of hypotension episodes of SBP less than 90 mmHg amongst patients who had such episodes.
Using ANOVA and Tukey's post hoc test, we compared the pre dialysis, post dialysis and the mean value during the hypotension episodes of each of the SBP, DBP, MBP, SV, CO and TPR in group 1. Statistically significant drops from the pre dialysis values of the SBP, DBP and MBP were shown during the episode of hypotension. No significant changes in HR, SV, CO or TPR were encountered during those episodes of hypotension. Also there were no significant changes between all pre and post dialysis haemodynamic variables in group 1 as shown in table 28.

Table 28. Comparison between predialysis, post dialysis and the averaged values of haemodynamic variables during the hypotension episode (SBP less than 90mmHg) (ANOVA and Tukey's post hoc test) (n = 7)

Variable	A Predialysis	B mean value during episode	C Post dialysis	A vs. B	A vs. C	B vs. C
SBP (mmHg)	128 (18)	80 (5)	117 (23)	*	ns	*
MBP (mmHg)	97 (13)	62 (3)	88 (13)	*	ns	*
DBP (mmHg)	76 (15)	50 (4)	69 (9)	*	ns	*
HR (bpm)	76 (10)	76 (6)	79 (9)	ns	ns	ns
SV (ml)	70 (29)	53 (14)	62 (11)	ns	ns	ns
CO (l/m)	5.3 (2.1)	4 (1.2)	4.9 (0.9)	ns	ns	ns
TPR (MU)	1.37 (0.72)	1.213 (0.31)	1.184 (0.25)	ns	ns	ns

Table 29. Total duration of hypotension episodes of SBP less than 90 mmHg for more than 10 minutes (n=7)

Pts. who had SBP <90 > 10 min	Total duration of episode (min)
Pt 3	161
Pt 4	26.2
Pt 8	43.5
Pt 14	12.8
Pt 18	13.5
Pt 22	25.8
Pt 25	102.8

6.7.2.4 Comparison between pre and post dialysis haemodynamic variables in group 2

In group 2, a comparison between the pre and post dialysis haemodynamic variables using a paired t test showed a significant decrease in the SBP, MBP and SV, along with a significant increase in the HR. The DBP, CO and TPR remained unchanged (Table 30).

Table 30. Comparison of pre and post dialysis haemodynamic variables in group 2 (paired t test)

	Pre dialysis	Post dialysis	*P* value
HR (bpm)	73 (11)	81 (14)	0.009*
SBP (mmHg)	147 (24)	131 (23)	0.003*
MBP (mmHg)	99 (16)	93 (15)	0.036*
DBP (mmHg)	76 (16)	72 (12)	0.15
SV (ml)	99 (37)	81 (35)	0.024*
CO (l/m)	7.1 (2.7)	6.5 (2.9)	0.26
TPR (MU)	1.28 (1.19)	1.18 (0.83)	0.75

6.7.2.5 Comparison between group 1 and group 2

Comparisons between group 1 and 2 in terms of the pre dialysis haemodynamic variables, post dialysis haemodynamic variables, age, inter-dialytic weight gain and vintage (number of years on haemodialysis) using un-paired t tests are displayed in tables 31 - 33. None of the comparisons showed a significant difference.

Table 31. Comparison of the predialysis haemodynamic variables in both groups (unpaired t test)

Predialysis	Group 1 Hypotension	Group 2 No hypotension	*P* value
HR (bpm)	76 (10)	73 (11)	0.6
SBP (mmHg)	128 (18)	147 (24)	0.08
MBP (mmHg)	97 (13)	99 (16)	0.7
DBP (mmHg)	76 (15)	76 (16)	0.99
SV (ml)	70 (29)	99 (37)	0.08
CO (l/m)	5.3 (2.1)	7.1 (2.7)	0.14
TPR (MU)	1.37 (0.72)	1.28 (1.19)	0.85

Table 32. Comparison of the post dialysis haemodynamic variables in both groups (unpaired T test)

Post dialysis	Group 1 Hypotension	Group 2 No hypotension	*P* value
HR (bpm)	79 (9)	81 (14)	0.72
SBP (mmHg)	117 (23)	131 (23)	0.18
MBP (mmHg)	88 (13)	93 (15)	0.41
DBP (mmHg)	69 (9)	72 (12)	0.61
SV (ml)	62 (11)	81 (35)	0.18
CO (l/m)	4.9 (0.9)	6.5 (2.9)	0.17
TPR (MU)	1.18 (0.25)	1.18 (0.83)	0.98

Table 33. Comparison of different factors for association with hypotensive episodes using an unpaired t test

	Group 1 Hypotension	Group 2 No hypotension	*P* value
Age (yrs)	58.4 (22.8)	62.4 (17.4)	0.64
Interdialytic wt. gain (Kg)	1.86 (1.25)	1.88 (1.03)	0.96
Vintage (yrs)	4.4 (6.4)	1.6 (1.2)	0.08

6.7.3 Discussion

Major advances in the area of haemodialysis have been accomplished over the last few years. This has aided in providing a better quality of life for patients on maintenance haemodialysis. Nevertheless, significant hypotension still continues to be the most common complication of haemodialysis, occurring in 25% to 50% of maintenance haemodialysis sessions.[2, 3] Intradialytic hypotension is likely to cause a state of hypoperfusion that may affect the integrity of vital organs such as the heart and the brain. Emerging evidence suggests that intradialytic hypotension may indirectly cause chronic heart failure through aggravating a condition known as atherosclerosis independent myocardial stunning, which commonly occurs in patients undergoing chronic haemodialysis.[61-64] Also, it has been shown that intradialytic hypotension causes a severe orthostatic drop in the cerebral blood flow velocity.[203] Furthermore, several studies have reported an association between intradialytic hypotension and an increased risk of mortality.[6, 202, 204-206] Therefore, it is necessary to identify and manage intradialytic hypotension as early as possible during haemodialysis sessions in order to prevent its complications.

In the current clinical practice BP monitoring during routine haemodialysis sessions is carried out using intermittent NIBP devices, usually 2-3 readings are taken during the whole 4 hour session including the pre and post dialysis readings. This might carry the risk of missing episodes of hypotension especially if they were asymptomatic. Asymptomatic hypotension is not unlikely to occur in a cohort of patients on chronic haemodialysis who may have gained tolerance to haemodialysis induced hypotension.

In our service evaluation, we utilised a noninvasive continuous beat-by-beat haemodynamic monitor (Finometer) to assess the incidence of significant hypotension episodes. We also identified the corresponding changes in other haemodynamic variables, including, the HR, SV, CO and TPR in a cohort of patients on chronic haemodialysis.

We also identified both, the maximum decreases in the BP encountered during conventional haemodialysis, and the incidence of transient intradialytic hypotension. Moreover, we characterised the changes that occurred in the HR, SV, CO and TPR during both, the maximal decrease in the BP and the intradialytic hypotension episodes. Lastly, we compared the age, Interdialytic weight gain and vintage on haemodialysis of the patients who had an episode of SBP lower than 90 mmHg for more than 10 minutes with those who did not.

In the cohort of 25 patients, acute significant BP drops were encountered during the course of haemodialysis. The mean percentage drops of the SBP, DBP and MBP from their corresponding baseline values were 39%, 38% and 38% respectively. There was a statistically significant drop from baseline values of the corresponding SV and CO with a mean percentage change of 21% and 18% respectively. A drop in the TPR from its baseline value equivalent to a mean percentage change of 22% was also shown, but it was not statistically significant. HR remained stable during the course of haemodialysis.

In this cohort of patients, 32%, 28% and 28% had an episode of more than 30% decrease from baseline values of the SBP, DBP and MBP for more than 10 minutes respectively, and 28% had an episode of SBP less than 90 mmHg for more than 10 minutes. The mean (SD) duration when the BP was less than 30% of the baseline value was 21 (39), 21 (43) and 18 (36) minutes for the SBP, DBP and MBP respectively. The mean (SD) duration when the SBP was less than 90 mmHg was 55 (56) minutes.

On further analysing the lower than 90 mmHg SBP for more than 10 minutes episodes of intradialytic hypotension, we found that there were no corresponding significant changes in any of the HR, SV, CO or TPR during the episode of hypotension indicating a failed cardiovascular compensatory mechanism to haemodialysis induced hypovolaemia. There were also no significant changes between any of the predialysis and post-dialysis haemodynamic variables in group 1.

On the other hand in group 2, a statistically significant decrease in the post-dialysis SBP, MBP and SV, along with a significant increase in the HR, from corresponding pre dialysis values was shown.

We also attempted to point out any possible differences between the patients who developed hypotension and those who did not. The results showed no statistically significant differences on comparing groups 1 and 2 in terms of predialysis and post-dialysis haemodynamic variables, or any of the patient characteristics. However, in this small sample size a trend of difference was shown in the predialysis SV in both groups. The mean (SD) SV for groups 1 and 2 was 70 (29) and 99 (37) ml respectively; $p = 0.08$. These results are subject to type 2 error, and they could give an indication of the likelihood of differences between the 2 groups, hence, they may help in future sample size calculations. Moreover, the predialysis SBP and SV were 23% lower in group 1 than group 2, which is considered a clinically significant difference (more than 20% change from baseline)[193], indicating that hypotension that was encountered in group 1 may have been due to a preload defect.

Kinet and colleagues studied the haemodynamic response to intradialytic hypotension in 14 patients on regular haemodialysis who were not known to have any cardiovascular abnormalities. The patients were monitored using both, a pulmonary artery catheter and an intra-arterial catheter during a conventional haemodialysis session. Hypotension was defined as a more than 30 mmHg decrease of MBP from the baseline value regardless of the duration. In agreement with our findings of high incidence of intradialytic hypotension, they showed a 43% incidence of intradialytic hypotension and the mean (SE) MBP during intradialytic hypotension was 55 (4.1) mmHg. They also showed agreement with our findings of an unchanged HR and TPR during intradialytic hypotension. [206]

Several studies have demonstrated the independent association of intradialytic hypotension with mortality.[6, 204, 205] A study by Tisler and colleagues assessed the effect of both, frequent intradialytic hypotension (f-IDH) and occasional intradialytic hypotension (o-IDH) on patient survival. 958 maintenance haemodialysis patients were the subject of the study. Intradialytic hypotension episodes were defined as an SBP lower than 90 mmHg or a drop in the SBP of more than 30 mmHg from the baseline value which only responds to fluid administration. f-IDH was defined as more than 9 IDH episodes and o-IDH was defined as 1 to 2 IDH episodes in a period of 10 months observation. 85 patients from the group with no-IDH were assigned as a control group. The 3 groups of f-IDH, o-IDH and no-IDH were further followed up for a period that ranged between 0.3 to 37 months and the mortality rate was compared between the 3 groups. Their results showed mortality rates of 58%, 47% and 39% for the f-IDH, o-IDH and the no-IDH groups respectively during the follow up period. These results indicate that the mortality rates in the f-IDH groups are significantly higher than the o-IDH and the no-IDH groups.[202]
Hence, it is important to identify the exact incidence and patho-physiology behind intradialytic hypotension, to be able to properly manage it and avoid its hazardous complications.
Further studies that are designed to follow up patients for recurrence of intradialytic hypotension and for the incidence of mortality amongst the patients who suffer intradialytic hypotension are warranted.

6.7.4 Conclusion

Significant hypotension is commonly encountered during maintenance haemodialysis, which is possibly due to a deficient predialysis preload. Transient Intradialytic hypotension in patients on chronic haemodialysis can be explained by a failed compensatory cardiovascular response to haemodialysis induced hypovolaemia.

6.8 Results: Assessment of the Incidence of significant hypertension during maintenance haemodialysis

This section presents an assessment of the incidence and magnitude of hypertension during maintenance haemodialysis as detected by the Finometer.

6.8.1 Data handling and statistics

The haemodynamic data required for the assessment of the incidence of intradialytic hypertension was retrieved from both, the 25 patients' Finometer raw data sheets and master spreadsheet 3, which were both, discussed in details in sections 6.3.2.4 and 6.3.2.4.3 respectively.

The Prism software was used for statistical analysis of our data.

Firstly, we used master spreadsheet 3 to bring the values of the SBP, DBP, MBP, HR, SV, CO and TPR during the BP peaks, their baseline values and their percentage changes from baseline values. We then transferred all the gathered haemodynamic data to the Prism software, and carried out a paired t test to compare the values of each of the SBP, DBP, MBP, HR, SV, CO and TPR during the BP peaks with their baseline values.

We then used three definitions of hypertension episodes that were based upon changes from baseline values, namely, a more than 30% increase in each of the SBP, DBP and MBP for more than 10 minutes.

We also used two more definitions of hypertension that imply absolute figures rather than relative changes including, an SBP more than 160 mmHg as a reflection of moderate to severe hypertension, and an SBP more than 180 mmHg as a reflection of severe hypertension, both for a duration of more than 10 min. We gathered all the data needed for these assessments of BP elevations that involved set definitions of hypertension from the Finometer's raw data spreadsheets, as described earlier.

We further assigned our patients into 2 groups according to the occurrence of SBP more than 180 mmHg for more than10 min episodes into: a hypertension episode group (group 3) and a no hypertension episode group (group 4).

In group 3, we used ANOVA and Tukey's post hoc test to compare the pre-dialysis, post-dialysis and mean values of all variables recorded during the hypertension episode. The mean values of all the variables during the hypertension episode were calculated using the "conditional formatting" tool, which was used to highlight all the cells in the SBP column that contained values higher than 180 in each of the 25 patients' Finometer's raw data sheets. We then transferred the whole rows of all variables which contained a highlighted SBP higher than 180 into a new clear excel sheet, and from that data on the new excel sheet we calculated the mean and standard deviations of each of the variables. ANOVA and Tukey's post hoc test is discussed in section 4.2.2, and conditional formatting is discussed in sections 5.3.2.4 and 6.3.2.4.

We also calculated the total time spent during each of the defined hypertension episodes (30% decreases in SBP, DBP, MBP, SBP higher than 160 mmHg and SBP higher than 180 mmHg) from the 25 patients' Finometer's raw data sheets, as described in section 6.3.2.4.

In group 4, we compared pre and post dialysis SBP, DBP, MBP, HR, SV, CO and TPR using a paired t test.

Lastly, we compared both groups 3 and 4 in terms of, predialysis SBP, DBP, MBP, HR, SV, CO and TPR, and post dialysis SBP, DBP, MBP, HR, SV, CO and TPR using an un-paired t test. We also compared the 2 groups in terms of age, Interdialytic weight gain and vintage on haemodialysis using an unpaired t test.

6.8.2 Results

6.8.2.1 Maximum increases in the BP encountered during haemodialysis

The percentage change of the highest blood pressure reading from baseline values is shown in table 34; the changes in SBP, DBP and MBP were all statistically significant. The corresponding changes in the HR, CO, SV and TPR are displayed in table 35; TPR showed a statistically significant increase, whereas SV and CO showed statistically significant decreases in comparison to baseline values. HR remained stable.

Table 34. Percentage change of highest BP readings (peaks) from baseline as detected by the Finometer (n = 25)

	Baseline	Peak	% change from baseline	*P value*
SBP (mmHg)	141 (24)	180 (32)	28%	< 0.0001*
DBP (mmHg)	76 (15)	109 (24)	43%	< 0.0001*
MBP (mmHg)	99 (15)	136 (27)	37%	< 0.0001*

Table 35. The change in HR, CO, SV &TPR during the BP peak (n = 25)

	Baseline	Reading during BP Peak	% change from baseline	*P* value
HR (beats/min)	74 (11)	77 (13)	4%	0.3013
CO (l/min)	6.6 (2.6)	4.8 (2.7)	27%	0.0002*
SV (ml)	91 (37)	64 (37)	30%	0.0001*
TPR (MU)	1.3 (1.06)	3.08 (2.81)	136%	0.0043*

6.8.2.2 Incidence of hypertension episodes

We defined our five hypertension episodes as, a more than 30 % increase of the SBP, DBP or MBP from the baseline value for more than 10 minutes, and an SBP of more than 160 mmHg and more than 180 mmHg for more than 10 minutes indicating moderate to severe hypertension and severe hypertension respectively.
Of the 25 patients, 3, 8 and 4 patients had an episode of more than 30% increase from baseline values of the SBP, DBP and MBP respectively for more than 10 minutes. The mean (SD) duration when the BP was 30% higher than the baseline value was 22 (1.5), 44 (49) and 44 (34) minutes for the SBP, DBP and MBP respectively.
13 patients had an episode of SBP higher than 160 mmHg for more than 10 minutes. 8 of whom were known hypertensive. The mean (SD) duration when the SBP was more than 160 mmHg was 60 (55) minutes.
4 patients had an episode of SBP higher than 180 mmHg for more than 10 minutes, they were all known hypertensive. The mean (SD) duration when the SBP was more than 180 mmHg was 79 (61) minutes.
Table 36 displays the total durations of episodes of both, SBP more than 160 mmHg and SBP more than 180 mmHg amongst our patients.

Table 36. Total durations of hypertension episodes of both, SBP more than 160 mmHg and SBP more than 180 mmHg that were encountered for more than 10 minutes

Pts. who had SBP > 160 > 10 min (n=13)	Total duration of episode (min)	Pts. who had SBP > 180 > 10 min (n=4)	Total duration of episode (min)
Pt 1	40	Pt 5	74
Pt 5	128	Pt 6	159
Pt 6	204	Pt 15	72
Pt 7	88	Pt 20	10
Pt 11	55		
Pt 12	28		
Pt 13	11		
Pt 14	13		
Pt 15	13		
Pt 19	43		
Pt 20	84		
Pt 21	49		
Pt 22	25		

6.8.2.3 An assessment of the changes in all haemodynamic variables during the episodes of severe hypertension

Using the haemodynamic data of the 4 patients who suffered an episode of SBP greater than 180 mmHg (group 3) during their haemodialysis sessions, we applied ANOVA and Tukey's post hoc test to compare the pre dialysis, post dialysis and the mean values of the SBP, DBP, MBP, HR, SV, CO and TPR during the episode of severe hypertension.

A significant elevation was encountered in the SBP and MBP during the hypertension episode in comparison with the post dialysis readings. However, the DBP, HR, SV, CO and TPR remained stable during the hypertension episode. Also there were no significant changes between all pre and post dialysis haemodynamic variables in group 3 (Table 37).

Table 37. Comparison between predialysis, post dialysis and the averaged values of haemodynamic variables during the hypertension episode of SBP greater than 180mmHg) (ANOVA and Tukey's post hoc test) (n = 4)

Variable	A Predialysis	B mean value during episode	C Post dialysis	A vs. B	A vs. C	B vs. C
SBP (mmHg)	177 (15)	196 (8)	151 (29)	ns	ns	*
MBP (mmHg)	111 (13)	129 (4)	101 (14)	ns	ns	*
DBP (mmHg)	83 (20)	94 (8)	73 (11)	ns	ns	ns
HR (bpm)	72 (5)	72 (11)	74 (7)	ns	ns	ns
SV (ml)	88 (37)	63 (18)	75 (34)	ns	ns	ns
CO (l/m)	6.3 (2.6)	4.4 (0.8)	5.7 (2.8)	ns	ns	ns
TPR (MU)	2.08 (2.3)	2.17 (0.42)	1.75 (1.47)	ns	ns	ns

6.8.2.4 Comparison of pre and post dialysis haemodynamic variables in group 4

In group 4, a comparison between the pre dialysis and post dialysis haemodynamic variables using a paired t test showed a significant decrease in SBP and SV, along with a significant increase in the HR. The DBP, MBP, CO and TPR remained unchanged (Table 38).

Table 38. Comparison of pre and post dialysis haemodynamic variables in group 4 (paired t test)

	Pre dialysis	Post dialysis	*P* value
HR (bpm)	74 (11)	82 (13)	0.0034*
SBP (mmHg)	135 (18)	122 (20)	0.016*
MBP (mmHg)	96 (14)	90 (14)	0.0733
DBP (mmHg)	75 (15)	71 (11)	0.2007
SV (ml)	91 (37)	76 (32)	0.0131*
CO (l/m)	6.7 (2.7)	6.1 (2.6)	0.1625
TPR (MU)	1.2 (0.65)	1.1 (0.46)	0.5401

6.8.2.5 Comparison between group 3 and group 4

Comparisons between group 3 and 4 in terms of the pre dialysis haemodynamic variables, post dialysis haemodynamic variables, age, inter-dialytic weight gain and vintage (number of years on haemodialysis) are displayed in tables 39 - 41. Both, the pre dialysis and the post dialysis SBP values were significantly higher in group 3 than in group 4. None of the other comparisons showed significant differences.

Table 39. Comparison of the predialysis haemodynamic variables in both groups (un-paired t test)

Predialysis	Group 3 Hypertension	Group 4 No hypertension	*P* value
HR (bpm)	72 (5)	74 (11)	0.6348
SBP (mmHg)	177 (15)	135 (18)	0.0002*
MBP (mmHg)	111 (13)	96 (14)	0.0734
DBP (mmHg)	83 (20)	75 (15)	0.3448
SV (ml)	88 (37)	91 (37)	0.8751
CO (l/m)	6.3 (2.6)	6.7 (2.7)	0.7869
TPR (MU)	2.08 (2.3)	1.16 (0.65)	0.113

Table 40. Comparison of the post dialysis haemodynamic variables in both groups (un-paired t test)

Post dialysis	Group 3 Hypertension	Group 4 No hypertension	*P* value
HR (bpm)	74 (7)	82 (13)	0.2497
SBP (mmHg)	151 (29)	122 (20)	0.0213*
MBP (mmHg)	101 (14)	90 (14)	0.1557
DBP (mmHg)	73 (11)	71 (11)	0.7217
SV (ml)	75 (34)	76 (32)	0.9238
CO (l/m)	5.7 (2.8)	6.1 (2.6)	0.7661
TPR (MU)	1.75 (1.47)	1.07 (0.846)	0.0804

Table 41. Comparison of different factors for association with hypertensive episodes using an un-paired t test

	Group 3 Hypertension	Group 4 No hypertension	*P* value
Age (yrs)	74.5 (7.1)	58.8 (19.2)	0.1245
Interdialytic wt. gain (Kg)	1.88 (0.48)	1.88 (1.15)	0.9984
Vintage (yrs)	2.4 (1.8)	2.4 (3.9)	0.9994

6.8.3 Discussion

Hypertension is a major risk factor for cardiovascular disease.[207] It is prevalent amongst chronic kidney disease patients, hence, the high incidence of cardiovascular disease in these patients.[208, 209] The Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VII) defined hypertension as an SBP ≥ 140 mmHg and / or a DBP ≥ 90 mmHg, and it recommended to treat hypertension in chronic kidney disease patients to a target BP of < 130/80 mmHg.[121]

Emerging evidence suggests that high predialysis BP and post-dialysis BP are associated with a high risk of mortality.[209, 210] However, there is lack of data to assess the incidence and long term effects of hypertension during the course of conventional haemodialysis sessions, as this would have required intra-arterial catheterisation for continuous monitoring of the BP, which is an invasive procedure that is not routinely employed to avoid the risk of complications. As mentioned earlier, maintenance haemodialysis sessions, BP is monitored on intermittent basis 2-3 times using the conventional NIBP devices, which may carry the risk of missing hypertensive events.

We utilised a noninvasive continuous beat-by-beat haemodynamic monitor that works through a finger cuff in an attempt to gain a better insight of the exact incidence and magnitude of hypertension during the entire sessions of conventional haemodialysis.

Our results showed that significant acute elevations in the BP were encountered during haemodialysis. The mean percentage elevation of the SBP, DBP and MBP from their baseline values during these acute BP elevations were 28%, 43% and 37% respectively. There was a statistically significant drop from baseline values of the corresponding SV and CO with a mean percentage change of 30% and 27% respectively, and a statistically significant elevation of the TPR from its baseline value with a mean percentage change of 136%. HR remained stable.

In this cohort of patients, 12%, 32% and 16% had an episode of more than 30% increase from baseline values of the SBP, DBP and MBP for more than 10 minutes respectively. 52% of the patients had an episode of SBP more than 160 mmHg for more than 10 minutes, and 16% had an episode of SBP more than 180 mmHg for more than 10 minutes. The mean (SD) duration when the BP was 30% higher than the baseline value was 22 (1.5), 44 (49) and 44 (34) minutes for the SBP, DBP and MBP respectively. The mean (SD) durations when the SBP was higher than 160 mmHg and higher than 180 mmHg were 60 (55) and 79 (61) minutes respectively.
As mentioned earlier we assigned our patients into 2 groups according to the incidence of episodes of SBP higher than 180 mmHg for 10 minutes into: group 3 (hypertension episode group), and group 4 (no hypertension episode group).
In group 3, a significant elevation was encountered in the SBP and MBP during the hypertension episode. However, the DBP, HR, SV, CO and TPR remained stable during the hypertension episode. Also there were no significant changes between all pre and post dialysis haemodynamic variables.
In group 4, the post dialysis SBP and SV were significantly lower than their pre dialysis values, and the post dialysis HR was significantly higher than its pre dialysis value. However, the DBP, MBP, CO and TPR remained unchanged. The post dialysis drop in SBP which was associated with a drop in the SV in group 4, and the fact that in group 3 the SBP remained high even after dialysis, may serve as potential evidence that the severe hypertension episodes that were encountered in those patients during the haemodialysis sessions resulted from volume depletion. An issue of debate is that in group 3 the SV remained unchanged after haemodialysis induced further volume removal. This may be explained by an increased sympathetic stimulation with a resultant increased myocardial contractility in an attempt to keep the SV stable, as SV is dependent upon both, preload and myocardial contractility.

On comparing group 3 and group 4, we found that both, the pre dialysis and the post dialysis SBP values were significantly higher in group 3 than in group 4. These findings may further support our explanation of the cause of severe hypertension that is to be due to volume depletion, as the BP was higher in group 3 than in group 4 from the start of haemodialysis and it has not improved by haemodialysis induced fluid removal, since it remained higher in group 3 till the end of haemodialysis. There were no significant differences between groups 3 and 4 in any of the other pre dialysis and post dialysis haemodynamic variables. Also, the age, inter-dialytic weight gain and the vintage on haemodialysis were not different in both groups.

It should be mentioned that the Finometer in contrast with the NIBP monitors that are conventionally used during maintenance haemodialysis, has the merit of providing a more detailed insight of the haemodynamics, with the ability to record variables other than the BP and HR including, the SV, CO and TPR. This extra information about the haemodynamics may be implied by nephrologists for proper management of patients during haemodialysis in terms of hypertension and volume status adjustment, hence, preventing negative outcomes.

There is lack of data to assess the incidence of hypertension during haemodialysis and its association with mortality. Nevertheless, the relationship between predialysis and post-dialysis hypertension, and cardiovascular morbidity and mortality has been reported in several studies.

Zager and colleagues studied the effect of predialysis and post-dialysis elevated SBP and DBP on cardiovascular mortality in 5,433 patients on maintenance haemodialysis. Moderate elevation of the predialysis BP was encountered in 27% of their patients, and was defined as SBP 160-179 mmHg and DBP 110 mmHg or DBP 100-109 mmHg and SBP < 180 mmHg. Moreover, the incidence of severe / very severe elevations of the pre-dialysis BP was 5%, and was defined as SBP ≥ 180 mmHg and / or DBP ≥ 110 mmHg. Their results also showed an increased incidence of mortality in association with severe post-dialysis hypertension. Pre-dialysis hypertension was not associated with an increased risk of mortality in their study.[211] Likewise, Foley and colleagues also reported an increased risk of mortality in association with a high post-dialysis SBP in 11,142 patients on maintenance haemodialysis.[209]

In a bigger study sample of 16,959 patients on maintenance haemodialysis, Stidley and colleagues demonstrated an increased risk of mortality in association with a predialysis SBP ≥ 150 mmHg.[210]

Further studies to confirm our findings of the high prevalence of intradialytic hypertension and to assess the effects intradialytic hypertension on morbidity and mortality are encouraged.

6.8.4 Conclusion

Significant elevations in the BP are commonly encountered, and are sustained for considerable periods during the course of maintenance haemodialysis.
Acute hypertension can be explained by a significant decrease in the preload, which is over-corrected by a significant increase in the afterload.
Episodes of sustained severe hypertension during haemodialysis can be explained by pre dialysis volume depletion.

6.9 Results: Assessment of the sensitivity of the conventional NIBP monitoring in detecting maximum changes in BP in comparison with the Finometer during maintenance haemodialysis

In this section, we compared the ability of the conventional NIBP monitoring and the continuous noninvasive haemodynamic monitoring (Finometer) in detecting BP aberrations that occur during sessions of maintenance haemodialysis.

6.9.1 Data handling and statistics

We obtained the baseline SBP, DBP and MBP (NIBP1) readings and the post dialysis SBP, DBP and MBP (NIBP2) readings from master spreadsheet 2. We then obtained the SBP, DBP, MBP and HR readings during the Finometer's BP peaks and the BP troughs from master spreadsheets 3. Master spreadsheets 2 and 3 are discussed in details in sections 6.3.2.4.2 and 6.3.2.4.3 respectively.

We then transferred these readings to the Prism software and carried out 3 main comparisons using a paired t test. Initially, we compared the baseline NIBP (SBP, DBP and MBP) readings with their corresponding post dialysis NIBP (SBP, DBP and MBP) readings. We then compared the baseline NIBP (SBP, DBP and MBP) readings with the Finometer's SBP, DBP and MBP readings during BP peaks, and the Finometer's SBP, DBP and MBP readings during BP troughs. We also calculated the percentage changes of each of the post dialysis NIBP (SBP, DBP and MBP) readings, the SBP, DBP and MBP readings during the Finometer's BP peaks and the SBP, DBP and MBP readings during the Finometer's BP troughs, from their corresponding SBP, DBP and MBP NIBP baseline values.

The time lag between both the highest and the lowest blood pressure values recorded by the Finometer and their next available NIBP measurement, were obtained from master spreadsheet 3.

6.9.2 Results

6.9.2.1 BP changes in response to haemodialysis as detected by the NIBP device

We assessed the magnitude of changes in BP that were detected by the NIBP device by comparing its 2 sets of pre dialysis and post dialysis readings of SBP, DBP and MBP using a paired t test for each comparison.

A statistically significant decrease in the post dialysis SBP was shown in comparison to the pre dialysis SBP, but no significant differences were shown between the post and pre dialysis readings of either of the DBP and MBP.

The percentage changes of the NIBP'S post dialysis readings from their corresponding pre dialysis readings were 8%, 4% and 4% for the SBP, DBP and MBP respectively (table 42).

Table 42. Comparison of the 2 sets of NIBP readings that were taken during the whole period of haemodialysis using a paired t test (n = 25)

	Baseline NIBP 1 (pre dialysis reading)	NIBP 2 (post dialysis reading)	% change of NIBP 2 from baseline NIBP 1	*P value*
SBP (mmHg)	141 (25)	130 (23)	8 %	0.0479*
DBP (mmHg)	77 (13)	74 (10)	4 %	0.2802
MBP (mmHg)	97 (14)	93 (14)	4 %	0.2418

6.9.2.2 BP troughs detected by the Finometer during haemodialysis

We assessed the absolute values of SBP, DBP and MBP during the maximum decrease (trough) in BP per patient as detected by the Finometer. Then we compared these values with their corresponding baseline NIBP values of SBP, DBP and MBP using a paired t test.

The Finometer's SBP, DBP and MBP values during the BP trough were all significantly lower than their corresponding baseline NIBP SBP, DBP and MBP values, equating to a 39%, 39% and 37% decrease respectively (table 43).

Table 44 displays the time lag between the BP trough and the next available NIBP measurement, which was > 2 hours in 14 patients, 1 to 2 hours in 6 patients and less than 1 hour in 5 patients. The mean (SD) of the time lag between the BP trough and the next available NIBP measurement was 2 hours and 7 minutes.

Table 43. Percentage change of lowest BP readings (troughs) detected by the Finometer from baseline NIBP readings using a paired t test (n = 25)

	Baseline NIBP1	Trough Finometer	% change of trough from baseline NIBP	*P value*
SBP (mmHg)	141 (25)	86 (26)	39 %	<0.0001*
DBP (mmHg)	77 (13)	47 (11)	39 %	<0.0001*
MBP (mmHg)	97 (14)	61 (16)	37 %	<0.0001*

Table 44. Time lag between lowest blood pressure readings detected by the Finometer and next available NIBP readings

Time lag	< 1 hour	1-2 hours	> 2 hours
n of patients (n = 25)	5	6	14

6.9.2.3 BP peaks detected by the Finometer during haemodialysis

We also assessed the absolute values of SBP, DBP and MBP during the maximum increases in BP (peaks) per patient as detected by the Finometer. Then we compared these values with their corresponding baseline NIBP values of SBP, DBP and MBP using a paired t test.

The Finometer's SBP, DBP and MBP values during the BP peak were all significantly higher than their corresponding baseline NIBP SBP, DBP and MBP values, equating to a 28%, 42% and 39% increase respectively (table 45).

Table 46 displays the time lag between the BP trough and the next available NIBP measurement, which was > 2 hours in 14 patients, 1 to 2 hours in 4 patients and less than 1 hour in 7 patients. The mean (SD) of the time lag between the BP peak and the next available NIBP measurement was 2 hours and 13 minutes.

Table 45. Percentage change of highest BP readings (peaks) detected by the Finometer from baseline NIBP readings (n = 25)

	Baseline NIBP1	Peak Finometer	% change of peak from baseline NIBP	*P value*
SBP (mmHg)	141 (25)	180 (31)	28 %	<0.0001*
DBP (mmHg)	77 (13)	109 (23)	42 %	<0.0001*
MBP (mmHg)	97 (14)	135 (27)	39 %	<0.0001*

Table 46. Time lag between highest blood pressure readings detected by the Finometer and next available NIBP readings

Time lag	< 1 hour	1-2 hours	> 2 hours
n of patients (n = 25)	7	4	14

6.9.3 Discussion

As mentioned earlier, haemodynamic instability is not unlikely to occur during haemodialysis. This mainly is due to the removal of vast amounts of fluids from the circulation in a relatively short period of time. Also, hypertension is highly prevalent amongst patients on maintenance haemodialysis, to which they are usually prescribed vasodilator drugs such as ACEi and CCB. These vasodilator drugs are known to affect the integrity of the patients' compensatory cardiovascular response to haemodialysis induced hypovolaemia.

Theoretically, maintenance haemodialysis sessions would be best monitored by intra-arterial catheterisation. However, its routine use is not justified due to its invasive nature and the risk of complications. Routine haemodialysis sessions are conventionally monitored by the intermittent oscillometric NIBP devices, only 2-3 measurements are usually taken during the whole 4 hour session of haemodialysis including a predialysis and a post-dialysis reading. This may carry the risk of missing BP aberrations especially that patients on maintenance haemodialysis are acclimatised to vast haemodynamic changes, which may cause those BP aberrations to be symptomless. Therefore, additional readings which are prompted by patient symptoms will not be attempted by the attending staff.

We utilised an accurate noninvasive continuous beat-by-beat BP monitor that works through applying a finger cuff (Finometer) to test the sensitivity of the conventional NIBP devices in detecting BP aberrations.

Our result showed that current practice of measuring NIBP is not reliable in detecting BP aberrations and that the Finometer provides a more comprehensive surveillance of the BP during maintenance haemodialysis.

As mentioned earlier, only 2 NIBP readings were taken for all our patients during the entire session of haemodialysis (a predialysis and a post-dialysis NIBP reading). This was because none of our patients had symptoms suggestive of hypotension; therefore, no extra NIBP measurements were attempted by the attending staff.
NIBP detected an 8%, 4% and 4% decrease in the post-dialysis SBP, DBP and MBP readings from their corresponding baseline (predialysis) NIBP readings respectively. Only the change in the SBP showed statistical significance. However, this 8% change in the SBP is not considered of clinical importance.
Continuous BP monitoring using the Finometer on the other hand detected statistically significant drops of 39%, 39% and 37% in SBP, DBP and MBP from baseline NIBP readings respectively, and statistically significant elevations of 28%, 42% and 39% in SBP, DBP and MBP from baseline NIBP readings respectively.
The mean time lag between BP troughs that were detected by the Finometer and their next available NIBP was 2 hours and 7 minutes, whereas the mean time lag between BP peaks that were detected by the Finometer and their next available NIBP was 2 hours and 13 minutes.
As previously discussed, the policy in our haemodialysis unit in regards to the frequency of NIBP measurements, was to take a pre dialysis and a post dialysis measurement. Extra measurements were to be taken whenever the patient experiences symptoms suggestive of hypotension. Policies involving the frequency of NIBP measurements may be different in other units. Therefore, the applicability of our results may be questioned by the fact that only two NIBP readings (predialysis and a post-dialysis) were taken for all of our patients during their haemodialysis sessions, as none of our patients has experienced symptoms suggestive of hypotension, which would have prompted extra BP measurements to be taken.

Symptomless hypotension that was observed in all our patients who have developed intradialytic hypotension is possibly explained by the tolerance that patients on chronic haemodialysis might have gained to the vast haemodynamic changes that they are subjected to 3 times per week during their continuous haemodialysis sessions.

There is lack of data in literature to describe the sensitivity of conventional NIBP in detecting BP aberrations during maintenance haemodialysis. Studies to explore this potential are warranted, due to its impact on patient safety.

6.9.4 Conclusion

Monitoring the BP noninvasively on continuous basis using the Finometer is more reliable than the conventionally used protocols of intermittent NIBP measurements during maintenance haemodialysis in detecting BP aberrations, especially that patients on chronic haemodialysis may have gained tolerance to hypotension, which may rather pass unnoticed.

6.10 Summary

In this service evaluation, we aimed to assess the adequacy of patient safety provided by the conventionally used protocols of intermittent NIBP measurements during maintenance haemodialysis sessions, in a cohort of patients who as previously mentioned are known to have co-morbid conditions such as hypertension and autonomic neuropathy, and are on various medications including anti-hypertensive drugs. These factors are likely to affect their compensatory cardiovascular responses to haemodialysis induced hypovolaemia, which normally keeps the blood pressure stable in response to hypovolaemia.

In order to complete this assessment, we explored the following inter-related research issues:

Firstly, we assessed the feasibility of using the Finometer for monitoring of maintenance haemodialysis by, evaluating the success rate of the Finometer in providing haemodynamic monitoring, and by comparing its BP measurements that were averaged over 10 second intervals with those obtained by the NIBP monitors during maintenance haemodialysis. Our results showed that adequate Finometer recordings were generated in 86% of cases, and that the Finometer is accurate in terms of BP monitoring. Hence, the Finometer is a feasible option for BP monitoring during maintenance haemodialysis.

Secondly, we assessed the gross haemodynamic changes that occur in response to haemodialysis. Our results showed that a significant drop in the SBP and MBP was encountered post-dialysis; this was accompanied by a significant drop in the SV and CO, and a significant rise in the HR. TPR remained unchanged. It was also shown that there was inter-patient variability in terms of the timing and magnitude of haemodynamic responses to haemodialysis.

Thirdly, we assessed the incidence, magnitude and duration of significant hypotension during maintenance haemodialysis, and we identified the corresponding changes in other haemodynamic variables too. Our results showed that during maintenance haemodialysis, the BP acutely dropped to significantly low values, which were associated with significant drops in SV and CO, TPR and HR remained stable. Sustained hypotension episodes of SBP less than 90 mmHg for more than 10 minutes were encountered in 28% of our patients, and there were no associated significant changes in any of the HR, SV, CO and TPR, indicating a total failure of the compensatory cardiovascular mechanisms to haemodialysis induced hypovolaemia. The compensatory cardiovascular mechanisms to haemodialysis induced hypovolaemia are discussed in details in section 2.2.3.

As previously mentioned, we have assigned the patients into two groups according to the incidence of hypotension episodes of SBP less than 90 mmHg for more than 10 minutes into group 1 (hypotension episode group) and group 2 (no hypotension episode group). No statistical significant differences were shown on comparing groups 1 and 2 in terms of predialysis and post-dialysis haemodynamic variables, or any of the patient characteristics. However, in this small sample size a trend of difference was shown in the predialysis SV in both groups. The mean (SD) SV for groups 1 and 2 was 70 (29) and 99 (37) ml respectively; $p = 0.08$. These results are subject to type 2 error, and they could give an indication of the likelihood of differences between the 2 groups, hence, they may help in future sample size calculations.

Fourthly, we assessed the incidence, magnitude and duration of significant hypertension during maintenance haemodialysis, and we identified the corresponding changes in other haemodynamic variables as well. Our results showed that significant acute BP elevations were encountered during haemodialysis, which were associated with a decreased SV and CO, along with a significantly increased TPR and a stable HR. We also demonstrated that sustained moderate to severe hypertension (SBP more than 160 mmHg) for more than 10 minutes occurred in 52% of the patients, and that sustained severe hypertension (SBP more than 180 mmHg) for more than 10 minutes occurred in 16% of the patients.

As discussed earlier, we have assigned the 25 patients into two further groups according to the incidence of severe hypertension episodes of SBP more than 180 mmHg for more than 10 minutes into group 3 (hypertension episode group) and group 4 (no hypertension episode group). In group 3, a significant elevation was encountered in the SBP and MBP during the hypertension episode. However, the DBP, HR, SV, CO and TPR remained stable during the hypertension episode. Also there were no significant changes between all pre and post dialysis haemodynamic variables.

Fifthly, we assessed the sensitivity of the conventional NIBP devices in detecting BP aberrations that are encountered during maintenance haemodialysis in comparison to the Finometer. We found that the NIBP conventionally set to take 2-3 readings during the haemodialysis session, was oblivious to all BP aberrations that were detected by the Finometer. It is also worth mentioning that 2 of our patients (patient 14 and 22) suffered both, an intradialytic hypotension episode of SBP < 90 mmHg and an intradialytic hypertension episode with SBP > 160 mmHg for more than 10 minutes in the same haemodialysis session.

Owing to our results and to the fact that both, intradialytic hypotension and hypertension are associated with poor patient outcomes [6, 204-206, 209, 210], it is obvious that the conventional NIBP monitors do not provide adequate patient safety during maintenance haemodialysis sessions, and that noninvasive continuous haemodynamic monitoring by the Finometer provides a safer option to maintenance haemodialysis patients.

We have also demonstrated a failed cardiovascular response to haemodialysis induced hypovolaemia with resultant hypotension. This was explained by the failed TPR response to haemodialysis induced hypovolaemia that was shown during both, the acute drops in BP and the intradialytic hypotension episodes.

We believe that the ability of the Finometer to give a better insight of the haemodynamic changes that occur at the time of intradialytic BP aberrations, may aid physicians to understand the patho-physiology behind those BP aberrations in cohorts of patients on chronic haemodialysis, subsequently, enabling the early detection and appropriate targeted management of those haemodynamic mishaps.

The major limitation to our work was the small sample size. As mentioned earlier, we have been granted ethics approval to perform an observational study, which will be a continuation of our work on a bigger scale.

In conclusion, continuous haemodynamic monitoring offers a safer option for patients on regular haemodialysis than conventional NIBP monitoring, through better detection of the frequently occurring BP aberrations and through aiding to diagnose their cause, hence, giving the physicians a better chance for prompt and proper management of these BP aberrations.

7 General discussion and conclusion

Induction of anaesthesia and haemodialysis are two clinical settings where vast changes in the haemodynamics are likely to occur, due to the introduction of drugs and techniques that have direct effects on the cardiovascular system in the former, and due to the removal of large volumes of fluids from the patients' circulation in a short period of time in the latter.

We tested the adequacy of current practice of BP measurement protocols in clinical settings of routine induction of anaesthesia and maintenance haemodialysis. This was accomplished by the following:

Initially, we assessed the feasibility of using the Finometer in both clinical settings of induction of anaesthesia and haemodialysis, by assessing its success rate in monitoring the BP and by comparing its measurements with those obtained by the conventional NIBP monitors for accuracy. Our results showed that the Finometer was successful and accurate in both our evaluations of induction of anaesthesia and haemodialysis, reflecting its feasibility for use in cohorts of patients undergoing routine induction of anaesthesia and maintenance haemodialysis.

Using the Finometer for haemodynamic monitoring during routine induction of anaesthesia and maintenance haemodialysis, we assessed the incidence, magnitude and duration of both, hypotension episodes and hypertension episodes. As mentioned earlier, both, significant hypotension and significant hypertension episodes that are encountered in anaesthesia and haemodialysis are known to be associated with poor patient outcomes. We found a high incidence of both significant hypotension and hypertension in induction of anaesthesia and haemodialysis. Furthermore, with the Finometer having the merit of recording haemodynamic variables such as the HR, SV, CO and TPR, we were able to obtain extra information about the patho-physiology of such BP aberrations.

We further assessed the sensitivity of the conventional intermittent NIBP devices in detecting the maximum changes in BP that occurred during routine induction of anaesthesia and maintenance haemodialysis in comparison with continuous noninvasive BP monitoring using the Finometer. It needs to be mentioned that we did not interfere with the frequency of the NIBP measurements that was predetermined by the attending anaesthetists or nephrologists. Our results clearly demonstrated that in cohorts of patients undergoing induction of anaesthesia and maintenance haemodialysis, where major haemodynamic changes are likely to occur, continuous noninvasive BP monitoring using the Finometer is superior to conventional intermittent NIBP measurement protocols in detecting BP aberrations. In conclusion, significant episodes of both, hypotension and hypertension commonly occur in routine induction of anaesthesia and maintenance haemodialysis. Continuous haemodynamic monitoring by the Finometer is more reliable than the conventionally used protocols of intermittent NIBP measurements in detecting these changes. The Finometer also provides extra haemodynamic information that can be used in pinning out the exact haemodynamic patho-physiology behind these BP aberrations.

These findings clearly suggest that continuous noninvasive haemodynamic monitoring using the Finometer is a safer option to patients undergoing routine induction of anaesthesia and maintenance haemodialysis than the conventional BP measurement protocols that involve BP measurements taken intermittently using NIBP devices.

8 Future directions

This thesis demonstrated that continuous noninvasive finger arterial pressure monitoring is feasible in cohorts of patients undergoing induction of anaesthesia and maintenance haemodialysis. Moreover, it was demonstrated that its use during induction of anaesthesia and maintenance haemodialysis may help improve the quality of patient care provided.

Our findings in this thesis have generated several related hypotheses and unanswered questions, which are discussed in the following sections.

8.1 Use of the Finometer in operating theatres

We assessed the feasibility of using the Finometer solely during the period of induction of anaesthesia. We have specifically chosen the time of induction of anaesthesia as we anticipated that major haemodynamic changes would occur, as a resultant of the simultaneous administration of several drugs and the employment of different techniques in a short period of time, which all have a direct effect on the cardiovascular system.

Further to our findings, an assessment of the feasibility of using the Finometer during the whole surgical procedure is warranted and we suggest that it includes the following:

- An assessment of the accuracy of the Finometer in terms of CO monitoring in comparison with a validated CO measurement technique.
- An assessment of whether if extra information provided by the Finometer can be used for fluid optimisation prior to surgery, and the impact of this on haemodynamic stability during anaesthesia.

As discussed in section 5.8, we used the Finometer to haemodynamically monitor one patient during the whole period of general anaesthesia in an attempt to illustrate the importance of running a service evaluation / study that assesses the feasibility of using the Finometer during the whole period of anaesthesia.

8.2 Use of the Finometer in haemodialysis

As previously mentioned, our findings in regards to the patients undergoing maintenance haemodialysis are limited by the small sample size. We were obliged to terminate our service evaluation and seek ethics approval after showing results that involved patient safety issues. However, we have been granted ethics approval for running an observational study, which will be a continuation of our assessment of the adequacy of patient safety provided by the currently used NIBP devices in maintenance haemodialysis on a bigger scale. We are currently in the process of collecting data.

We recommend the adoption of a study aiming to assess if patients who had an episode of hypotension respond in the same way in successive sessions. Also, to assess if the haemodynamic response of patients who have DM differs from that of those who do not have DM.

Lastly, a study to assess the effect of haemodialysis on endothelial function is encouraged.

8.3 Use of the Finometer in intensive care units

The feasibility of using the Finometer in critically ill patients is an area that needs to be explored. Hypothetically, if the Finometer was found feasible, it would help save valuable time and effort, due to the fact that it is reliable and easily applicable in a few minutes.

In patients who require invasive haemodynamic monitoring, it may be used temporarily to bridge the time period when lengthy invasive procedures are being installed to the patient. Moreover, its use in patients who are more stable may help avoid complications and extra costs of invasive procedures.

We recommend that the assessment of the feasibility of the Finometer in critically ill patients includes the following:

- An assessment of the success rate of the Finometer in generating haemodynamic recordings, especially that the critically ill patients have a high incidence of shock and vasoconstricted extremities. As mentioned earlier, vasoconstricted extremities may affect the ability of the Finometer's pulse plethysmograph to detect a pulse waveform from the finger.
- An assessment of the accuracy of the Finometer in terms of BP monitoring in comparison with the intra-arterial measurements.
- An assessment of the accuracy of the Finometer in terms of CO monitoring in comparison with a validated CO measurement technique.

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