OHST OXFORD HIGHER SPECIALTY TRAINING

Edited by
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Tanya Jones
Daniel Martin

ADVANCED TRAINING IN ANAESTHESIA

the essential curriculum

Oxford Higher Specialty Training: Advanced Training in Anaesthesia

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The Essential Curriculum

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JP

To Maryam and Oscar, and to my parents, Joan and the late Colin.

TJ

A huge thank you to Nick Stephenson, for all the reading, patience, and support.

DM

To Georgina, and my long-suffering family and friends.

All

Also to the late Dr John Ruston, FRCA (1955–2013), Consultant Anaesthetist to the Royal Free Hospital. We miss the benefits of his wisdom and experience.

Foreword

Drs Prout, Jones, and Martin have endeavoured to provide a comprehensive reference text for all those involved in the practice and safe delivery of anaesthesia, with the direct aim of following the Royal College of Anaesthetists published syllabus for the final FRCA examination. Succinct and clearly laid out, it enables readers to build on their knowledge of basic science, and provides fresh insight into the applications of basic science applied to clinical anaesthesia. Modern anaesthesia encompasses vast topics, and although a relatively young medical specialty, change is inevitable. The wealth of knowledge in medicine and how this impacts on the safe delivery of anaesthesia expands exponentially. The FRCA syllabus for examinations in anaesthesia is now clearly defined, but this is just the beginning. Interpretation and emphasis is always going to need guidance, and the authors have aspired to provide that guidance.

The book is divided into two main categories: the first is dedicated to applied basic science, and is followed by the application of basic science into clinical anaesthesia. This is exactly the stance taken by the Royal College of Anaesthetists with the final FRCA examination. The book is thoughtfully laid out, with very clear subject headings, in which information on clinical topics is easily available. It provides practical advice, based on sound physiology and pathophysiology to provide guidance for the safe delivery of modern anaesthesia, in the context of patients with much co-morbid disease. Appropriate references are provided at the end of each chapter for further in depth reading.

With the ageing population, anaesthesia will be required for an increasing number of individuals, with an ever expanding array of inherited and acquired conditions. Preoperative risk analysis features prominently in the chapters, with a commitment to optimising the medical conditions of the patient prior to anaesthesia and surgery. Recommendations for levels of monitoring go hand in hand with the choice of anaesthetic techniques for delivering safe anaesthesia, in order to ensure the best possible outcome for patients.

This is a concise reference text for revision purposes. It enables readers to build on their academic knowledge, and provides fresh insight into the applications of basic science relevant to safe clinical anaesthesia. The inclusion of over seventy enthusiastic young authors has ensured modern interpretation, and brought both great diversity and lateral thought to the book.

The book will be indispensable for candidates involved in sitting the final FRCA examination. Interestingly, it will also be of great value to those of us who sat the examination some time ago. Access to information in the 21st century is instant, but appropriate emphasis is always going to need guidance.

We have come a long way since W.T.G. Morton, William Squire, John Snow, and Joseph Clover began giving ether and chloroform to allow surgical intervention without time constraint. I am sure that they would all be amazed by the increasingly sophisticated and precise administrations of the modern speciality, particularly as it is delivered to so many people with such diverse conditions of ill-health.

Advanced Training in Anaesthesia will successfully complement other key medical texts as a reference guide that will be indispensable to those involved in the safe delivery of anaesthesia to an increasingly aged and co-morbid population.

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Preface

The principal aim of this book is to assist candidates preparing for final examinations in anaesthesia, both in the UK and elsewhere.

We very much hope, however, that the book will find a place beyond the requirements of exam preparation. We have tried to produce a stand-alone account of the essentials of our specialty and its subspecialties that will provide a ready source of reference in most situations.

The Final FRCA (Fellowship of the Royal College of Anaesthetists) examination in the UK is a major hurdle in anaesthetic training, representing the highest professional qualification in the specialty and the gateway to specialist training at an advanced level.

The book attempts to follow closely the recently revised college syllabus, published in August 2010.[1] The syllabus is extensive, comprising both applied basic sciences, and the clinical practice of anaesthesia, intensive care, and pain management. Any subject listed in the syllabus may appear in the examination: we have, therefore, adhered to it closely and attempted to be comprehensive in our presentation of topics.

This book aims to cover the required knowledge in the necessary detail, and is designed as a companion volume to *Training in Anaesthesia: The Essential Curriculum*, published by Oxford University Press in 2010 and which is aimed at the Primary FRCA. Knowledge of the Primary syllabus is assumed by the Final examiners and is often a stumbling block in the Final examination.

It cannot be stressed too highly that pure basic science topics are frequently examined in the Final FRCA, and candidates would be most unwise not to take account of this during their revision. Together, the two volumes are intended to be a comprehensive guide to the FRCA examination.

In this volume, topics in applied basic science are presented in a systems-based format as laid out in the college syllabus. The sections that follow cover all the major clinical subspecialties. The double-page spread is intended to provide a succinct format for learning, yet containing all the important detail.

References and suggestions for further reading from the recent literature are included for readers who wish to explore subjects in more depth.

The editors have been fortunate to recruit both distinguished contributors who are leaders in their field, but also trainees—who have made an important contribution to ensure that the resulting information meets their needs.

We are hugely grateful to everyone at Oxford University Press, most especially to Christopher Reid who offered such encouragement after our initial approach, to Fiona Richardson and Geraldine Jeffers who displayed powers of extreme patience (sorely tested!) whilst awaiting the manuscript, and to Abigail Stanley and Jane Williams for seeing the project through to publication and beyond.

We hope that this will be the first of many editions and look forward to your feedback such that future editions can evolve according to the needs and wishes of the readership we seek to serve.

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Tanya Jones
Daniel Martin
London 2013

[1] www.rcoa.ac.uk/system/files/TRG-CCT-ANNEXC.pdf

Contents

Abbreviations

6MWT	Six-minute walk test
AAA	Abdominal aortic aneurysm
AAGBI	Association of Anaesthetists of Great Britain and Ireland
AASM	American Academy of Sleep Medicine
ABG	Arterial blood gas
ABPM	Ambulatory blood pressure monitoring
ACC	American College of Cardiology
ACEI	Angiotensin converting enzyme inhibitor
ACT	Activated clotting time
ACTH	Adrenocorticotrophic hormone
ADH	Anti-diuretic hormone
ADP	Adenosine diphosphate
ADQI	Acute dialysis quality initiative
AED	Antiepileptic drug
AEP	Auditory evoked potential
AF	Atrial fibrillation
AFOI	Awake fibreoptic intubation
AG	Anion gap
AHA	American Heart Association
AHI	Apnoea-hypopnoea index
AKI	Acute kidney injury
ALA	Aminolaevulinic acid
ALS	Advanced Life Support
cAMP	cyclic adenosine monophosphate
ANP	Atrial natriuretic peptide
ANS	Autonomic nervous system
AP	Anteroposterior
APACHE	Acute Physiology and Chronic Health Evaluation
APC	Activated protein C
APH	Antepartum haemorrhage
APTT	Activated partial thromboplastin time
AR	Absolute risk
ARR	Absolute risk reduction
ARA	Angiotensin receptor antagonist
ARDS	Acute respiratory distress syndrome
ARVD	Arrhythmogenic right ventricular dysplasia
ASA	American Society of Anesthesiologists
ASD	Atrial septal defect
AT	Anaerobic threshold *or* antithrombin *or* angiotesin
ATLS	Advanced Trauma Life Support
ATN	Acute tubular necrosis
ATP	Adenosine triphosphate
AV	Atrioventricular
AVN	AV node/nodal
AVNRT	AV nodal re-entrant tachycardia
BiPAP	Bi-level positive airways pressure
BMR	Basal metabolic rate
BNP	Brain natriuretic peptide
BP	Blood pressure
BPEG	British Pacing and Electrophysiology Group
BPF	Bronchopleural fistula
BTS	British Thoracic Society
CABG	Coronary artery bypass grafting
CAC	Coronary artery calcium
CAD	Coronary artery disease
CARP	Coronary Artery Revascularisation Prophylaxis
CATS	Childrens' Acute Transport Service (UK)
CCB	Calcium channel blocker
CCF	Congestive cardiac failure
CCO	Critical care outreach
CCOM	Continuous cardiac output monitoring
CCTA	Coronary CT angiography
CHD	Congenital heart disease
CI	Confidence interval
CICV	Can't intubate, can't ventilate
CIN	Contrast-induced nephropathy
CMAP	Compound muscle action potential
CMRI	Coronary MRI
$CMRO_2$	Cerebral metabolic rate of oxygen consumption
CMV	Cytomegalovirus
CNS	Central nervous system
CO	Cardiac output *or* carbon monoxide
CO_2	Carbon dioxide
COPD	Chronic obstructive pulmonary disease
COX	Cyclo-oxygenase
CPAP	Continuous positive airways pressure
CPB	Cardiopulmonary bypass
CPET	Cardiopulmonary exercise testing
CPP	Cerebral perfusion pressure
CRBSI	Catheter-related bloodstream infection
CRMD	Cardiac rhythm management device
CRP	C-reactive protein
CRT	Cardiac resynchronization therapy

CSE	Combined spinal epidural
CSF	Cerebrospinal fluid
CT	Computed tomography
CTPA	Computed tomography pulmonary angiography
CVC	Central venous catheter
CVP	Central venous pressure
CVS	Cardiovascular system
CW	Continuous wave
CXR	Chest X-ray
DAS	Difficult Airway Society
DASI	Duke Activity Status Index
DC	Direct current
DCM	Dilated cardiomyopathy
DHCA	Deep hypothermic circulatory arrest
DI	Diabetes insipidus
DIC	Disseminated intravascular coagulation
DNA	Deoxyribonucleic acid *or* Did not attend
DPP	Dipeptidyl peptidase
DPPC	Dipalmitoyl phosphatidylcholine
DSE	Dobutamine stress echocardiography
DVT	Deep vein thrombosis
EACA	Epsilon-aminocaproic acid
EBV	Epstein–Barr virus
ECF	Extracellular fluid
ECG	Electrocardiogram
ECHO	Echocardiography
ECT	Electroconvulsive therapy
EDV	End-diastolic volume
EEG	Electroencephalogram
ELISA	Enzyme-linked immunosorbent assay
EMG	Electromyogram
EMI	Electromagnetic interference
ENT	Ear, nose, and throat
ERCP	Endoscopic retrograde cholangiopancreatography
ERPC	Evacuation of retained products of conception
ESA	European Society of Anaesthesiology
ESC	European Society of Cardiology
ESLD	End-stage liver disease
ESRD	End-stage renal disease
ETT	Endotracheal tube
EVAR	Endovascular aneurysm repair
EVD	External ventricular drain
EVLW	Extravascular lung water
EWS	Early warning score
FBC	Full blood count
FEV_1	Forced expiratory volume in one second
FFP	Fresh frozen plasma
FMV	Facemask ventilation
FNA	Fine needle aspiration
FRC	Functional residual capacity
FT	Flow time
FVC	Forced vital capacity
GA	General anaesthesia
GABA	γ-aminobutyric acid
GCS	Glasgow Coma Scale
GEDV	Global end-diastolic volume
GFR	Glomerular filtration rate
GI	Gastrointestinal
GIFTASUP	Guidelines on intravenous fluid therapy in adult surgical patients
GLP	Glucagon-like peptide
cGMP	cyclic guanosine monophosphate
GORD	Gastro-oesophageal reflux disease
Gp	Glycoprotein
G6PD	Glucose-6-phosphate dehydrogenase
GCSE	Generalised convulsive status epilepticus
GTN	Glyceryl trinitrate
GTP	Guanosine triphosphate
GUCH	Grown-up congenital heart disease
HAPE	High altitude pulmonary oedema
Hb	Haemoglobin
HCM	Hypertrophic (obstructive) cardiomyopathy
HDL	High density lipoprotein
HDU	High dependency unit
HES	Hydroxyethyl starch
HFO	High-frequency oscillation
HFPEF	Heart failure with preserved ejection fraction
HFREF	Heart failure with reduced ejection fraction
HIT	Heparin-induced thrombocytopenia
HOPE	Heart Outcomes Prevention Evaluation
HPA	Hypothalamic–pituitary–adrenal (axis)
HR	Heart rate
HRT	Hormone replacement therapy
5-HT	5-hydroxytryptamine
IABP	Intra-aortic balloon pump
IAP	Intra-abdominal pressure
ICD	Implantable cardioverter defibrillator
ICF	Intracellular fluid
ICP	Intracranial pressure
ICRP	International Commission on Radiological Protection
ICS	Intraoperative cell salvage *or* Intensive Care Society
IHD	Ischaemic heart disease
IL	Interleukin
INR	International normalized ratio
IOP	Intraocular pressure
IPPV	Intermittent positive pressure ventilation
ISWT	Incremental shuttle walk test
ITU	Intensive therapy unit
IV	Intravenous
IVC	Inferior vena cava
LA	Local anaesthetic
LAD	Left anterior descending (coronary artery)
LAP	Left atrial pressure
LASER	Light amplification by stimulated emission of radiation
LAUP	Laser-assisted uvuloplasty
LBBB	Left bundle branch block
LDL	Low density lipoprotein

LED	Light-emitting diode
LFTs	Liver function tests
LiDCO	Lithium dilution cardiac output
LIMA	Left internal mammary artery
LMWH	Low-molecular-weight heparin
LODS	Logistic Organ Dysfunction Score
LOS	Lower oesophageal sphincter
LV	Left ventricular
LVAD	Left ventricular assist device
LVEDP	Left ventricular end-diastolic pressure
LVEDV	Left ventricular end-diastolic volume
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
LVOT	Left ventricular outflow tract
MAP	Mean arterial pressure
MA	Mean acceleration
MAP	Mean arterial pressure
MELD	Model for end-stage liver disease
MEP	Motor evoked potential
MET	Metabolic equivalent (of task)
MEWS	Modified early warning system
MI	Myocardial infarction
MIBG	Meta-iodobenzylguanidine
MILS	Manual in-line stabilization
MODS	Multiple Organ Dysfunction Score
MOF	Multiple organ failure
MPAP	Mean pulmonary artery pressure
MPI	Myocardial perfusion imaging
MPM	Mortality Prediction Model
MRI	Magnetic resonance imaging
NAP	National Audit Project
NASPE	North American Society of Pacing and Electrophysiology
NBM	Nil by mouth
NCEPOD	National Confidential Enquiry into Patient Outcome and Death
NGT	Nasogastric tube
NICE	National Institute for Health and Clinical Excellence
NIV	Non-invasive ventilation
NHS	National Health Service (UK)
NMBA	Neuromuscular blocking agent
NMDA	N-methyl-D-aspartic acid
NNT	Number needed to treat
NO	Nitric oxide
NOD	Nucleotide oligomerization domain
NOS	Nitric oxide synthetase
NPSA	National Patient Safety Agency
NREM	Non-rapid eye movement
NS	Normal saline
NSAID	Non-steroidal anti-inflammatory drug
NSTEMI	Non ST-elevation myocardial infarction
NSVT	Non-sustained ventricular tachycardia
NTS	Nucleus (of) tractus solitarius
NYHA	New York Heart Association
ODM	Oesophageal Doppler monitor
OLV	One lung ventilation
OPCAB	Off-pump coronary artery bypass
OR	Odds ratio
OSA	Obstructive sleep apnoea
PA	Pulmonary artery
PAC	Pulmonary artery catheter
PAO_2	Alveolar partial pressure of oxygen
PaO_2	Arterial partial pressure of oxygen
PAP	Pulmonary artery pressure
PAH	Pulmonary arterial hypertension
PAOP	Pulmonary artery occlusion pressure
PCA	Patient-controlled analgesia
PCEA	Patient-controlled epidural analgesia
PCI	Percutaneous coronary intervention
PDA	Patent ductus arteriosus or posterior descending (coronary) artery
PDEI	Phosphodiesterase inhibitor
PDPH	Post-dural puncture headache
PE	Pulmonary embolism
PEA	Pulseless electrical activity
PEEP	Positive end-expiratory pressure
PFO	Patent foramen ovale
PHT	Pulmonary hypertension
PICC	Peripherally-inserted central catheter
PiCCO	Pulse contour cardiac output
PICU	Paediatric intensive care unit
PMN	Polymorphonuclear neutrophil
PMP	Pain management programme
PND	Paroxysmal nocturnal dyspnoea
PNI	Peripheral nerve injury
PNS	Parasympathetic nervous system
POCT	Point of care testing
POISE	PeriOperative Ischaemia Study Evaluation
POMS	Postoperative Morbidity Survey
PONV	Postoperative nausea and vomiting
POSSUM	Physiological and Operative Severity Score for Enumeration of Mortality and Morbidity
PPCM	Peripartum cardiomyopathy
PPHN	Persistent pulmonary hypertension of the newborn
PPV	Pulse pressure variation
PRCs	Packed red cells
PRES	Posterior reversible encephalopathy syndrome
PRR	Pattern recognition receptor
PT	Prothrombin time
PTFE	Polytetrafluoroethylene
PV	Peak velocity
PVR	Pulmonary vascular resistance
PVB	Paravertebral block
PVR	Pulmonary vascular resistance
PW	Pulsed wave
RAAA	Ruptured abdominal aortic aneurysm
RAAS	Renin–angiotensin–aldosterone system
RCoA	Royal College of Anaesthetists (UK)
RCM	Restrictive cardiomyopathy

RCT	Randomized controlled trial
RCV	Red cell volume
REM	Rapid eye movement
RFTs	Respiratory function tests
RIFLE	Risk-Injury-Failure-Loss-Endstage
RIG-1	Retinoic acid-inducible gene-1
RIJV	Right internal jugular vein
ROC	Receiver operating curve
ROS	Reactive oxygen species
ROTEM®	Rotational thromboelastometry
RR	Relative risk
RRR	Relative risk reduction
RRT	Renal replacement therapy *or* rapid response team
RS	Respiratory system
RSI	Rapid sequence induction
RV	Right ventricular
RVOT	Right ventricular outflow tract
SAH	Subarachnoid haemorrhage
SAM	Systolic anterior motion
SAPS	Simplified Acute Physiology Score
SBP	Systolic blood pressure
SCD	Sudden cardiac death
SCI	Spinal cord injury
SIADH	Syndrome of inappropriate antidiuretic hormone (secretion)
SID	Strong ion difference
SIRS	Systemic inflammatory response syndrome
SLE	Systemic lupus erythematosus
SNS	Sympathetic nervous system
SR	Systematic review
SSRI	Selective serotonin reuptake inhibitor
SOB	Shortness of breath
SOFA	Sequential Organ Failure (score)
SSEP	Somatosensory evoked potential
SSRI	Selective serotonin reuptake inhibitor
STEMI	ST-elevation myocardial infarction
SvO_2	Mixed venous oxygen saturation
SV	Stroke volume
SVR	Systemic vascular resistance
SVV	Stroke volume variation
TBI	Traumatic brain injury
TBSA	Total body surface area
TCA	Tricyclic antidepressant
TCI	Target controlled infusion
TEBI	Thoracic electrical bioimpedance
TEBR	Thoracic electrical bioreactance
TEG®	Thromboelastography
TF	Tissue factor
TFPI	Tissue factor pathway inhibitor
TGA	Transposition of the great arteries
TIA	Transient ischaemic attack
TIPS	Transjugular intrahepatic portosystemic shunt
TIVA	Total intravenous anaesthesia
TLC	Total lung capacity
TLR	Toll-like receptor
TNF	Tumour necrosis factor
TOE	Transoesophageal echocardiography
ToF	Train of four
tPA	Tissue plasminogen activator
TPN	Total parenteral nutrition
TPDT	Transpulmonary dilutional technique
TPN	Total parenteral nutrition
TSH	Thyroid-stimulating hormone
TTE	Transthoracic echocardiography
TUR	Transurethral resection
UA	Unstable angina
UFH	Unfractionated heparin
UPPP	Uvulo-palato-pharyngoplasty
VAD	Ventricular assist device
VATS	Video-assisted thoracoscopic surgery
VF	Ventricular fibrillation
VKA	Vitamin K antagonist
VMA	Vannilyl mandelic acid
VOTO	Ventricular outflow obstruction
VRII	Variable rate insulin infusion
VSD	Ventricular septal defect
VT	Ventricular tachycardia *or* ventilatory threshold
VTE	Venous thromboembolism
vWF	Von Willebrand's factor
WHO	World Health Organization

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Part 1

Applied Basic Science

Chapter 1

Cardiovascular system

1.1 An approach to cardiovascular risk assessment

Perioperative risk

Patients undergoing surgery may suffer complications that result in life-altering morbidity or even mortality. Assessment of perioperative risk involves consideration both of the premorbid state of the patient along with the nature, extent, and urgency of the surgery to be performed.

Risk may be modified by optimization of the patient's underlying medical conditions and appropriate management intra- and postoperatively.

Whilst no surgical intervention is without risk, a thorough knowledge of how to identify and manage those patients identified as 'high risk' may lead to improved outcomes.

Perioperative cardiovascular complications are a major source of mortality and morbidity with an overall incidence of cardiac death in the region of 0.5–1.5%. Tissue injury secondary to surgery triggers a stress response that can detrimentally affect the cardiovascular system. Myocardial oxygen demand may rise and lead to ischaemia, arrhythmia, infarction, and heart failure. In addition, inter-compartmental fluid shifts, haemodynamic stresses, altered coagulation and disruption of regular medications can significantly exacerbate cardiovascular pathology.

Cardiac risk index

The first widely used cardiac risk index was proposed by Goldman et al. in 1977 with the aim of evaluating cardiac risk in non-cardiac surgery. Nine criteria were identified by multivariable analysis that independently predicted increased risk (see Box 1.1).

Box 1.1 Goldman risk criteria

- Preoperative 3rd heart sound and/or raised jugular venous pressure
- Myocardial infarction (MI) in the preceding 6 months
- >5 premature ventricular contractions per minute
- A cardiac rhythm other than sinus rhythm or the presence of premature atrial contractions on preoperative electrocardiogram (ECG)
- Age >70 years
- Intraperitoneal, intrathoracic, or aortic surgery
- An emergency operation
- Significant aortic stenosis
- Poor general medical condition.

From *The New England Journal of Medicine*, Goldman et al., 'Multifactorial Index of Cardiac Risk in Noncardiac Surgical Procedures', 297, 16, Copyright © 1977, Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

The Goldman criteria were modified in 1986 by Detsky et al. to form the Modified Cardiac Risk Index, and again in 1999 by Lee et al, resulting in the Revised Cardiac Risk Index. In the latter, patients are categorized according to the presence of 0, 1, 2, or ≥3 risk factors (see Box 1.2).

A number of taskforce guidelines have been published by the American College of Cardiology (ACC)/American Heart Association (AHA) and European Society of Cardiology (ESC)/European Society of Anaesthesiology (ESA). These contain a series of consecutive suggestions which create a framework for perioperative cardiovascular evaluation in non-cardiac surgery.

Box 1.2 Revised Cardiac Risk Index criteria

- High-risk surgical procedure
- History of ischaemic heart disease
- History of congestive heart failure
- History of cerebrovascular disease
- Preoperative insulin therapy for diabetes
- Preoperative serum creatinine >177μmol/L.

With kind permission from Springer Science+Business Media: *Journal of General Internal Medicine*, 'Predicting cardiac complications in patients undergoing non-cardiac surgery', 1, 4, 1986, pp. 211–19, AS Detsky et al.

The 2007 ACC/AHA guidelines stratify cardiac conditions into those that require immediate investigation, those that may be associated with increased risk, and those that are not (see Box 1.3). The 2009 ESC/ESA guidelines outline a stepwise approach to evaluating a patient, with the aim of creating an individualized cardiac risk assessment. They make suggestions regarding optimization prior to surgery, and emphasize the lack of evidence to support preoperative coronary revascularization as a risk reduction strategy (see section 1.5 and Box 1.4).

Box 1.3 Guidelines for preoperative cardiac evaluation

Active cardiac conditions requiring further evaluation:

- Unstable coronary syndromes
- Decompensated heart failure
- Significant arrhythmias
- Severe valvular disease.

Clinical risk factors that may impact upon outcome:

- History of ischaemic heart disease
- History of compensated or prior heart failure
- History of cerebrovascular disease
- Diabetes mellitus
- Renal insufficiency.

Factors not proven to increase perioperative risk:

- Advanced age
- Abnormal ECG
- Rhythm other than sinus
- Uncontrolled systemic hypertension.

Reprinted from Journal of American College of Cardiology, 50, 17, Fleisher et al., 'ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery), pp. e159–e242, Copyright 2007, with permission from Elsevier and American College of Cardiology, Foundation of the American Heart Association Inc.

Box 1.4 A stepwise approach to cardiac risk assessment

1. Assess the urgency of the surgical procedure.
2. Does the patient have an unstable cardiac condition (for example, unstable angina or acute heart failure)? If so, assess and treat.
3. Assess the risk of the surgical procedure.
4. Consider the patient's functional capacity.
5. Review (and aim to continue) chronic aspirin therapy.
6. Consider pharmacological interventions ± non-invasive testing in patients found to have reduced functional capacity.
7. Review the results of non-invasive tests to determine whether or not intervention is appropriate (for example, revascularization).

The risk attached to the surgical procedure itself is categorized according to the 30-day incidence of adverse cardiac events (cardiac death or MI). Three categories of surgical risk are identified (Table 1.1).

Table 1.1 Risk of cardiac death or myocardial infarction within 30 days of surgery

Low risk: <1%	Intermediate risk: 1–5%	High risk: >5%
Breast	Abdominal	Aortic and major vascular surgery
Dental	Carotid	Peripheral vascular surgery
Endocrine	Peripheral arterial angioplasty	
Eye	Endovascular aneurysm repair	
Gynaecology	Head and neck surgery	
Reconstructive	Neurological	
Minor orthopaedic	Major orthopaedic	
Minor urology	Major urology	

Referral for preoperative investigations

An ECG should be performed in all patients who have cardiac risk factors, and should be considered in those without risk factors who are scheduled for intermediate or high-risk surgery. Non-invasive investigations must be specifically aimed at identifying and quantifying underlying left ventricular dysfunction, myocardial ischaemia, and valvular dysfunction. These include the exercise ECG (stress test) and echocardiography (ECHO). The rationale for these tests should be similar to that applied to patients with symptoms of cardiovascular disease in the non-surgical setting. An investigation should be ordered only when the results of the test would lead to a clear change in the perioperative management strategy (see section 1.4). In the case of emergency surgery, investigations are limited by the timeframe in which the operation must be performed.

Patient age

The chronological age of a patient accounts for only a small increase in overall perioperative risk, and in isolation is, therefore, a poor predictor of complications. However, increasing age is associated with accumulating comorbidities, each of which requires careful consideration preoperatively and may contribute to increased risk. The prevalence of cardiovascular disease increases with age along with a decline in respiratory and renal function.

Measures of functional capacity

Functional capacity is the ability to perform physical exercise and can be assessed by questioning or formal testing. Physical fitness correlates with the ability to increase systemic oxygen delivery in order to match the rise in oxygen consumption (VO_2) in the perioperative period that accompanies major surgery.

The Duke Activity Status Index (DASI)

Simple questioning about perceived maximal activity can provide an insight into limitations during daily life. The DASI is a questionnaire that requires the patient to indicate whether he or she can perform specific tasks and assigns scores accordingly. The scores from the DASI are known as a metabolic equivalent of task (MET), where 1 MET (see Box 1.5) is equivalent to basal metabolic rate (a VO_2 of approximately 3.5mL/kg/min).

Box 1.5 Metabolic equivalents of task (METs)

1 MET:	Eating, washing.
3 METs:	Walking 100m on flat ground.
4 METs:	Walking up one flight of stairs.
10 METs:	Strenuous sporting activities.

The sum of METs from the DASI (maximum is 58.2) can then be used to estimate an individual's peak oxygen uptake:

$$\text{Estimated peak } VO_2\ (\text{mL/kg/min}) = (0.43) \times \text{DASI} + 9.6$$

The DASI has been shown to correlate well with perioperative outcome. The inability to perform exercise at less than 4 METs is associated with an increased incidence of postoperative complications. This form of assessment is, however, liable to bias if the patient's completion of the questionnaire is inaccurate.

The incremental shuttle walk test (ISWT)

During an ISWT, the patient must walk back and forth between two markers placed 10m apart on flat ground. The pace is to the sound of a tone that begins at 30m per minute and increases by 10m per minute each minute after that. The subject must continue walking until exhausted or unable to complete the 10m distance within the time of two tones. The outcome measured is the total distance walked. There is a linear relationship between systemic VO_2 and walking distance and when compared to treadmill testing, peak VO_2 can be accurately predicted from the ISWT distance.

Cardiopulmonary exercise testing (CPET)

CPET can provide detailed information that may allude to underlying cardiopulmonary limitations and disease. It is a non-invasive test with minimal associated risks. It requires the patient to exercise until exhaustion on a bicycle ergometer whilst respiratory gas exchange is measured at the mouth. Oxygen uptake and carbon dioxide production is calculated and along with heart rate, these data can be used to calculate a number of variables that may assist perioperative risk stratification (see section 1.2).

Further reading

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1.2 Cardiopulmonary exercise testing

A cardiopulmonary exercise test (CPET) provides objective measures of cardiovascular, respiratory, and circulatory physiology that are related to physical fitness, pathophysiology, and perioperative survival. This is in contrast to many alternative assessment modalities, which are only able to summarize resting single organ function. CPET is a dynamic measure of functional capacity and is used widely in the field of sports and exercise medicine.

The physiology of exercise

The primary measure of the CPET is oxygen uptake (VO_2), which is expressed in either mL/min or normalized for the patient's weight as mL/kg/min. Oxygen uptake increases linearly during progressively more strenuous exercise and two points of significance during this increase are the ventilatory threshold (VT), commonly referred to as the anaerobic threshold (AT), and maximal oxygen uptake (VO_2max). The latter is a plateau in VO_2 that is reached at maximal exercise capacity and is a reliable measure of physical fitness. If no plateau is achieved, the maximum VO_2 attained is referred to as VO_2 peak. VO_2max is determined by factors that govern oxygen delivery such as respiratory, cardiovascular, and circulatory function and influenced by gender, age, level of physical fitness, and a degree of genetic inheritability. Consideration of the Fick equation emphasizes the importance of oxygen delivery in determining VO_2 max and highlights the mathematical coupling between VO_2 and oxygen delivery (see Box 1.6).

Box 1.6 The Fick equation for oxygen consumption

$$VO_2 = (HR \times SV) \times (CaO_2 - CvO_2)$$

CaO_2 = arterial oxygen content; CvO_2 = mixed venous oxygen content; HR = heart rate; SV = stroke volume

AT is the VO_2 during an increasing exercise load at which metabolism switches to a predominantly anaerobic source of energy rather than an aerobic one. It coincides with the point at which there is a sharp upwards inflection in the serum lactate concentration and production of additional carbon dioxide.

Practical considerations

To perform a CPET requires an exercise stimulus, a means of measuring gas exchange at the nose or mouth, and a system to collate the data. Exercise on an electronically braked bicycle ergometer produces the most repeatable data and is preferable to a treadmill in a clinical setting. For patients with lower limb incapacity it is possible to perform a CPET using a hand-crank system.

Breath-by-breath gas analysis provides the most reliable means of data collection and can be achieved via a tight fitting mask or mouthpiece. The concentration of oxygen and carbon dioxide is measured along with gas flow; computer software then calculates the volume of each gas inspired and expired per minute. Many other respiratory values can also be calculated. Additional physiological measurements are collected during the test, including heart rate, ECG, and non-invasive blood pressure.

The commonest exercise protocol is one of a continuous 'ramped' workload based upon predictions of the patient's VO_2 max. According to age, gender, weight, and level of physical fitness a ramp gradient is selected that will result in a test lasting 10–12min. Perioperative patients commonly require a ramp of 10 to 15 watts per minute.

The CPET has a reported mortality of 2–4 per 100 000 tests and is conducted in the presence of an exercise physiologist and physician. A variety of contraindications to CPET exist (see Box 1.7).

Box 1.7 Contraindications to CPET

Absolute

- Acute MI
- Unstable angina
- Unstable arrhythmias
- Syncope
- Endocarditis or myocarditis
- Severe aortic stenosis
- Uncontrolled heart failure
- Acute pulmonary embolism
- Aortic dissection
- Uncontrolled asthma
- Pulmonary oedema
- Resting SaO_2 ≤85%
- Respiratory failure
- Other medical disorders affecting performance
- Inability to cooperate.

Relative

- Left main stem disease
- Moderate valvular stenosis
- Severe untreated hypertension
- Arrhythmias
- High-degree AV block
- Hypertrophic cardiomyopathy
- Pulmonary hypertension
- Advanced pregnancy
- Electrolyte abnormalities.

Patients are asked to pedal on the bicycle ergometer for as long as possible, stopping only when exhausted. A clinician may halt a test if concerned with the patient's condition or data.

Data presentation

Data are traditionally presented in a 'nine-panel plot' that consists of nine graphs of different physiological measurement collected during the CPET (Fig. 1.1). Salient values such as VT, VO_2 max (or peak), the ventilatory equivalents for oxygen (Ve/VO_2) and carbon dioxide (Ve/VCO_2) will be highlighted and accompanied by a description of the nine-panel plot and of the patient's performance during exercise. From this information clinicians should be able to derive an indication of perioperative risk.

Determination of anaerobic threshold

For perioperative patients the most frequently reported measurement from the CPET is AT. Cardiopulmonary disease that limits systemic oxygen delivery will reduce both AT and VO_2 max.

The commonest method of determining AT from the nine-panel plot is by the 'V-slope' method. At a cellular level, anaerobic metabolism generates lactate and hydrogen ions. The latter combine with bicarbonate and lead to increased carbon dioxide production:

$$H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow H_2O + CO_2$$

This increase in carbon dioxide production can be detected at the mouth during exercise. After the test, in a plot of VO_2 against VCO_2 there will be a marked change in the slope of the line, and the VO_2 at which this occurs is the AT (Fig. 1.2).

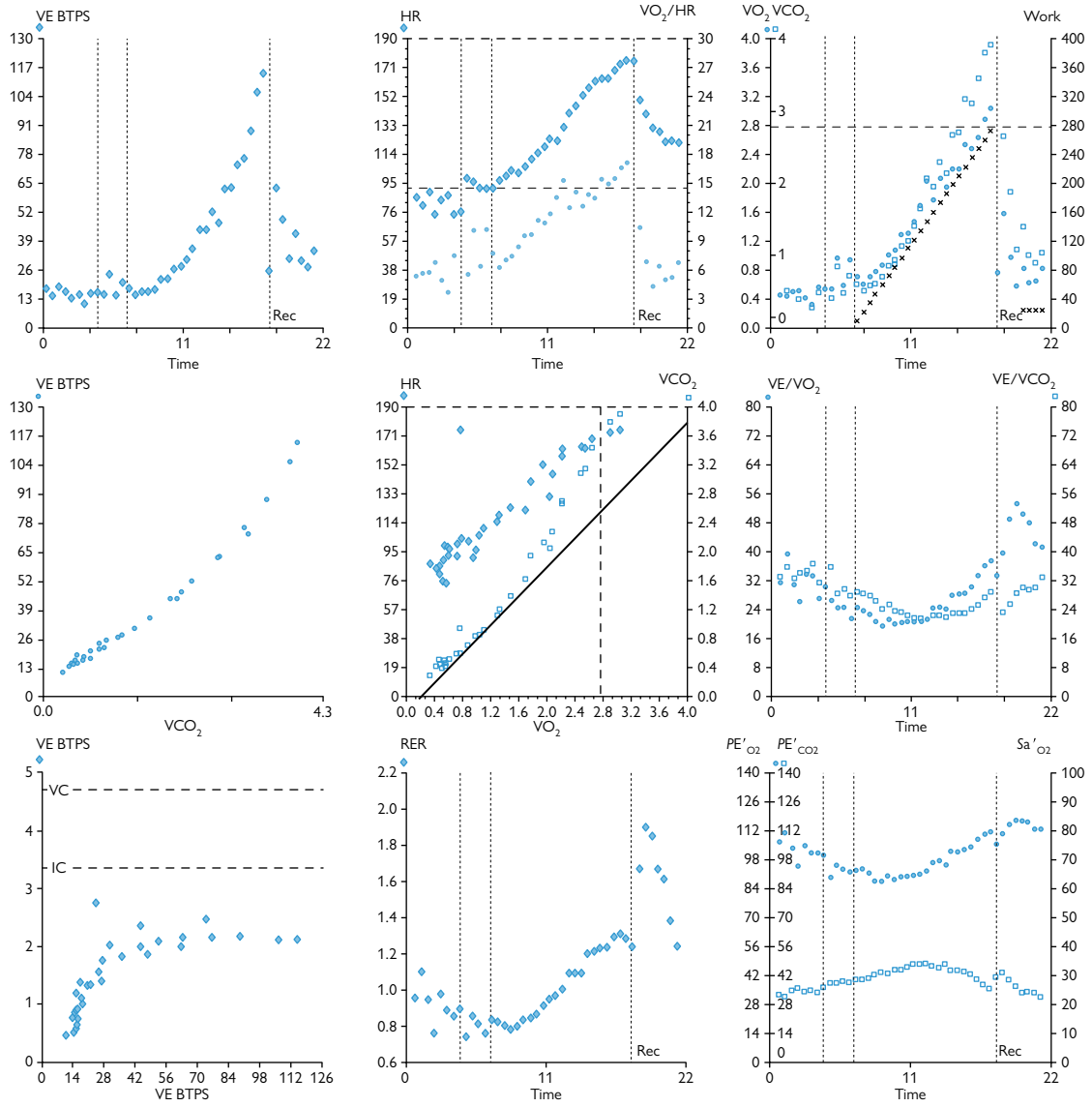

Fig. 1.1 Cardiopulmonary exercise testing: a nine-panel plot. Reproduced from Neil Agnew, 'Preoperative cardiopulmonary exercise testing', *Continuing Education in Anaesthesia, Critical Care, and Pain*, 2010, 10, 2, pp. 33–37, by permission of Oxford University Press and the *British Journal of Anaesthesia*. doi:10.1093/bjaceaccp/mkq001.

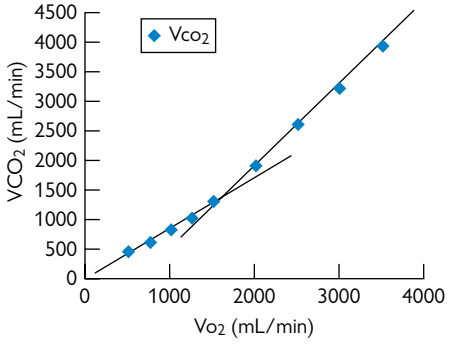

Fig. 1.2 V-slope method for determining ventilator threshold. Reproduced from *Postgraduate Medical Journal*, Albouaini et al., 83, 985, pp. 675–682, copyright 2007, with permission from BMJ Publishing Group Ltd. doi:10.1136/hrt.2007.121558.

It can be estimated by placing a line with a slope of 1 against the VO_2: VCO_2 plot and marking the point of inflection. A number of other changes occur at AT that can be used to verify its presence:

- The respiratory exchange ratio (RER) is the ratio of carbon dioxide output and oxygen uptake (VCO_2/VO_2). It is roughly equivalent to the respiratory quotient (RQ) during strict steady state resting conditions and rises to >1.0 at AT.
- The ventilatory equivalents for oxygen and carbon dioxide are calculated by dividing minute volume (Ve) by the expired volume of the desired gas (Ve/VO_2). This dimensionless value can be considered as a measure of ventilatory efficiency, indicating the magnitude of minute volume required to expire a litre of oxygen (or carbon dioxide). Both Ve/VO_2 and Ve/VCO_2 rise after AT, the latter occurring slightly later than the former.
- End-tidal oxygen rises at AT.

Clinical significance of CPET results

Physicians have used CPET for many years to determine the cause of dyspnoea in patients and to investigate respiratory and cardiovascular disorders. Only recently has CPET gained popularity for the preoperative assessment of high-risk surgical patients.

A low AT is associated with poor outcome postoperatively, and high risk is suggested when the AT is <11mL/kg/min. Knowledge of a patient's AT can facilitate postoperative triage to a specific level of care. In this way, patient outcome may be improved, length of hospital stay reduced, and resources saved.

Studies have confirmed the usefulness of CPET in specific cohorts of patients including those undergoing aortic aneurysm repair, oesophagectomy, and liver transplantation.

The ventilatory equivalent for oxygen (Ve/VO_2) is also a useful indicator of functional capacity. The ability to train patients and improve physical fitness prior to surgery is an interesting prospect as part of preoperative optimization.

Oxygen pulse is a term that describes the oxygen uptake per heartbeat. It is calculated as VO_2/heart rate. Rearrangement of the Fick equation shows that it is equal to $SV \times (CaO_2 - CvO_2)$ that is, the product of stroke volume and oxygen extraction. Oxygen pulse is depicted on the nine-panel plot and generally increases during exercise. A flattening off of this upwards trajectory is a strong indicator of cardiac limitation and usually a sign of ischaemic heart disease.

Further reading

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1.3 Special investigations in the assessment of cardiac disease

The initial approach to assessing cardiac risk (cardiac death or non-fatal MI) in patients undergoing non-cardiac surgery is described in section 1.1. In summary, *three* components contribute to this risk:

- Patient-specific variables
- Exercise capacity
- Surgery-specific risk.

Patients at low risk generally require no further evaluation before surgery.

Patients at high risk (e.g. those with symptoms of unstable coronary disease) frequently undergo coronary angiography.

Patients who are judged to be at intermediate risk on clinical criteria are essentially a heterogeneous group in whom non-invasive testing seeks to identify a subgroup with significant cardiac disease (Fig. 1.3).

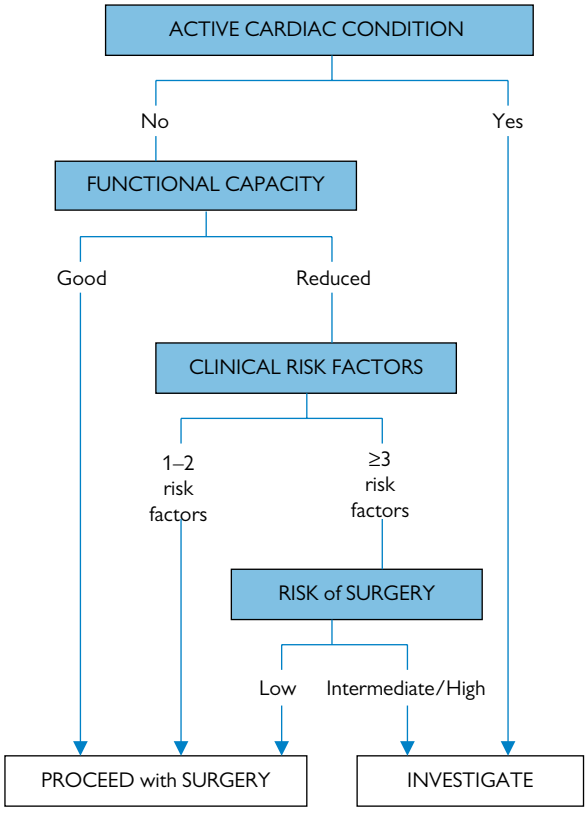

Fig. 1.3 Algorithm for special investigations before non-cardiac surgery.

Non-invasive testing

Non-invasive testing should be seen as more than simply a screening tool for potential revascularization. The aim of non-invasive tests (ECG, ECHO and stress imaging) is to identify patients with myocardial ischaemia or those with valvular or left ventricular (LV) dysfunction. The results may underpin perioperative management decisions such as choice of anaesthetic technique or the type of surgery undertaken. Non-invasive testing generally has a high *negative* predictive value but a low *positive* predictive value in terms of the likelihood of adverse perioperative cardiac events.

Resting ECG

In patients with established ischaemic heart disease (IHD), changes on the 12-lead ECG may be of prognostic significance. Current guidelines suggest an ECG should be performed in patients with one or more risk factors who are undergoing intermediate- or high-risk surgery. The ECG may of course be normal or non-specific even in the presence of active ischaemia or infarction.

Resting echocardiography

Resting ECHO is of only limited value in terms of assessing perioperative risk. This probably relates to a failure to detect even severe underlying ischaemic heart disease. The main indications for preoperative ECHO are as in the non-surgical population:

- To evaluate valve function in patients with a murmur.
- To assess LV function in patients with heart failure or dyspnoea of unknown origin.

Stress testing

Stress tests (exercise ECG, stress ECHO, and stress radionuclide myocardial perfusion imaging) have a high negative predictive value (>90%) for postoperative cardiovascular events—that is, a negative test is associated with a very low incidence of adverse events and predicts a safe procedure. The positive predictive value (see section 10.1) is, however, low (about 20%). By its nature, stress testing primarily detects flow-limiting lesions rather than non-flow-limiting plaques. The latter may often be the source of perioperative MI through plaque rupture. The positive predictive value will be further reduced if a positive result is the impetus for a change in management, for example, revascularization, initiation of drug therapy, or selection of a different surgical procedure.

Current recommendations in respect of preoperative stress testing may be summarized as shown in Box 1.8.

Box 1.8 Indications for preoperative stress testing

- *Recommended* for patients with ≥3 cardiac risk factors undergoing high-risk surgery.
- *Not recommended* for patients undergoing low-risk surgery.
- *May be considered* in patients undergoing intermediate-risk surgery or in patients with ≤2 risk factors undergoing high-risk surgery.

A variety of stress testing modalities is available. They can be classified according to:

- Type of stress: exercise, vasodilatation (dipyridamole/adenosine) or dobutamine.
- Measure of induced ischaemia: ECG changes, myocardial perfusion defects (rMPI), or wall motion abnormalities (ECHO).

Exercise ECG

Exercise ECG testing without myocardial imaging has long been used to detect myocardial ischaemia. In respect of assessing perioperative risk, *exercise tolerance* is more important than ECG changes. A patient who is unable to perform moderate exercise and/or reach 85% of maximal heart rate is at higher risk of a postoperative cardiac event—even in the absence of diagnostic ECG changes.

Limitations to exercise stress testing include:

- The presence of other conditions which may prevent many patients from exercising and/or achieving target heart rate, e.g. lung disease, arthritis, peripheral vascular disease.
- The presence of resting ECG abnormalities (e.g. bundle branch block, digoxin therapy, female sex) may prevent detection of ischaemia.

Stress radionuclide myocardial perfusion imaging (rMPI)

The use of dipyridamole-thallium imaging in patients undergoing major non-cardiac surgery has been widely investigated. The negative predictive value is high (98%) but the positive predictive value is low (only 18%). Thus a positive test result is only a weak predictor of a perioperative cardiac event.

The presence of reversible ischaemic defects in >1 segment of the myocardium may be a stronger predictor of an adverse outcome, especially if in the presence of other risk factors (age, diabetes, etc.).

Stress echocardiography

Stress (either exercise-induced or pharmacological) two-dimensional transthoracic echocardiography (TTE) combines information on resting LV function, valvular abnormalities, and on the presence and extent of inducible ischaemia.

It has a number of clinical applications:

- Diagnosis of coronary artery disease (CAD): by showing inducible wall motion abnormalities).
- Assessment of myocardial viability prior to revascularization.
- To identify a 'culprit' lesion in a patient with known coronary artery stenosis.
- Risk stratification of patients with known or suspected cardiac disease (including prior to non-cardiac surgery).

Dobutamine stress echocardiography (DSE) has become increasingly popular, especially for patients unable to perform an exercise-based stress test. Dobutamine increases heart rate and myocardial contractility. In the presence of significant coronary stenosis, regional ischaemia can therefore be expected in response to dobutamine, manifesting as area(s) of reduced contractility. DSE has a good safety profile, but may provoke arrhythmias and/or hypotension in susceptible patients. Minor arrhythmias (e.g. atrial or ventricular premature beats) occur in up to a third of patients. DSE should be avoided in patients with significant hypertension or arrhythmia. The presence of an abdominal aortic aneurysm has previously been cited as a relative contraindication to DSE—but evidence suggests stress testing in this population is safe and that the risk of rupture is very small.

Other non-invasive tests

Stress testing remains the preferred non-invasive approach to the detection of coronary disease. Sometimes, however, an equivocal result will suggest a need for an anatomical assessment of the coronary arteries in order to confirm or refute the clinical suspicion. Cardiac catheterization is expensive and carries a small but significant risk of serious complications. Novel coronary imaging techniques (computed tomography (CT) and magnetic resonance imaging (MRI)) are emerging, with the hope of improvements in both cost and safety.

Computed tomography and magnetic resonance imaging

Coronary artery calcium (CAC) can be detected by CT. The presence of CAC is highly sensitive (but less specific) for the presence of significant coronary artery stenosis. There is, at present, no evidence of benefit in respect of using a CAC score in routine screening of asymptomatic patients, but the technique has been widely marketed in this regard.

Both CT and MRI have recently emerged as potentially exciting non-invasive techniques to actually visualize both native coronary arteries and bypass grafts. The current limitations of coronary CT angiography (CCTA) and coronary MRI (CMRI) are likely to be overcome as the technology improves. MRI is likely to be preferred in younger patients due to concerns about the radiation doses associated with CCTA. There are as yet no data in respect of either technique in the setting of preoperative risk stratification.

Cardiopulmonary exercise testing

This provides a global assessment of exercise capacity, especially in relation to cardiovascular and respiratory function. The underlying physiology of CPET and its potential applications are discussed in section 1.2.

Coronary angiography

Coronary angiography remains the definitive means by which to confirm the presence of CAD. It is, however, an invasive procedure that carries with it the potential for life-threatening complications.

The indications for preoperative coronary angiography are highly limited, and are essentially identical to those that apply in the non-operative setting (see Box 1.9). This reflects the lack of evidence that preoperative coronary revascularization improves outcome (see section 1.5).

Box 1.9 Indications for preoperative coronary angiography

Recommended for:

- Acute ST elevation MI (STEMI)
- Non-STEMI and unstable angina
- Refractory angina unresponsive to medical therapy.

May be considered for:

- Stable patients undergoing high- or intermediate-risk surgery.

Before a preoperative angiogram is performed, it should be established that the patient is a candidate for *preoperative* revascularization—in addition to an acceptance that this may have implications in respect of potential postponement of surgery and/or introduction of antiplatelet therapy. Should an angiogram confirm an indication for revascularization, then a wide discussion (between patient, cardiologist, surgeon, and anaesthetist) should inform the decision as to the most appropriate therapy (see section 1.5).

Further reading

Priebe H-J (2011). Preoperative cardiac management of the patient for non-cardiac surgery: an individualized and evidence-based approach. *Br J Anaesth*, 107:83–96.

1.4 Scoring systems for outcome in anaesthesia, surgery, and critical care

The 'ideal scoring system' to predict individual outcome following anaesthesia or admission to intensive care does not exist. There are, however, many systems that seek to predict likely outcome within a population or group of patients.

The scores variously account for past medical history, physiology, and concurrent illness. Similarly, they may be based on single time points or on repeated evaluation. The predictive value of the scores varies from population to population and indeed should be only applied to those groups of patients in which they have undergone validation. Predicted outcomes include mortality and morbidity.

A classification of scoring systems is difficult. Simple classifications might be based on predicted outcome, method of scoring (e.g. anatomical, physiological, organ system, intervention based) or pathology (trauma, general surgical, neurosurgical, and so on). As classification is non-standard, it is important for the anaesthetist to be able to consider the different range of scores available, their components, and applicable population(s).

Critical care scoring systems

Acute Physiology and Chronic Health Evaluation (APACHE) score

The APACHE score was introduced in 1981. It combined 34 patient variables (on admission to ICU) and a chronic health evaluation to produce a severity score, which correlated with mortality.

APACHE II was published in 1985 and was a simpler version with only 12 variables and altered weighting. The score continued to be a single measure based on admission physiology and correlated well with in-hospital mortality across a number of populations. The score was widely adopted.

APACHE III was introduced in 1991 and was intended to predict individual patient mortality. The score is more complex and the software for calculation was held under copyright. It has not been as widely adopted as APACHE II despite potentially better accuracy.

Simplified Acute Physiology Score (SAPS)

The SAPS was introduced in 1984 as a 14-variable alternative to the physiology component of APACHE. It was superseded by SAPS II in 1993 (and subsequently SAPS III), which expanded the variables to 17 and incorporated regression calculations. It reflects scores calculated within the first 24h of critical care admission and is an alternative to the APACHE score.

Mortality Prediction Model (MPM)

The MPM and its successor MPM II are designed to predict mortality on ICU admission and at 24h. There are also variations on the model that allow prediction at 48h and 72h. The models assess multiple physiological and chronic health parameters and predict mortality following complex logistic regression.

Sequential Organ Failure (SOFA) score

Originally the Sepsis-Related Organ Failure Score, this was subsequently validated in non-sepsis organ dysfunction and is now interchangeably known as the SOFA. The score was developed by a working group of the European Society of Intensive Care Medicine (1996). Six systems are analysed: respiratory, cardiovascular, central nervous, hepatic, renal, and coagulation. This score allows repeated measures over time to assess improvement or deterioration and the rate of such change. Mean and highest SOFA scores have been shown to be useful predictors of outcome comparable with SAPS II.

Multiple Organ Dysfunction Score (MODS)

Similar to SOFA, the MODS examines six organ systems (cardiovascular, renal, respiratory, hepatic, haematological, neurological) and produces a weighted score depending on degrees of dysfunction. The score can be repeated on a daily basis to monitor progression. The score uses a unique variable (pressure-adjusted heart rate, a product of HR and the ratio of central venous pressure (CVP): mean arterial pressure (MAP)) to assess cardiovascular function. It correlates well with mortality, although some evidence suggests that the SOFA cardiovascular component is a better predictor than that of MODS.

Logistic Organ Dysfunction Score (LODS)

The LODS is broadly similar to the MODS and SOFA scores but less widely used. A more complex calculation is involved but claims to take into account both the relative severity among organ systems and the degree of severity within an organ system.

Scoring systems used in perioperative care

American Society of Anesthesiologists Physical Status (ASA-PS)

The ASA-PS has been in use in a form similar to that used today since 1963. It encompasses six categories, 1–6 (originally five), to describe the underlying fitness of patients. The addition of the 'E' suffix allows distinction of emergency operations and the 'P' suffix has been proposed for pregnancy. It is a simple system that is quick and easy to use (Table 1.2). This very simplicity, however, means that there can be significant inter-observer variation in ASA grading.

Table 1.2 The ASA-PS

ASA score	
1	Healthy individual
2	Mild systemic disease
3	Severe systemic disease
4	Severe systemic disease—a constant threat to life
5	Moribund—not expected to survive 24h
6	Brain-stem dead—organ donation

Physiological and Operative Severity Score for Enumeration of Mortality and Morbidity (POSSUM)

The POSSUM was originally conceived for surgical audit. The system combines 12 physiological and six operative parameters to give an estimated morbidity and mortality. The scoring system tends to overestimate risk in low-risk patients and at the extremes of age. The scores have been adapted since introduction. P-POSSUM uses a different equation to produce more accurate mortality data. V-, Cr-, and O-POSSUM have been introduced for vascular, colorectal, and oesophagogastric surgical groups respectively. The scoring systems have been widely

validated, although nevertheless can over- or underestimate risk depending on cohort.

The score is, however, difficult to use for preoperative risk prediction, since the operative data (e.g. peritoneal soiling or blood loss) are at that point unknown.

Postoperative Morbidity Survey (POMS)

The POMS was described in the late 1990s. The nine-point enquiry into different organ systems allows quantification of patient morbidity. Postoperative morbidity of any kind can have significant bearing on outcomes such as length of stay. Although, given its nature, not useful as a predictive score, it can be used to assess therapy and compare units or techniques.

Postoperative Nausea and Vomiting (PONV) scores

A number of scoring systems exist for PONV. The Apfel score assigns 1 point each to certain risk factors: female sex, previous PONV, non-smoker, and postoperative opioid use. The total score allows a prediction of PONV risk.

An alternative is the Koivuranta score that uses a 5-point scale adding motion sickness and surgery length whilst omitting opioid use.

Surgical scoring systems

Numerous scores exist within the various surgical subspecialities. Indeed some (e.g. the POSSUM score) are widely used by both anaesthetists and surgeons.

Trauma scores

Multiple trauma scores exist and are either physiological (Revised Trauma Score), anatomical (Injury Severity Score, Abbreviated Injury Score), or a combination of the two (Trauma Injury Severity Score). They are variably able to predict outcome for multiply injured patients.

Neurosurgery

The Glasgow Coma Scale (GCS) is widely used throughout medicine although originally was (and remains) a tool for assessing conscious level following traumatic brain injury. The scale assesses motor, verbal, and eye opening function with a maximum score of 15 and a minimum of 3 (see Table 6.3). The T suffix can be appended for intubated patients, replacing the verbal component and altering the range to 2T–10T.

Subarachnoid haemorrhage is graded by the World Federation of Neurosurgical Societies (WFNS) on a 5-point scale with mortality for grade V haemorrhage approaching 90%.

Hepatobiliary

The Child–Turcotte–Pugh score (see Table 4.4) was originally conceived to predict operative mortality for patients with liver disease. A 5-point physiological score stratifies patients into one of three categories (A, B, and C). Child's C liver disease has been associated with high mortality. The MELD (Model for End-stage Liver Disease) score is often used to classify patients with liver disease prior to transplantation.

Several scores have been used to assess the severity of acute pancreatitis including Glasgow and Ranson's criteria, although the APACHE score has also been used in patients admitted to the intensive care unit.

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1.5 Perioperative management of the cardiac patient requiring non-cardiac surgery

Sections 1.1–1.3 dealt with cardiac risk assessment in respect of patients undergoing non-cardiac surgery. This initial approach encompasses an appraisal of clinical predictors of risk (presence of angina, heart failure, diabetes, renal insufficiency, etc.), together, most importantly, with a consideration of the patient's functional status and the perceived risk attached to the proposed surgical procedure.

This section deals with certain important management strategies aimed at reducing perioperative risk. These include:

- Drug therapy: β-blockers, statins, and management of antiplatelet therapy.
- Revascularization: percutaneous coronary intervention (PCI) vs coronary artery bypass grafting (CABG).

Drug therapy

Pre-optimization of a patient's *medical* therapy aims to confer protection through plaque stabilization and reduction of ischaemia.

β-blockers

β-blockers have long been suggested to reduce cardiovascular risk in patients undergoing non-cardiac surgery, although studies have yielded conflicting results.

Mangano et al. (1996) demonstrated an improved outcome 2 years after acute β-blockade (atenolol for 1 week post-operatively) in non-cardiac surgical patients. Other studies produced less convincing results, but it was suggested that atenolol be given preoperatively to all patients with actual coronary disease or those at risk.

A large, multinational randomized study, the POISE (PeriOperative Ischaemia Study Evaluation) trial was set up aiming to clarify the situation. Patients receiving metoprolol had a reduced 30-day incidence both fatal and non-fatal of MI and cardiac arrest, but all-cause mortality was *increased,* with an excess of hypotension, bradycardia, and stroke. The findings therefore ran contrary to the practice of advocating β-blocker therapy in all patients perceived to be at risk.

Potential limitations of the POISE trial include:

- Arguably a high dose of metoprolol (100mg twice a day) was used, and it was unadjusted for heart rate within the inclusion criteria.
- Therapy was initiated only 2–4h before surgery, which may have increased the risk of perioperative hypotension and bradycardia, whilst perhaps not allowing sufficient time for other benefits (e.g. anti-inflammatory effects) to develop.

Nonetheless, the POISE trial cast doubt upon the benefit of widespread prophylactic β-blockade, and suggested that benefit was likely to reside in a smaller percentage of high-risk patients.

A reasonable consensus of the current understanding would be:

- High-risk patients may still derive benefit from perioperative β-blockade: the POISE study showed evidence of cardiac protection.
- In patients scheduled for high-risk (major vascular) surgery who have known CAD, documented myocardial ischaemia or a high Revised Cardiac Risk Index, β-blocker therapy should be initiated perioperatively.
- If β-blocker therapy is initiated, in high-risk patients or for high-risk surgery, this should begin preferably 1 month before surgery, with careful dose titration, and pre- and perioperative monitoring of heart rate (target 60–80 beats per minute) and blood pressure (systolic >100mmHg). HDU admission may be indicated postoperatively. The benefits and risks should be discussed carefully with the patient, in particular, the increased risk of stroke.
- If β-blockers are used, long-acting β-1 cardioselective agents (atenolol or bisoprolol) may be most effective.
- If the risks appear to outweigh benefits (e.g. in patients with a history of previous stroke), initiation of β-blocker therapy may reasonably be withheld, even in high-risk cases.
- In patients already receiving chronic β-blocker therapy, this should be continued.

Statins

Statins (3-hydroxy-3-methylglutaryl coenzyme-A reductase inhibitors) are, of course, widely used clinically to reduce elevated levels of cholesterol and so decrease the risk of atherosclerosis.

They may, however, significantly reduce cardiovascular mortality and morbidity irrespective of an individual's cholesterol status.

In addition to being highly efficacious in lowering LDL (low-density lipoprotein) and cholesterol, and raising HDL (high-density lipoprotein), they also have a variety of so-called *pleiotropic* effects (see Box 1.10).

Box 1.10 Lipid-lowering and pleiotropic effects of statins

Lipid-lowering effects:

- Decreased cholesterol and LDL
- Increased HDL.

Pleiotropic effects:

- Increased endothelial production of NO synthetase
- Decreased endothelin-1 production
- Improved thrombogenic profile
- Decreased inflammation and C-reactive protein (CRP) levels
- Plaque stabilization
- Reduced atherosclerosis.

There is growing evidence to support the use of statins perioperatively, with improvements in both short- and long-term outcomes after cardiac and non-cardiac surgery.

Several randomized controlled trials (RCTs) and observational studies have demonstrated improved outcome in the perioperative period, probably related to the pleiotropic effects of statins, including plaque stabilization and reduced thrombogenesis.

In the DECREASE III trial, for example, elective vascular surgical patients were randomized to receive fluvastatin 80mg once a day or placebo for 30 days pre- and post-op. The incidence of detectable ischaemia (troponin rises or ECG changes) and of cardiovascular mortality in the treatment group was roughly halved.

The current evidence would suggest that statin therapy should be initiated in all high-risk patients who are not already receiving them, and that chronic therapy should, wherever possible, not be discontinued in the perioperative period.

Management of antiplatelet therapy during the perioperative period

The management of antiplatelet therapy in patients requiring non-cardiac surgery is an important and increasing clinical problem, most especially in patients who have undergone previous PCI. About 5–10% of patients with coronary stents undergo non-cardiac surgery within a year of stent implantation. The essential factors to consider are:

- Risk of stent thrombosis or acute coronary syndrome if antiplatelet therapy is discontinued.
- Risk of bleeding if therapy is continued.

Coronary artery *angioplasty* was first reported in 1977. *Bare metal stents* were introduced a decade later in response to high restenosis rates after angioplasty alone. However, the incidence of restenosis following intimal hyperplasia remains up to 30%.

Stent insertion causes damage to the endothelial surface, and the result of interactions between stent, blood, and the vessel wall is neointimal hyperplasia and increased thrombogenicity.

In 2003, *drug-eluting stents* (typically releasing sirolimus or paclitaxel) emerged as a solution to restenosis, although a 5–10% risk of stent thrombosis remains.

Three classes of antiplatelet drugs (see section 1.20) are available to prevent stent thrombosis:

- Aspirin
- Thienopyridines (clopidogrel and prasugrel)
- GP IIb/IIIa inhibitors (tirofiban and abciximab).

Typically, aspirin and clopidogrel are used in combination ('dual anti-platelet therapy') following stent implantation to reduce platelet activation.

Stent thrombosis is a serious complication, carrying a 20% mortality. Premature discontinuation of dual antiplatelet therapy is the most powerful independent predictor of stent thrombosis.

The greatest risk to the patient undergoing non-cardiac surgery with a stent *in situ* is from interruption of dual anti-platelet therapy, particularly if this occurs during the first 12 months following insertion (Box 1.11; see also section 1.20).

Box 1.11 Summary of guideline recommendations for patients with stents undergoing non-cardiac surgery

- Defer elective surgery for 6 weeks following bare metal stent insertion and 6–12 months following drug-eluting stent insertion.
- If surgery cannot be deferred:
  - Continue dual antiplatelet therapy perioperatively where possible.
  - If not, continue aspirin and stop clopidogrel 5–7 days preoperatively.
  - Restart clopidogrel as soon as possible postoperatively.

Premature discontinuation of antiplatelet therapy for minor procedures is rarely justified. Most surgical procedures can in fact be safely performed in the presence of dual platelet therapy, or at least with aspirin alone.

The role of 'bridging therapy' in high-risk individuals who stop dual antiplatelet therapy remains unclear. Unfortunately, heparins have minimal antiplatelet effect, rendering them theoretically unsuitable as bridging therapy. Tirofiban has a short half-life (2h), and may be a more attractive agent. Bleeding time returns to normal 4h after cessation of a tirofiban infusion.

Revascularization

In patients with stable coronary disease, the indications for revascularization include left main stem or severe triple-vessel disease.

Most patients with stable coronary disease who are scheduled for non-cardiac surgery do not benefit from prophylactic revascularization. In addition, any reduction in risk from revascularization must be balanced against the risks of the revascularization procedure itself, coupled with the risks of interrupting clopidogrel therapy in patients with recently inserted stents.

The Coronary Artery Revascularization Prophylaxis (CARP) trial compared preoperative revascularization (PCI or CABG) with medical therapy in patients with stable coronary disease scheduled for major vascular surgery. No significant differences in outcome were identified.

The decision to revascularize is usually based on the results of non-invasive testing, the indications for which are discussed in section 1.3. Angiography should be performed in patients with high-risk features on non-invasive testing (e.g. a reversible large anterior wall defect), and in patients with high-risk unstable angina.

CABG should be undertaken in patients with established indications for the procedure, typically significant left main stem disease, or triple vessel disease with impaired LV function.

If the disease is amenable to PCI, then consideration should be given to bare metal stent insertion, deferring surgery for 4–6 weeks if possible following the procedure.

Further reading

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1.6 Dynamic pressure measurements

Pressure monitoring is a core component of anaesthesia practice. Common methods of measuring dynamic pressure changes in theatre or in the critical care unit include *direct* techniques (cannulation of systemic and/or pulmonary arteries and central veins), but also *indirect* techniques including echocardiography (see section 1.8).

Physical principles: pressure versus flow

Vascular cannulation allows *pressure* measurement, whilst other measures of cardiac function, such as cardiac output and oxygen delivery, reflect *flow*. The relationship between pressure and flow is described using familiar equations (see Box 1.12) according to whether the flow is assumed to be laminar or non-laminar.

Box 1.12 Pressure: flow relationships

Laminar flow (the Hagen–Poiseuille equation):

$$\text{Flow} = \frac{\text{Pressure gradient} \times \text{radius}^4 \times \text{pi}}{\text{Tube length} \times \text{viscosity} \times 8}$$

Non-laminar/turbulent flow:

$$\text{Flow} \propto \frac{\text{Radius}^2 \times \sqrt{\text{pressure gradient}}}{\text{Length} \times \text{density}}$$

At the organ level, a pressure gradient is required to maintain flow. If the organ is contained in a non-distensible structure, a rise in pressure within the organ may lead to parenchymal injury with reduction in flow. This is seen in a variety of circulations including cerebral (raised intracranial pressure), cardiac and coronary (tamponade), hepatic (capsular swelling), and pulmonary (hyperinflation).

Arterial lines

There are numerous indications for inserting an arterial line, both for haemodynamic monitoring, and to facilitate blood sampling (see Box 1.13).

The anatomical site is chosen according to a variety of factors including:

- Anticipated ease of cannulation
- Risk of distal ischaemia (perceived higher risk with proximal insertion site)
- Patient positioning and intraoperative access
- Risk of catheter-related sepsis
- Concurrent monitoring requirements.

Box 1.13 Indications for arterial line insertion

Continuous monitoring

Blood pressure:

- Cardiovascular instability (current or anticipated)
- Non-invasive technique impractical (obesity, burns, etc.) or unreliable (e.g. atrial fibrillation).

Cardiac output:

- Pulse contour analysis (see section 1.7).

Sampling

- Anticipated bleeding (e.g. vascular, cardiac, liver surgery)
- Poor gas exchange
- Anticipated changes in coagulation (e.g. cardiac, liver surgery)
- Repeated sampling required (e.g. diabetic ketoacidosis).

Interpretation of the arterial waveform

Pressure and flow within the proximal aorta reflect the interaction between the heart and the arterial tree. When LV pressure exceeds aortic pressure, blood flows into the ascending aorta. The driving force behind this pressure difference depends on LV contractility, size and shape, and on the heart rate. Assuming no valvular obstruction, opposition to flow is due to *vascular impedance*, which has three components:

- Resistance: related to blood viscosity and vascular geometry.
- Inertia: a function of the mass of blood to be accelerated.
- Compliance: representing the distensibility of the vasculature.

During LV systole, the arterial pressure rises rapidly since blood is being pumped into the arterial tree faster than it can be redistributed. As the ventricle begins to relax, so the pressure falls as aortic blood flow declines. When aortic pressure exceeds LV pressure, the aortic valve closes, generating a small pressure wave—the *incisura* or dicrotic notch, on the arterial waveform (Fig. 1.4). Thereafter, arterial pressure continues to fall towards diastolic pressure before the next systole.

The shape of the aortic pulse wave changes as it is transmitted peripherally: pulse pressure and systolic pressure increase, and the initial upstroke (the anacrotic limb) rises more steeply. The dicrotic notch migrates from a sharp, early position in the waveform to a later, smoother oscillation.

A variety of physiological and pathological factors affect the shape of the arterial waveform (see Box 1.14).

Box 1.14 Some factors affecting arterial waveform morphology

Physiological

- *Ageing:* higher systolic pressure and increased pulse wave velocity; loss of diastolic wave.
- *Exercise:* increased pulse pressure (proportional to stroke volume).

Pathological

- *Arteriosclerosis:* increased systolic pressure + pulse pressure.
- *Aortic stenosis:* 'anacrotic' pulse with slow rise, late peak, low pulse pressure.
- *Aortic regurgitation:* 'collapsing' pulse—rapid upstroke, rapid decline, wide pulse pressure.

Central venous cannulation

There are many indications for central venous catheterization:

- Haemodynamic monitoring (CVP, SvO_2, etc.)
- Drug and fluid administration (total parenteral nutrition (TPN), vasopressors, cytotoxic agents, etc.)
- As a route for other procedures (pulmonary artery (PA) catheter, cardiac pacing, liver biopsy, etc.)
- Renal replacement therapy or plasmapheresis
- Poor peripheral venous access.

Interpretation of CVP waveform

The normal CVP waveform is shown in Fig. 1.5.

A wave: atrial contraction

The a wave is pre-systolic. It is caused by right atrial contraction and therefore it is absent in atrial fibrillation. Large a waves occur

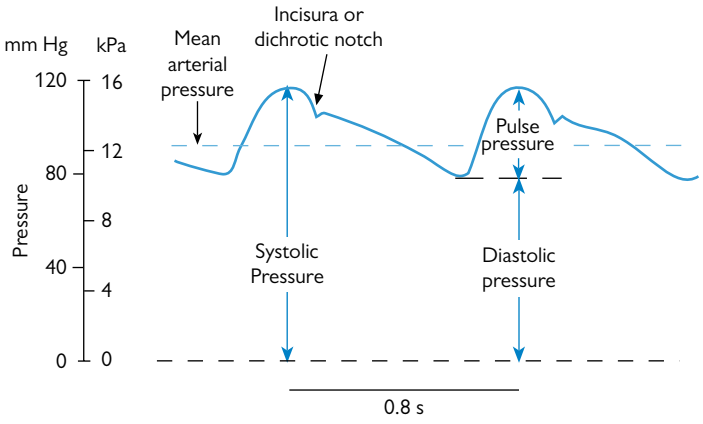

Fig. 1.4 The normal arterial waveform. Reproduced from Pocock and Richards, *Human Physiology: The Basis of Medicine*, third edition, 2006, Figure 15.24, page 285, with permission from Oxford University Press.

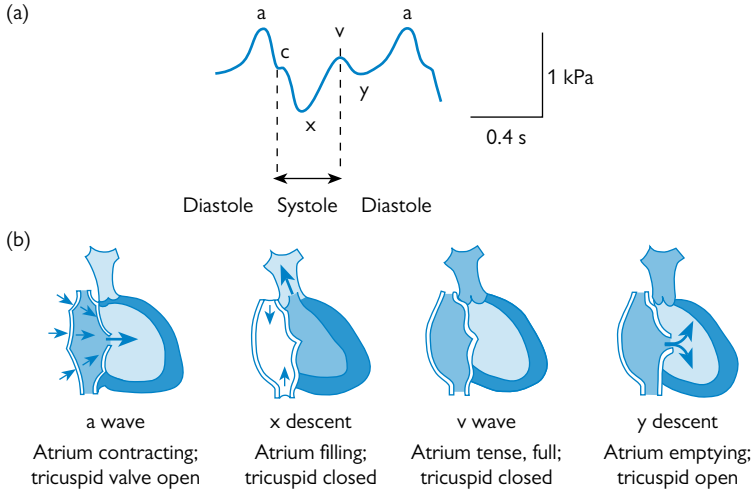

Fig. 1.5 The normal CVP waveform. Reproduced from Pocock and Richards, *Human Physiology: The Basis of Medicine*, third edition, 2006, Figure 15.15, page 275, with permission from Oxford University Press.

when the right atrium is contracting against increased resistance. This happens in three situations:

- Tricuspid stenosis
- Tricuspid valve normal but closed:
  - Regularly: junctional rhythms
  - Irregularly: AV dissociation:
    - — Ventricular tachycardia (VT)
    - — 3rd-degree heart block
- Increased resistance to right ventricular (RV) filling:
  - Pulmonary hypertension
  - Pulmonary stenosis.

C wave

Unclear origin. Possibly due to:

- Closure of the tricuspid valve
- Bulging of the tricuspid valve into the right atrium during RV isovolumetric contraction
- Transmitted pulsations from the carotid artery.

X descent: atrial relaxation

Occurs during ventricular systole. The CVP decreases because of both atrial relaxation and a downward displacement of the tricuspid valve.

The x descent is larger when the atrium is compressed as in constrictive pericarditis or cardiac tamponade. The x descent is smaller when the right ventricle is dilated, or there is tricuspid regurgitation.

V wave: venous filling of the atria

Occurs in late systole and is due to the increasing volume of blood in the right atrium against a closed tricuspid valve. Tricuspid regurgitation causes the v wave to become more prominent and may obliterate the x descent.

Y descent: yawning open of the tricuspid valve

Occurs when the tricuspid valve opens and the ventricle fills, reducing pressure in the atria. Several variations of the y wave have been characterized:

- Rapid, deep y descent: tricuspid regurgitation
- Rapid, short y descent: constrictive pericarditis, right sided diastolic failure (restrictive RV disease)
- Slow y descent (obstruction to RV filling): tricuspid stenosis, right atrial myxoma.

Complications of central venous cannulation

Many complications have been associated with central line insertion, occurring both at the time of the procedure, and subsequently (Table 1.3).

Table 1.3 Complications of central venous cannulation	
Immediate	**Late**
Bleeding Pneumothorax Arterial puncture Dysrhythmia Air embolism Thoracic duct injury	Infection Thromboembolism Catheter migration (e.g. right atrial perforation causing pericardial tamponade)

Particular emphasis has been placed recently on *infectious* complications, since CVCs constitute the largest single source of bloodstream infection in hospitalized patients.

Catheter-related bloodstream infections (CRBSIs) are attributable to four elements: skin colonization, intraluminal or hub contamination, secondary seeding from a current bloodstream infection, and contamination of the infusate (rare). The following reduce the risk of developing a CRBSI:

- Subclavian rather than jugular or femoral approach
- Absence of septic focus elsewhere
- Inserted with maximal barrier precautions
- Totally implantable < tunnelled < non-tunnelled
- Silver-impregnated collagen cuff, or heparin-bonded catheters
- Single-lumen catheters
- Dressings containing sterile gauze, or transparent occlusive dressings
- Catheter site care by specialist teams
- Peripherally inserted central catheters (PICCs).

Interpretation of CVP data

The CVP is often used to assess preload and fluid responsiveness. Volume expansion is considered first-line therapy in haemodynamically unstable patients. However, CVP correlates poorly with circulating blood volume, and the correlation between a change in CVP and a change in stroke volume or cardiac index is poor.

Pulmonary artery catheterization

Flow-directed pulmonary artery catheters (PACs) were developed in the 1970s and initially used to guide fluid therapy following acute MI. They continue to be used for haemodynamic monitoring, but not without controversy (see section 1.7). A variety of data may be obtained from the PAC, either directly or indirectly (see Box 1.15).

Box 1.15 Data obtained from the PAC

Direct

- *Pressure monitoring:* PAC gives direct measurements of central venous, right-sided intracardiac, pulmonary arterial and pulmonary capillary wedge pressures.
- *Mixed venous oxygen saturations*: can be measured directly from the catheter tip either continuously or intermittently.

Indirect

- *Cardiac output*: using thermodilution, PACs can be used to estimated cardiac output using the Stewart–Hamilton equation.
- *Vascular resistance*: pulmonary and systemic vascular resistance can be calculated by combining pressure and flow (cardiac output) data.

Interpretation of the PAC waveform

The pressure trace obtained from a PAC undergoes characteristic changes from chamber to chamber (Fig. 1.6). It is therefore important to have pressure transduction displayed (with an appropriate scale) during insertion and subsequent manipulations.

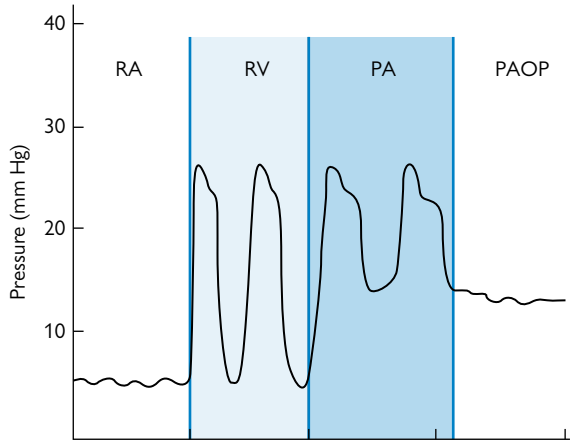

Fig. 1.6 Pressure waveforms recorded during PAC insertion. Reproduced from Catherine Spoors and Kevin Kiff, *Training in Anaesthesia*, 2010, Figure 10.41, Page 285, with permission from Oxford University Press.

Zeroing and referencing

Two separate processes are required when setting up a transduction system for a PAC:

- Zeroing: the process by which the transduction system is exposed ('opened') to air establishing the atmospheric reference pressure (taken as 'zero').
- Referencing: the process by which the air–fluid interface of the transducer is placed at a set level to negate the effects of the weight of the catheter tubing and fluid column. This point (the 'phlebostatic level') is usually taken as the intersection between a coronal plane passing midway between the anterior and posterior surfaces of the chest and a transverse plane lying at the junction of the 4th intercostal space and the sternal margin.

Dynamic response assessment

After placement, the dynamic response of the system to physiological pressure swings should be tested. Response depends on the resonant frequency of the system and damping. Briefly opening and closing the valve in the continuous flush device, producing a square wave followed by a gradual return to baseline, can assess both of these factors. Underdamping exists if there is excessive oscillation before returning to baseline; overdamping exists if there are no oscillations.

- *Underdamping:* caused by short tubing, or resonance within the system due to the natural frequency of the system being too near the oscillatory frequencies of the arterial pressure wave.
- *Overdamping:* most commonly due to air bubbles within the tubing but also from three-way taps, clots, vasospasm, narrow/long/compliant tubing or from kinks in the cannula or tubing.

Interpretation of pressure waveforms

PACs typically only display the *right ventricular trace* during insertion, but some recent devices allow continuous display of RV systolic and diastolic pressures. Normal RV pressures vary from 15–25mmHg systolic and 3–12mmHg diastolic.

- Raised RV systolic pressure: is seen in pulmonary hypertension, pulmonary embolism or left-sided heart failure. In pulmonary stenosis, RV pressure is raised, with a steep fall when the catheter enters the pulmonary artery.
- Raised RV diastolic pressure: is seen in cardiomyopathy, RV ischaemia or infarction, pericardial tamponade or constriction, or in RV failure secondary to pulmonary hypertension.

The *pulmonary artery pressure (PAP) waveform* is similar to the systemic arterial pressure tracing, but at lower pressures. The migration of the PAC into the PA from the RV is evident on the waveform when the diastolic pressure reading increases to 8–15mmHg.

Raised PAP may be seen with normal or high PVR though in practice there is a large degree of overlap between these two groups:

- Raised PAP with high PVR: pulmonary embolism, pulmonary arterial hypertension, hypoxic pulmonary vasoconstriction.
- Raised PAP with normal PVR: mitral valve disease, left-to-right shunts.

The *pulmonary capillary wedge pressure (or pulmonary artery occlusion pressure, PAOP) waveform* is similar to the CVP trace, and described by the same nomenclature (although the c wave, here reflecting *mitral* valve closure, is often not seen). The normal PAOP is between 6mmHg and 15mmHg. Similarities between PAOP and CVP traces extend to the abnormalities seen within them:

- Raised a wave: increased resistance to LV filling, regardless of cause: mitral stenosis, LV systolic or diastolic dysfunction, volume overload, decreased LV compliance (e.g. due to myocardial ischaemia or infarction).
- Raised v wave: occurs when systole results in retrograde flow, e.g. in mitral regurgitation or VSD complicating MI.

Timing of PAC pressure readings

Since spontaneous and positive pressure breathing produce opposite effects on pleural and alveolar pressure, and these pressures influence PAOP, all PAOP readings should be recorded at end-expiration, when intrathoracic pressure is equal to atmospheric pressure.

Potential errors in PAOP interpretation as a surrogate for preload

For pulmonary artery wedge pressure to accurately reflect LV preload, a number of measures must be equivalent. Preload is represented by LV end diastolic volume, measured by assessing LV end diastolic pressure, which in turn is represented by left atrial pressure. Assuming the tip of the PAC lies in West's zone 3 of the lung (where the arterial and venous pressures both exceed the alveolar pressure throughout the cardiac cycle), a continuous column of blood is created between the tip of the catheter and the left atrium.

However if any of these assumptions does not hold, PAOP may not represent LV preload accurately. Readings should be interpreted with caution in a variety of situations: LV diastolic failure, mitral valve disease, raised intrathoracic pressure (e.g. positive end expiratory pressure (PEEP)) or raised pulmonary vascular resistance.

Complications related to PACs

These include all the complications of central venous cannulation together with other procedure-specific risks (see Box 1.16).

Box 1.16 Complications of PA catheterization

- All the complications of central venous cannulation
- Dysrhythmias during insertion (one series reports sustained VT in 3% of cases)
- Knotting of the catheter
- Balloon rupture
- Pulmonary infarction or haemorrhage
- Damage to valves or myocardium
- Mistaken positioning, measurement, or interpretation, and the consequences of decisions thus taken.

1.7 Cardiac output measurement

Cardiac output (CO) monitoring is a routine component of management in respect of critically ill patients in the intensive care unit, and, increasingly, in other areas, including the operating theatre.

Its use rests on the premise that inadequate CO results in organ dysfunction and/or failure, and that maintaining organ perfusion will result in improved patient outcome.

The ideal monitor (see Box 1.17) remains elusive, and there are few high-quality data to support the use of any one existing technique over another.

Box 1.17 Properties of the ideal cardiac output monitor

- Non-invasive or minimally invasive
- Widely applicable in all patient groups (awake/sedated/anaesthetized)
- Real-time beat-to-beat results
- Accurate, precise, and validated
- Short learning curve for implementation and analysis
- Operator independent
- Cost effective
- Safe—with minimal complications.

Bedside measurements and biochemical markers

Assessment of cardiac output using *clinical indicators* (e.g. peripheral skin temperature or neurological status) or *commonly measured parameters* (heart rate, arterial blood pressure, CVP, and urine output) is subject to many confounding factors, including pre-existing cardiovascular disease, intercurrent interventions (e.g. therapeutic cooling), and the effects of intercurrent drug therapy, and correlates poorly with cardiac output.

Biochemical markers such as lactate and acid–base status add to the clinical picture and the trends in these measurements can certainly be used to monitor efficacy of therapy. However, absolute values do not correlate well with CO, and abnormalities tend to be a late feature of inadequate CO.

The pulmonary artery catheter (PAC)

In respect of 'bedside' techniques, the PAC remains the 'gold standard' against which other modalities are validated.

Fick first measured CO in 1870, using the arterio-venous oxygen difference (via mixed venous oxygen saturation sampling) and oxygen consumption (via spirometry). Stewart then adapted the technique to use indicator (indocyanine green) dilution in 1897 followed half a century later by Felger's introduction of thermodilution using boluses of cold fluid.

The PAC was introduced in the 1970s bringing CO measurement to the bedside. To measure CO, the area under the indicator dilution curve (change in concentration of dye as sampled from the PAC or temperature measured by a thermistor at the catheter tip, plotted semi logarithmically against time) is calculated using the Stewart–Hamilton equation. Important assumptions include:

- Complete mixing of blood and indicator (dye or cold fluid) with no loss
- Blood flow remains constant

Errors are thus inevitable in the presence of cardiac shunts, arrhythmias, regurgitant valvular disease, and conditions where there is a marked variation in body temperature (bypass, therapeutic hypothermia) or due to technical difficulties (misplacement or intra/interoperator variation in measurement technique).

By definition, dilutional techniques are intermittent in nature and studies need to be repeated when physiological conditions change. Technological developments have permitted continuous CO monitoring (CCOM) by incorporating specialist thermistors into the PAC to assess either random temperature changes or the amount of energy required to maintain a set temperature. These systems take an average of several readings, and are not, therefore, real time.

The PAC is considered most invasive compared with other CO monitors, as it requires a catheter to be passed via the right atrium and ventricle to reside in a pulmonary artery, and carries a risk of important complications, including arrhythmias and pulmonary haemorrhage. Studies in the 1990s suggesting worse outcomes when using PACs in the critically ill were probably victims of selection bias (PACs were used in the sickest patients). A subsequent multicentre (PAC-Man) study re-evaluated use of the PAC against either no CO monitoring (CVP and clinical evaluation only) or other (non-specified) forms of CO monitoring and found no significant difference in outcome, good or bad, between the three groups.

The PAC remains useful in certain groups (particularly cardiac patients) since, in addition to basic CO parameters, it also provides PA pressures, right- and left-sided filling pressures (PAOP), *and* the potential to measure mixed central venous oxygen saturations.

Transpulmonary dilutional techniques

Invasive monitoring of arterial blood pressure and CVP is a basic standard of care for critically ill patients. New technologies have adapted these to estimate CO using transpulmonary dilutional techniques (TPDTs). The PiCCO® and the LiDCO® are those most widely studied and applied in practice.

TPDT effectively measures the change in concentration of an indicator between the venous and arterial blood—on either side of the pulmonary circulation. Again, it relies on complete mixing, and no loss of indicator, but has been validated in many patient populations when used to monitor physiological trends as a guide to therapy.

Temporal analysis of the transpulmonary dilution curve allows additional variables to be calculated from TPDT:

- *Extravascular lung water (EVLW)*: can be used to differentiate between cardiac and non-cardiac pulmonary oedema, and has been shown to be a predictor of mortality in critically ill patients with acute lung injury
- *Global end-diastolic volume* (GEDV): represents a *volume-based* assessment of preload that correlates well with stroke volume (SV). When compared to static pressure-based assessments of preload (CVP, PAOP) volume-based measurement has been shown to more reliably predict fluid responsiveness

Pulse contour analysis

Calibrated monitors

Both the PiCCO® and the LiDCO®, in addition to supporting the intermittent transpulmonary thermodilution technique (which is

used to calibrate the system), provide continuous computational analysis of the arterial pulse contour from an indwelling arterial line (see Box 1.18). Since the arterial waveform is dependent on the interaction between SV and systemic vascular resistance, calculated results are affected by changes in resistance, compliance, and impedance at the point of signal detection. For accuracy a good trace is mandatory.

Additional information obtained by pulse wave analysis includes derived 'dynamic' indices such as *stroke volume variation* (SVV), and *pulse pressure variation* (PPV). These indices are not surrogates for preload but can provide an indication that a fluid challenge may be effective in increasing CO. They are only validated in patients who are ventilated, with stable intrathoracic pressures and a constant tidal volume >8mL/kg. They are unreliable in spontaneously breathing patients, or where there is marked ventilator dyssynchrony.

Box 1.18 Comparison of PiCCO® and LiDCO® systems

PiCCO®

- Requires arterial cannula with thermistor tip (brachial or femoral) + central venous catheter.
- Measures area under systolic waveform (from ventricular ejection to dicrotic notch)—averaged over 30sec.
- 8-hourly calibration with cold fluid bolus (TPDT).

LiDCO®

- External sensor attached to conventional arterial line
- Uses harmonic waveform analysis (Fourier transformation).
- Calibrated by TPDT (lithium bolus)—inaccurate in the presence of lithium therapy or muscle relaxants.

Sources of error/limitations (both systems)

- Arrhythmias.
- Poor arterial trace.
- Requires recalibration when changing SVR.
- Use of intra-aortic balloon pump (IABP) or recirculation techniques.

Uncalibrated monitors

Less invasive systems incorporating alternative algorithms for pulse waveform analysis are available. Avoiding the need for intermittent calibration means there is no requirement for central venous access. Lack of calibration would suggest a potential for inaccuracy, but when used to follow trends in response to interventions, studies have shown these systems to be useful, especially in the perioperative setting. As with the calibrated systems, they depend on a high-quality arterial trace and a stable cardiac rhythm.

Examples include the FloTrac® and PRAM® (Pressure Recording Analytical Method) systems.

The oesophageal Doppler

The physical principles behind ultrasound and the Doppler effect are discussed in section 1.8.

Continuous wave Doppler gives a reliable measure of blood flow velocity, which is utilized to calculate stroke volume and hence cardiac output. Inaccurate positioning of the probe may affect results, and certain important assumptions are made during the calculations (see Box 1.19).

The oesophageal Doppler incorporates this technology within a thin semi-rigid tube, inserted either orally or nasally to measure blood flow in the descending thoracic aorta.

The probes are generally only tolerated in anaesthetized or sedated patients, and there is a steep learning curve for optimal use.

Box 1.19 Assumptions for calculations utilizing Doppler measurements

- Constant aortic blood flow: measured as area under velocity: time graph.
- Angle between Doppler beam and blood flow is within 30° of axial flow.
- Aortic radius (r) measurement:
  - Aorta assumed to be a true cylinder (r calculated from estimated cross-sectional area = πr^2).
  - Since r is squared, a small error in measurement will overestimate CO.
  - Derived either from normogram according to height, weight, age, and sex (Cardio Q®) or from direct M-mode measurement (HemoSonic®).
- Fixed ratio of blood supply upper to lower body (assumed 30% cephalic): in reality, this varies with age, pathology, intraoperative manipulations.

In addition to stroke volume and cardiac output, the oesophageal Doppler monitor (ODM) provides additional variables according to the prevailing haemodynamics (see Box 1.20).

Box 1.20 Additional variables from oesophageal Doppler monitoring

FTc (corrected flow time)

- Measured from beginning of upstroke until return to baseline (corrected to HR of 60 beats/min).
- Marker of fluid responsiveness.
- FTc is inversely proportional to SVR—hence FTc low in situations when SVR high (e.g. heart failure, vasopressor therapy) but fluid therapy would be inappropriate.

PV (peak velocity)

- Peak blood flow velocity during systole (cm/sec).
- Marker of contractility.
- Falls linearly with age.
- Affected primarily by LV contractility (low in heart failure/β-blocker therapy; high in inotropic states).

MA (mean acceleration)

- Measured from start of systole to peak velocity.
- Predominantly a marker of contractility.
- Affected by contractility > afterload > preload.

The ODM has been validated in various populations and is now recommended by NICE for perioperative care (see section 4.10).

Echocardiography

There is a wide body of literature supporting the use of TTE and TOE as a monitor of cardiac output, and TOE has good correlation with CO values obtained from PAC data.

The technique is described in more detail in section 1.8.

Thoracic bioimpedance and bioreactance

The techniques of thoracic electrical bioimpedance (TEBI) and bioreactance (TEBR) both rely on the assumption that the thoracic cavity is a cylinder perfused with fluid (blood). The fluid causes a resistance to a current passed between two fixed electrodes on the body wall, which changes according to the amount of fluid within.

Compared to bioimpedance, which measures changes in *amplitude*, bioreactance uses changes in *amplitude* and *frequency*

which, analogous to FM versus AM radio waves, is more reliable, has better signal fidelity, better noise filtering capacity and is not affected by the distance between electrodes. Since phase shifts can only occur with *pulsatile* flow bioreactance is not affected by changes in other thoracic cavity fluids (chest wall oedema, effusions, pulmonary oedema, pulmonary and venous circulations). Early studies of bioreactance monitors in clinical practice are encouraging, and further work is ongoing.

Summary

All of the techniques used to measure cardiac output (and derived indices) have specific limitations (see Table 1.4).

Which monitor to use depends upon the patient population, clinical scenario, available equipment, and institutional familiarity. All forms of monitoring are liable to error due to *human* as well as technical factors (see Box 1.21).

Table 1.4 Summary of characteristics of common forms of cardiac output monitoring

	Methods	Examples (indicator)	Invasiveness	Equipment	Continuous or Intermittent	Measured variables	Derived variables	Specific disadvantages	Limitations and errors
Dilution	Thermo dilution	PAFC	++++	CV, PAFC	Int	Temp, CVP, PAOP/PAP/ $ScvO_2$ CO		Invasive line in to RA	Incorrect position, respiratory swing –West's zones
							SV, SVR(I), PVR(I), LVSWI	Complications of centralline insertion	Calculations using non simultaneous data
								Lack of training/ familiarity	Intra/extra-cardiac shunts, arrhythmias
	Transpulmonary indicator dilution	PiCCO (thermal)	+++	CV, thermistor tipped FA/BA	Both	Temp, CVP, HR, ABP, CO	GEDV, EVLW, PPV	Specific line	Temperature shifts Rapid changes in vasculomotor tone Arrhythmias
		LiDCO (lithium)	+++	CV or PV, AL			TBV	Muscle relaxants	
								Lithium therapy	
		CO status (ultrasound)	+++	US				Primarily paediatric validation	
		VolumeView (thermal)	+++	CV, specific FA				Specific line	
Pulse analysis	Arterial pulse pressure waveform analysis	PiCCO	+++	CV, specific AL	Cont.	HR, ABP, CO	SVV, SV, SVR(I)	See above	Temperature shifts Rapid changes in vasculomotor tone Arrhythmias
		LiDCO	+++				PPV, SV, SVR(I)	See above	
		Vigileo and FLoTrac sensor	++					Specific kit	
		MostCare	++					Specific kit	
Ultrasound/ Doppler	Doppler-	CardioQ	++	Specific equipment, US machine	Cont.	HR, CO	FT, SV, SVR(I)	Oesophageal pathology	Turbulent flow, skilled operator
	Oesophageal	WAKI						Assumptions re aortic size	
	Doppler-	USCOM	±		Int.			May be difficult with trache/ETT	
	Suprasternal								
	Transoesophageal Echo		++		Int.			Oesophageal pathology	
	Transthoracic Echo		±		Int.			Image quality in critically ill	
	Bioimpedence	Lifegard TEBCO	±	Specific equipment	Cont.		PEP, LVET	Specific kit, validation	Peripheral oedema, pleural effusions
		Hotman							
		BioZ							
	Bioreactance	NICOM	±	Specific equipment	Cont.			Specific kit, validation	Unknown

AL: arterial line (any); BA: brachial arterial access; Cont.: continuous; CV: central venous access; FA: femoral arterial access; Int.: intermittent; PAFC: pulmonary artery flotation catheter; PV: peripheral venous access; US: ultrasound machine.

Box 1.21 Potential human errors in CO monitoring

- Lack of familiarity/training
- Complications during insertion or during use
- Poor positioning
- Poor calibration
- Lack of incorporation of data into entire clinical picture.

Users must be clear about what they are measuring and why, and which values are real and which are derived. This requires a thorough understanding of the physiology of critical illness, and of the techniques used and the physical principles upon which they are based, in order to avoid error. Ultimately, monitoring *per se* cannot improve outcome unless the data obtained are of high quality, *and* used in the correct manner to guide therapeutic interventions that have been shown to improve outcome.

Further reading

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de Waal EEC, Wappler F, & Buhre WF (2009). Cardiac output monitoring. *Curr Opin Anaesthesiol*, 22(1):71–7. doi:10.1097/ACO.0b013e32831f44d0.

1.8 Echocardiography in anaesthesia and intensive care

Echocardiography is increasingly seen as a safe and accurate method of haemodynamic assessment. In comparison with pressure and flow-based monitoring (see section 1.6), it has the additional advantage of potentially identifying the *cause* of the observed haemodynamics.

Physics of echocardiography

Ultrasound waves are the longitudinal compression of particles that are transmitted via a medium. They reflect off components of the medium according to its echogenicity, and are detected by the same probe. The waves are described in terms of *frequency* (number of oscillations per second, in units of Hertz, Hz) and *wavelength* (λ) in units of metres (m).

Frequency and wavelength are related according to the equation:

$$c = f\lambda$$

c = speed of the wave (m/s); f = frequency (Hz); λ = wavelength (m)

Within a constant medium, doubling the incident frequency will halve the wavelength.

The speed of sound varies according to the medium through which it passes, and is about 1500m/s in most soft tissues. Medical ultrasound typically uses sound wave frequencies of between 1MHz and 20MHz (1MHz = 10^6Hz), which is well above the human auditory spectrum of <20kHz.

The speed (c) of the waves is a function of the compressibility (κ) and density (ρ) of the material, according to the equation:

$$c = \sqrt{1/\kappa\rho}$$

Typical values for various body tissues are given in Table 1.5.

Table 1.5 Physical characteristics of different tissues relevant to ultrasound

Material	Density ρ (kg/m^3)	Speed c (m/s)
Air	1.2	330
Water	1000	1480
Blood	1060	1570
Fat	920	1450
Bone	1380–1810	4080

When an ultrasound wave passes from one medium to another, the frequency is constant. If the wave speed in the second medium changes, then the wavelength will also change:

$$\text{Frequency (f)} = c/\lambda$$

For example, if the speed of the wave in the medium halves, then the wavelength will also halve for the frequency to stay the same.

Generation of ultrasound

A transducer is a device that converts one form of energy to another. In the case of ultrasound this conversion is from electrical to mechanical (sound) energy, and back again when the sound wave returns. The transducer in nearly all medical ultrasound transducers is made of lead zirconate titanate (PZT), a crystalline ceramic, which generates a charge in response to mechanical stress, and vice versa. This quality is known as piezoelectricity. Returning sound waves are converted to electrical signals via the piezoelectric crystal and converted using software to images. The amplitude of the signal represents the echogenicity of the structure, and is indicated by increasing brightness on the screen.

The Doppler effect

This is the observation that the frequency of an observed wave changes when the source of the wave is moving relative to the observer. In respect of echocardiography, the *source* is the echo-reflective surface (blood or tissue) and the *observer* is the probe.

By measuring the change in frequency, the velocity of the source relative to the medium can be calculated. The Bernoulli equation uses the velocity of flow between the two chambers to calculate the *pressure difference* between them (allowing the technique to provide, for example, a pressure gradient in aortic stenosis). In its simplified form, the Bernoulli equation can be expressed as:

$$\Delta P = 4(V_2^2 - V_1^2)$$

V_1 = proximal velocity (m/s); V_2 = distal velocity (m/s); ΔP = instantaneous pressure gradient (mmHg)

The proximal velocity V_1 can usually be ignored, hence the equation simplifies even further to $\Delta P = 4\ V_2^2$

Colour Doppler

The Doppler effect can be used to indicate simply the direction of blood flow on a 2D image. This is known as colour Doppler. By convention, blood moving away from the probe is coloured blue, and blood moving towards the probe is coloured red (hence the acronym 'BART').

Ultrasound imaging modes

Five modes of echo image representation are recognized, but modern machines use only three (M-mode, 2D, and Doppler).

A (amplitude) mode

Horizontal axis represents *time* or *depth* into the patient. Vertical axis represents *amplitude* of the return echo.

B (brightness) mode

The two dimensions of the display are used to represent a cross section of the patient. The brightness represents the amplitude of the echoes received.

M (motion) mode

The display shows time (horizontal) and brightness (vertical) on the axes. A single plane is chosen by the operator and any echo reflection within this plane is displayed, against time, on the screen.

2D (two-dimensional) mode

Repeated sweeps of M-mode are displayed to reproduce images recognizable as 2D structures. Since multiple M-mode cuts are used to make up each frame, the temporal resolution is inferior to M-mode.

Doppler modes

The Doppler effect can be monitored and colour changes added to a 2D image (colour Doppler). Alternatively, the velocity along a given plane can be tested using either continuous waves (CW Doppler) or pulsed waves (PW Doppler). Collectively these are termed spectral Doppler.

Safety considerations in trans-oesophageal echocardiography (TOE)

In comparison with other imaging and monitoring modalities, TOE has an attractive safety profile: it does not require major vessel cannulation or transfer of a critically ill patient, and does not involve use of ionizing radiation. Significant remaining risks include:

- Physical trauma: to teeth, oropharynx, oesophagus, or stomach. Known oesophageal and/or gastric pathology is a relative contraindication.
- Thermal damage: the probe generates heat, which is normally absorbed by surrounding tissues. There is usually an automatic cut-out if the temperature rises too high.
- Bubble formation: local heat can cause dissolved gases to come out of solution ('cavitation').
- Cardiovascular instability: this is rare, but the procedure may provoke both vagal and sympathetic responses. Tachyarrhythmias and even MI have been reported.

The procedure may be carried out with topical local anaesthesia (LA), light sedation (with/without topical LA), conscious sedation or general anaesthesia (GA). The decision regarding which depends upon the indication for TOE, the clinical status of the patient, resources available, expertise available and patient preference. Of note, pain is often an indicator of significant complications (e.g. oesophageal trauma) and should not simply be relieved by the use of sedative drugs without due consideration as to the cause.

TOE data relevant to anaesthesia and critical care

TOE allows evaluation of several important cardiovascular parameters of immediate relevance to anaesthesia and critical care:

Left ventricular preload

In the presence of mitral regurgitation, LV preload can be estimated using the modified Bernoulli equation by measuring the peak flow velocity of the regurgitant jet to derive the left ventricular-atrial pressure gradient. Subtracting this from the peak systolic blood pressure yields an estimate of left atrial pressure (LAP).

Alternatively, a visual estimation of LV end-systolic and end-diastolic areas (obtained through a transgastric view) readily gives an estimation of volume status.

Global LV systolic function

Doppler TOE can be used to provide continuous measurement of *cardiac output*, classically by the LV outflow tract (LVOT) method: multiplying the LVOT cross-sectional area by the PW Doppler-derived time-velocity integral yields stroke volume.

Alternatively, the fractional change of LV cavity area measured via the transgastric view gives an estimate of *ejection fraction*.

Regional systolic LV function

This is based on a visual (and subjective) assessment of wall motion, graded as normokinesia, hypokinesia, akinesia or dyskinesia. Regional wall motion abnormalities corresponding to the anatomical distribution of the three major coronary arteries are potentially important indicators of ischaemia.

Other TOE observations

TOE will, of course, reveal other potentially important information, including (but not limited to):

- LV diastolic function
- RV function
- Valvular lesions (stenosis or regurgitation)
- Pericardial disease (effusion or constriction).

Intraoperative use of TOE

The use of TOE in *cardiac surgery* is well established: to confirm the diagnosis, refine anaesthetic and surgical management, and to assess the response to the intervention.

There is increasing interest in the use of TOE as a complementary monitoring tool in *non-cardiac surgery*. It is well recognized that perioperative *cardiac* complications constitute a major element of the risk associated with non-cardiac surgery. The factors that make up this risk—the patient's functional status, pre-morbid conditions, and the nature of the proposed surgery—are discussed elsewhere (sections 1.1–1.5).

TOE may be used to guide intraoperative fluid therapy and to identify possible myocardial ischaemia through regional wall motion assessment.

Intraoperative TOE may be especially applicable to certain non-cardiac surgical procedures:

- *Aortic surgery:* aortic occlusion produces an acute rise in afterload that may promote cardiac failure or ischaemia. Reperfusion is frequently associated with myocardial depression.
- *Liver transplantation:* TOE allows rapid identification of possible causes of haemodynamic instability, including hypovolaemia, RV failure, and embolic phenomena.
- *Major orthopaedic surgery:* may be associated with cardiovascular instability due to embolism of fat, air, or bone marrow.
- *Neurosurgery:* procedures in the sitting position carry a particular risk of air embolism. TOE may be used both to screen for a patent foramen ovale and to detect air embolism during surgery.
- *Surgery in the GUCH patient:* in some cases this will pose special challenges (see sections 1.19 and 14.9) and intraoperative TOE may be invaluable.

Use of TOE in critical care

TOE has potentially important applications in the critical care unit, employing the same principles and techniques as described previously. There are several critical care situations in which general consensus and/or evidence supports the use of TOE:

- The haemodynamically unstable patient
- Suspected aortic dissection
- Blunt or penetrating chest trauma
- Suspected pre-existing valvular or myocardial disease in the trauma patient
- Widened mediastinum and suspected aortic injury.

Further reading

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1.9 Perioperative arrhythmias

The term 'arrhythmia' denotes an abnormality in cardiac rate, rhythm, or conduction. The event may be asymptomatic, or it may cause symptoms such as palpitations, dizziness, or syncope. In some instances, an arrhythmia may result in sudden cardiac death.

Cardiac arrhythmias are an important cause of both morbidity and mortality during the perioperative period, yet there is relatively little guidance in the literature aimed at management in this specific setting.

Mechanisms of arrhythmia generation

Arrhythmias may arise through disorders of impulse *formation* or *conduction*. Essentially, three processes may occur—these are illustrated in Fig. 1.7:

- *Increased automaticity*: either the phase 4 depolarization slope is steeper, or the threshold potential lower.
- *Triggered activity*: 'after'-depolarizations may reach threshold potential—characteristic of the long QT syndrome.
- *Circus movement or re-entry*: non-uniform rates of conduction/refractory periods within a ring of excitable tissue may produce a self-sustaining circus movement: either structural (e.g. Wolff–Parkinson–White syndrome) or, more commonly, functional (e.g. myocardial ischaemia).

A variety of factors may precipitate arrhythmias perioperatively (see Box 1.22).

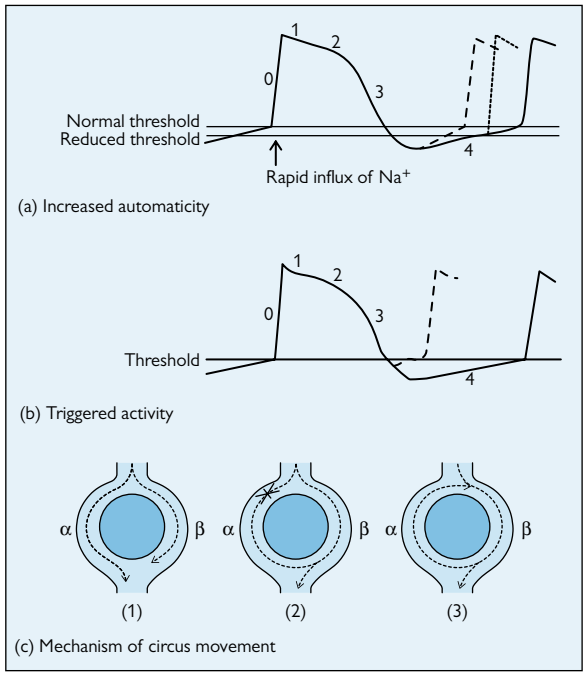

Fig. 1.7 Mechanisms of arrhythmogenesis. Image courtesy of Dua et al., 'Management of Perioperative Arrhythmias', *Indian Journal of Anaesthesia*, 2007, Figure 1, 51, 4, pp. 310–323, with permission.

Box 1.22 Common intraoperative factors predisposing to arrhythmias

- Pre-existing cardiac disease:
  - Ischaemic heart disease, cardiomyopathy, etc.
- Fluid and electrolyte imbalance:
  - Hypovolaemia, hypo- or hyperkalaemia, hypocalcaemia or hypomagnesaemia
- Light planes of anaesthesia/excessive stimulation:
  - Especially during endotracheal intubation
- Metabolic upset:
  - Hypo- or hypercarbia, acidosis or alkalosis, hypoxaemia, hypothermia or hyperthermia
- Anaesthetic and other drugs:
  - Volatile agents (e.g. halothane, enflurane), ketamine (blocks catecholamine re-uptake), others (e.g. suxamethonium, atropine, inotropes, β-blockers)
- Mechanical irritation:
  - Central lines, PACs, surgical retraction, etc.
- Vagal stimulation:
  - Peritoneal stretch, oculo-cardiac reflex, etc.
- Intracranial pathology:
  - Subarachnoid haemorrhage, raised intracranial pressure
- Endocrine disorders:
  - Phaeochromocytoma, thyrotoxicosis.

Approach to management

The overriding question is whether the arrhythmia is considered dangerous, or potentially so. If time permits, it is always desirable to record a definitive 12-lead ECG.

If the arrhythmia is causing a haemodynamic disturbance (hypotension, ischaemic ECG changes or signs of cardiac failure), it requires treatment: the degree of disturbance dictates the urgency required. Pseudo-arrhythmias (from diathermy, muscle artefact, or poor ECG electrode contact) should, of course, be ruled out.

Depending on the nature of the arrhythmia, and the clinical status of the patient, there are three categories of treatment:

- Electrical: cardioversion (or defibrillation) or pacing
- Simple clinical intervention: e.g. vagotonic manoeuvre
- Pharmacological.

In all instances, precipitating or aggravating factors should be identified and corrected, and there should be no hesitation in seeking early cardiological advice if needed.

The Resuscitation Council (www.resus.org.uk) provides detailed guidelines on arrhythmia management.

Management of individual rhythm disturbances

Bradycardia

Whilst a bradycardia is defined as HR <60 beats/min, it is perhaps better characterized as a heart rate that is inappropriately

slow for the haemodynamic state of the patient. Sinus bradycardia may of course be a normal finding in athletes, but is more usually associated with drug therapy (β-blockers, digoxin, etc.) ± ischaemic heart disease. Other causes include hypothermia and hypothyroidism.

Non-sinus bradycardias may be nodal in origin or occur in the setting of AV block. The presence of adverse signs (HR <40/min, associated hypotension or supercedent ventricular arrhythmias) is an indication for treatment. Anticholinergics (glycopyrronium/atropine) remain first-line (after elimination of obvious precipitants such as peritoneal stretch), but with initial caution in the presence of IHD.

Refractory bradycardias, and those where there is a high risk of deterioration to asystole (e.g. long pauses, Mobitz type II AV block, or 3rd-degree AV block with broad complexes) will require expert assistance and possibly transvenous pacing. Chronotropic infusions (isoprenaline or adrenaline) or transcutaneous pacing may be appropriate interim measures.

Atrial fibrillation

AF is common—it may be seen acutely in theatre, and, perhaps even more commonly, in high-dependency postoperative patients, in whom the incidence may be as high as 15%. It carries a significant mortality and morbidity.

The fundamental consideration remains the haemodynamic status of the patient, whilst the goal of treatment may be to restore sinus rhythm or to control the ventricular rate.

In essence, patients who are severely haemodynamically unstable should undergo prompt synchronized DC cardioversion.

In the case of haemodynamically stable patients with new-onset AF, there is a greater variety of options: DC cardioversion may still be considered, but a pharmacological approach is often employed. Intravenous amiodarone has a conversion rate of up to 80% (and, of course, has efficacy in a wide range of other acute arrhythmias), but there are reports of occasional severe acute pulmonary toxicity. A relatively new class 3 agent, ibutilide, is reported to have high conversion rates, even when amiodarone has been unsuccessful.

Whilst previously, the goal of therapy was to restore sinus rhythm, there is growing interest in *rate control* strategies as a primary endpoint, with similar or even improved mortality and morbidity. A variety of agents may be used, including digoxin, calcium antagonists (diltiazem or verapamil) and β-blockers.

Anticoagulation in AF is discussed in section 1.20.

AV nodal re-entrant tachycardia (AVNRT)

AVNRT is the commonest non-sinus, regular, narrow-QRS complex tachycardia. It is frequently seen in the emergency department and intensive care setting, but may also be encountered in theatre. In many cases, the ventricular rate is extremely high (180–240 beats/min). An awake patient will experience palpitations, light-headedness, and shortness of breath or anxiety. Vagal manoeuvres may slow AV conduction and terminate the arrhythmia. Intravenous adenosine has a rapid onset of action and an extremely short half-life, and is the drug of first choice. Longer-acting agents such as verapamil may be used: it is important *not* to administer verapamil to a patient receiving β-blocker therapy.

Ventricular tachyarrhythmias

Ventricular arrhythmias may be classified according to morphology (monomorphic vs polymorphic) and duration (sustained vs non-sustained). Episodes of non-sustained ventricular tachycardia (NSVT) may be seen in the absence of structural heart disease, but in those with heart disease, NSVT is a predictor of more serious subsequent arrhythmias. Magnesium may reduce the incidence of postoperative NSVT after cardiac surgery.

Sustained VT may be monomorphic (constant QRS amplitude) or polymorphic (continually changing QRS morphology). Monomorphic VT arises through a re-entry phenomenon: lignocaine was traditionally first-line therapy, but amiodarone is widely used.

In polymorphic VT, the critical deciding factor in choosing therapy is the QT interval during previous sinus rhythm. Polymorphic VT in the setting of a normal QT interval usually occurs in ischaemic heart disease and frequently degenerates into VF. Amiodarone or procainamide may be preferable to lignocaine. By contrast, polymorphic VT with a preceding prolonged QT interval (torsades de pointes) requires a different approach—therapy is focused at reversal of the QT prolongation. Electrolyte imbalance should be corrected, and intravenous magnesium is the first-line treatment. Both class I and III anti-arrhythmics may themselves prolong the QT interval (procainamide, for example, is contraindicated in torsades)—the incidence of torsades is lowest with amiodarone (see Box 1.23), which may, therefore, be a rational therapy for refractory polymorphic VT of unknown aetiology.

In all cases, it must be stressed that DC cardioversion remains first-line treatment in the unstable patient.

Box 1.23 Some causes of prolonged QT syndrome

Congenital

- Jervell–Lange–Nielsen and Romano–Ward syndromes.

Acquired

- Metabolic:
  - Hypokalaemia, hypocalcaemia, hypomagnesaemia
- Bradyarrhythmias:
  - Sinus node dysfunction
  - 2nd- or 3rd-degree AV block
- Antiarrhythmic drugs:
  - Quinidine, procainamide, disopyramide, amiodarone, sotalol
- Antimicrobial drugs:
  - Erythromycin, clarithromycin, some azole antifungals
- Antihistamines:
  - Terfenadine, astemizole
- Psychotropic drugs:
  - Thioridazine, phenothiazines, SSRIs, risperidone
- Other:
  - Droperidol, myocardial ischaemia, hypothermia.

Pulseless cardiac arrest

The four most common lethal rhythms are ventricular fibrillation (VF), pulseless VT, pulseless electrical activity (PEA), and asystole. The most critical intervention is immediate CPR, and in the case of a shockable rhythm (VF or VT), defibrillation should be performed as early as possible.

The exact mechanism of successful defibrillation remains unknown, but it may act to prolong the refractory period of the cardiac action potential. Most defibrillators now employ a biphasic shock waveform that possibly increases the termination rate of VF.

In the case of asystole or PEA, survival is poor unless a reversible cause (e.g. hyperkalaemia or hypovolaemia) is identified and treated.

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1.10 Pacemakers and defibrillators

There are important considerations in respect of patients with permanent pacemakers and/or implantable defibrillators who present for surgery. It is essential to have a basic understanding of the function of these so-called cardiac rhythm management devices (CRMDs) and a strategy for safe management during the perioperative period.

Overview of pacemakers

Pacemaker systems consist of an *impulse generator* (usually implanted in the subpectoral region) and *leads* (usually attached to the endocardium via a transvenous approach).

Pacemakers may be single chamber (RV), dual chamber (RA + RV), or even tri-chamber (RA+RV+LV)—the latter are used in resynchronization therapy for heart failure (see section 1.13), in which the LV lead is usually placed via the coronary sinus.

Single-chamber devices sense intrinsic activity within that chamber, which will either inhibit or trigger pacing activity. Dual-chamber systems seek to maintain atrioventricular synchrony to optimize cardiac output. Some systems incorporate a rate-modulating mode that enables patients without intact sinus node function to increase their heart rate in response to exercise—commonly used sensors detect motion/vibration or minute ventilation (via changes in thoracic impedance). It is crucial to be aware of such configurations preoperatively, since certain functions may need to be altered or disabled.

An internationally recognized 5-position code is used to describe pacemaker location and function (Table 1.6). The 5-position code is often shortened to the first 3, and the most commonly used mode is a dual chamber (DDD) mode. Multisite pacing (position V) refers either to the presence of more than one lead in a single chamber, or more commonly, biventricular pacing to promote resynchronization.

Implantable cardioverter defibrillators

Implantable cardioverter defibrillators (ICDs) have all the capabilities of a pacemaker, together with the potential for defibrillation (± overdrive pacing) of tachyarrhythmias (usually ventricular). ICDs measure each cardiac R–R interval, and categorize the rate as normal, too fast (short R–R) or too slow (long R–R). When enough short R–R intervals are detected, an antitachycardia event (pacing or shock) is begun. Most ICDs will also start pacing when the R–R interval is too long. Like pacemakers, ICDs are described by an international generic code (Table 1.7).

Preoperative assessment of patients with CRMDs

Preoperative evaluation should focus on three main questions (see Fig. 1.8):

1. What type of device is present?
2. How dependent is the patient on the device's pacing function, and what is the underlying escape rhythm (Box 1.24)?
3. What are the device settings and is it functioning correctly?

A detailed history and examination should determine the indication for the CRMD, any coexisting pathology, and the location of the impulse generator. Many patients with CRMDs will have important coexisting disease, including IHD, cardiomyopathy, valvular heart disease, or congenital heart disease.

Box 1.24 Major indications for pacemaker implantation

- 3rd-degree and advanced 2nd-degree AV block at any level.
- Higher level AV block of any type with associated bundle branch block.
- Sinus node dysfunction with documented symptomatic bradycardia.
- Bradycardia–tachycardia syndrome.
- Recurrent carotid sinus syncope.

Patients will ideally carry a card showing the make, model, and serial number of the device. Pacemaker dependency will be suggested by a preceding history of symptomatic bradycardia or AV node ablation. A chest X-ray (CXR), whilst not routinely required, will confirm whether the device is single- or dual-chamber and whether an ICD is *in situ* (visible shock coil on the ventricular lead).

A 12-lead ECG will demonstrate whether or not the pacing function is being used, and which chamber(s) are sensed and/or paced.

The only reliable assessment of a CRMD is direct interrogation by a cardiac electrophysiologist—this will reveal battery status, settings, pacemaker dependency, and event log (e.g. shock history); additionally, whether or not a magnet will convert the device to an asynchronous mode (Box 1.25).

Box 1.25 Key points in preoperative evaluation of CRMDs

- Has the device been interrogated by an electrophysiologist?
- Consider replacement if device nearing end of battery life.
- What is the patient's underlying rate and rhythm?
- Identify the magnet rate and rhythm.
- Ensure that rate-responsiveness functions (e.g. via minute ventilation) are turned off.
- Consider increasing the pacing rate to optimize oxygen delivery during major surgery.
- Disable antitachycardia therapy if ICD *in situ*.

Sources of electromagnetic interference (EMI) in theatre and use of magnets

EMI may cause pacemaker output to be inhibited, or it may produce inappropriate triggering. Additionally, the pacemaker may revert to an asynchronous mode that may provoke arrhythmias if there is a competing underlying rhythm.

The operating theatre environment may generate numerous sources of EMI (Box 1.26).

Box 1.26 Sources of EMI in theatre

- Surgical diathermy (esp. 'coag' or 'blend'); MRI
- External cardioversion or defibrillation; lithotripsy
- Radio-frequency ablation; electroconvulsive therapy (ECT).

Table 1.6 Generic pacemaker codes				
Position 1	**Position II**	**Position III**	**Position IV**	**Position V**
Chamber(s) paced	Chamber(s) sensed	Response to sensing	Rate modulation	Multi-site pacing
O = None	O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T = Triggered	R = Rate modulation	A = Atrium
V = Ventricle	V = Ventricle	I = Inhibited		V = Ventricle
D = Dual (A + V)	D = Dual (A + V)	D = Dual (T + I)		D = Dual (A + V)

Table 1.7 Generic defibrillator codes			
Position 1	**Position II**	**Position III**	**Position IV (or use pacemaker code)**
Shock chambers	Antitachycardia pacing chambers	Tachycardia detection	Antibradycardia pacing chambers
O = None	O = None	E = Electrogram	O = None
A = Atrium	A = Atrium	H = Haemodynamic	A = Atrium
V = Ventricle	V = Ventricle		V = Ventricle
D = Dual (A + V)	D = Dual (A + V)		D = Dual (A + V)

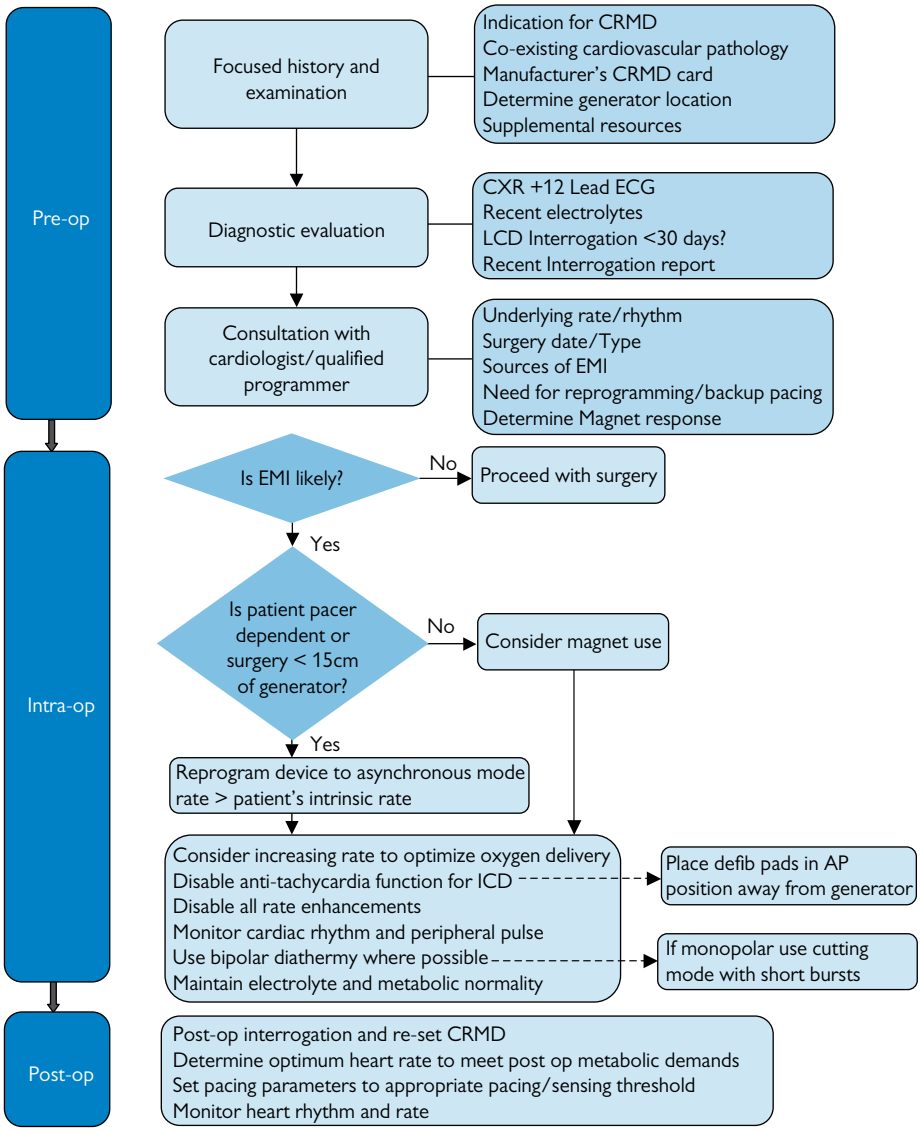

Fig. 1.8 Perioperative management of CRMDs. Reproduced from Navaratnam et al., 'Pediatric pacemakers and ICDs: how to optimize perioperative care', *Pediatric Anesthesia*, 21, 5, pp. 512–521, with permission, © 2011, Blackwell Publishing Ltd.

Modern devices are less susceptible, but the risk remains. Patients who are pacemaker dependent *and* in whom there is deemed a significant risk of EMI should be reprogrammed to an asynchronous mode at a rate higher than the patient's intrinsic rate. Rate-responsive functions, as discussed previously, should be disabled, as should the antitachycardia function of an ICD.

Reprogramming should take place under appropriate monitoring, and external defibrillator pads applied if an ICD has been disabled—these should be placed as far away from the pulse generator as possible.

It is usually advised that a magnet be made available for emergency use in theatre if EMI occurs. It is important to remember, however, that different devices respond in different ways. The device's individual magnet response settings can be revealed by interrogation as part of the preoperative work-up. In most cases, placing a magnet over the pulse generator will cause the pacemaker to revert to an asynchronous pacing mode (AOO, VOO, or DOO). ICDs will usually suspend antitachycardia therapy in the presence of a magnet.

The availability of a magnet does, not, however, replace the need for preoperative evaluation of a CRMD and for re-programming by a cardiac electrophysiologist if the risk of EMI is deemed significant.

Intra- and postoperative management of patients with CRMDs

ECG monitoring is essential, and the monitor settings should be altered to detect pacemaker activity. Pulse oximetry is, of course, routine, and the waveform should be displayed. For patients with significant cardiac disease or those undergoing major surgery, invasive arterial monitoring is invaluable. Major electrolyte disturbances, acid–base imbalance or hypoxaemia may affect pacemaker function and should be corrected.

If a device was altered preoperatively, it will of necessity require reprogramming postoperatively, and in the case of ICDs, full monitoring should continue until the anti-tachycardia function has been re-enabled.

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1.11 Cardiomyopathy

Cardiomyopathy is defined as a myocardial disorder in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valvular or congenital heart disease.

Classification

The phenotypes described are:

- Dilated cardiomyopathy (DCM)
- Hypertrophic (obstructive) cardiomyopathy (HCM)
- Restrictive cardiomyopathy (RCM)
- Arrhythmogenic right ventricular dysplasia (ARVD)
- Unclassified (encompassing Tako-tsubo cardiomyopathy and left ventricular non-compaction).

Each may be subclassified into familial/non-familial, genetic/non-genetic, and idiopathic/acquired forms (for a summary, see Table 1.8).

General investigations and perioperative management

The management of heart failure is discussed in section 1.13.

Brain natriuretic peptide (BNP) levels are useful in diagnosing and assessing the severity of both acute and chronic heart failure.

Echocardiography (see section 1.8) is crucial for objective assessment of both structural and functional cardiac abnormalities. Determining the LV ejection fraction (LVEF) allows for a broad classification of heart failure syndromes into two types:

- HFREF (heart failure with reduced ejection fraction): LVEF <50%
- HFPEF (heart failure with preserved ejection fraction): LVEF >50% with diastolic dysfunction.

Cardiac MRI may be useful in assessing possible aetiologies, since it may reveal cardiac inflammation, infiltration or fibrosis. Myocardial biopsy may be useful in cases of myocarditis and infiltrative diseases such as amyloidosis.

Certain categories of drug are disease modifying in HFREF (see Box 1.27).

Box 1.27 Drug therapy in HFREF

Disease modifying

- Angiotensin-converting enzyme inhibitors (ACEIs).
- β-blockers.
- Mineralocorticoid receptor antagonists (e.g. spironolactone).
- Angiotensin receptor antagonists (ARAs) if ACEI intolerant.

Drugs of less certain benefit

- Ivabradine—if HR >70/min (in addition to β-blocker, or as an alternative if β-blocker intolerant).
- Digoxin (even in sinus rhythm).
- Nitrates and hydralazine (alternative to ACEI or ARA).
- Diuretics (loop or thiazide) for fluid retention.

For HFPEF, there are no convincing data to suggest a survival benefit with ACEI or ARA therapy. Diuretics are useful for treating fluid retention. Comorbidities such as hypertension and myocardial ischaemia should be treated.

There are certain fundamental principles of perioperative management of patients with cardiomyopathies or heart failure (see Box 1.28).

Box 1.28 Perioperative management of heart failure syndromes

- Undertake risk scoring prior to anaesthesia (see sections 1.1–1.5).
- Optimize heart failure medication.
- Consider invasive monitoring, including TOE.
- Avoid tachycardia, and aim to maintain sinus rhythm (low threshold for DC cardioversion if arrhythmia develops).
- Avoid large-volume infusions.
- Consider inotropic support *only* if measured CO and patient's clinical state suggest indicated (patient's normal BP may be significantly lower than in normal population).
- If longstanding heart failure on maintenance diuretics, IV diuretics or even ultrafiltration may be required in the early postoperative period.

Dilated cardiomyopathy

DCM is the most common of the cardiomyopathies, defined by the presence of LV dilatation and systolic dysfunction (with or without RV dysfunction), in the absence of abnormal loading conditions or coronary artery disease.

In addition to familial and genetic causes, alcohol, viruses, tachycardia, nutritional deficiencies, pregnancy, and drugs (including chemotherapeutic agents) are known causes.

Many patients are asymptomatic, but may present acutely with decompensated heart failure. There is an important risk of life-threatening arrhythmias and sudden death, and symptomatic patients with LVEF <30% should be considered for an ICD. There is growing use of cardiac resynchronization therapy (see section 1.13).

In terms of surgical treatment, severely impaired patients may be candidates for cardiac transplantation. Other therapies have been tried, including LV volume reduction surgery (the Batista procedure), attempting to improve the mechanics of LV function.

Peripartum cardiomyopathy (PPCM)

PPCM is a form of DCM that occurs during the last month of pregnancy or within 5 months of delivery, in the absence of another cause for heart failure or structural and functional abnormality of the heart. The LV systolic function is reduced (LVEF <45%). Risk factors include: age >30 years, multiparity, African origin, multiple fetuses, history of pre-eclampsia, eclampsia, or hypertension, cocaine use, or oral tocolytic therapy.

Management goals are similar to those in all heart failure syndromes, but some important aspects are specific to PPCM (see Box 1.29).

Box 1.29 Specific management aspects in PPCM

- ACEIs, ARAs, and aldosterone antagonists are contraindicated in pregnancy (consider hydralazine).
- β-blockers (especially selective β1-receptor blockers such as bisoprolol) can safely be used during pregnancy.
- IV GTN can be given during pregnancy.
- Anticoagulation is recommended: pregnancy and the postpartum period are hypercoagulable states and in the context of LV systolic dysfunction there is a high risk of embolic events.
- Breastfeeding is not recommended, as the aim is to reduce prolactin levels, which is thought to play an important role in the pathophysiology of the condition, and bromocriptine may be considered.
- In cardiogenic shock, urgent mechanical circulatory support should be considered.
- Expedite delivery of patients with advanced or unstable heart failure.

Hypertrophic cardiomyopathy

Hypertrophic (obstructive) cardiomyopathy (HCM) is characterized by the presence of myocardial hypertrophy in the absence of an obvious precipitant such as hypertension or valvular heart disease. Several different subtypes exist, any of which may be associated with diastolic dysfunction, myocardial ischaemia or dynamic or fixed LV outflow tract (LVOT) obstruction. The dynamic LVOT obstruction is secondary to systolic anterior motion of the mitral valve apparatus (SAM), which may or may not result in mitral regurgitation. HCM is additionally a phenotypic presentation for several conditions e.g. Anderson–Fabry's disease or Friedreich's ataxia, and an association exists with bicuspid aortic valve, and Wolff–Parkinson–White syndrome.

Patients with HCM are at particular risk of *sudden cardiac death* (SCD). Risk factors include:

- Family history of SCD
- Severe LV hypertrophy (>30mm)
- Abnormal BP or HR response to exercise
- Sustained or multiple non-sustained VT on Holter monitoring.

β-blockers, verapamil, or disopyramide are treatments of choice in HCM, especially in the context of LVOT obstruction. Control of AF through pharmacotherapy or ablation (with anticoagulation as appropriate) is important, as AF is poorly tolerated. Patients with reduced ejection fraction should be on standard heart failure medication for HFREF.

Surgical management includes septal myomectomy for obstructive HCM and severe symptoms unresponsive to pharmacotherapy. An alcohol septal ablation procedure in the cardiac catheter laboratory may be a preferred strategy in selected patients. Dual chamber pacing can be considered although the benefits of this strategy are questionable. Patients with end-stage heart failure should be considered for cardiac transplantation.

Restrictive cardiomyopathy

RCM is defined as restrictive ventricular physiology in the presence of normal or reduced diastolic volumes (of one or both ventricles), normal or reduced systolic volumes, and normal ventricular wall thickness. However a degree of increased LV wall thickness is seen in some cases such as infiltrative disease (e.g. amyloidosis) or storage disease (Pompe's disease or Fabry's disease). RCM is rare in the developed world, where it is most commonly associated with cardiac amyloidosis.

Other potential causes include haemochromatosis, sarcoidosis, carcinoid syndrome, endomyocardial fibrosis (subtropical Africa, Asia, and central America) and radiation. The most important differential diagnosis is constrictive pericarditis, where surgical pericardectomy can be considered.

Table 1.8 Summary of essential features of the cardiomyopathies

	Dilated	Peri-partum	Hypertrophic	Restrictive	Arrhythmogenic
Sex	M > F	F	M = F	M = F	M = F
Prevalence	36:100 000	1:100–1:4000	1:500	1:1000–1:5000	1:5000
Aetiology	Multiple: 25% genetic (predominantly autosomal dominant, but X-linked with muscular dystrophies); drugs, alcohol, viral, nutritional	? pregnancy-related inflammation/altered prolactin processing	Predominantly autosomal dominant inheritance	Multiple–including deposition disorders and genetic	Predominantly autosomal dominant inheritance
Histology	Myocyte hypertrophy, fibrosis, lymphocyte infiltration	Lymphocytic infiltrate, myocyte oedema, variable fibrosis	Myocyte disarray and fibrosis	Myocyte hypertrophy, fibrosis, lymphocyte infiltration ± evidence of storage disease	Replacement of RV myocardium with adipose tissue and fibrosis
Examination	Features of LV ± RV failure May be functional mitral ± tricuspid regurgitation	Features of LV ± RV failure May be functional mitral ± tricuspid regurgitation	Double LV impulse, sharp rising pulse, ejection systolic murmur ± mitral regurgitation	Features of LV ± RV failure May be functional mitral ± tricuspid regurgitation	Features of RV ± LV failure
ECG	Normal or bundle branch block, tachyarrhythmias, abnormalities of ST segment, T wave, QT interval	Normal or bundle branch block, tachyarrhythmias, abnormalities of ST segment, T wave, QT interval	Usually abnormal, with features of LVH, various ST segment and T wave abnormalities	AF, sick sinus syndrome, VT, inferior Q waves, low QRS voltages	ECG normal at presentation in 40-50% May show RBBB, T wave inversion, epsilon waves, LBBB or VT
Outlook	Depends on aetiology	Ranges from full recovery to progressive fibrosis and DCM	Mortality 1% per year	Depends on aetiology	Depends on risk factors for sudden cardiac death

LBBB/RBBB: left/right bundle branch block

In RCM, the stroke volume is limited and small. Further, infiltrative disease involving the sino-atrial or atrio-ventricular node may lead to bradyarrhythmias in the perioperative situation. Maintenance of an adequate SVR and heart rate are key to maintain CO.

Arrhythmogenic right ventricular dysplasia

ARVD is an inherited disorder in which there is progressive replacement of RV myocardium by adipose and fibrous tissue. The principal complication is arrhythmia, and certain factors increase the risk of SCD in ARVD:

- Young age.
- Competitive sport activity.
- Family history of SCD.
- Significant RV involvement with impaired systolic function.
- Involvement of the LV.
- History of syncope or previous ventricular arrhythmia.

Such patients should undergo ICD placement and refrain from competitive athletics. Sotalol is often a highly effective antiarrhythmic agent in ARVD. Patients with intractable arrhythmias and progressive heart failure should be assessed for cardiac transplantation.

Further reading

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1.12 Inotropes and vasodilators

The development of a low cardiac output state necessitates urgent intervention to restore adequate perfusion before multiorgan failure develops. Current consensus recommends that inotropes and vasodilators be used *early* in selected patients whose shocked state persists despite volume resuscitation. Appropriate monitoring should be instituted to guide therapy (see sections 1.6 and 1.7). Inotrope therapy should be weaned as soon as adequate organ perfusion is restored and can be maintained.

Inotropes and inodilators

Adrenaline (epinephrine)

Adrenaline is an endogenous catecholamine formed by the methylation of noradrenaline (norepinephrine). It acts predominantly on cardiac β_1 and peripheral α_1 receptors, resulting in positive inotropic, chronotropic, and vasoconstrictor effects. The net effects on systemic vascular resistance (SVR) are less predictable than with noradrenaline, since adrenaline also causes concomitant peripheral β_2 receptor activation with vasodilatation.

Adrenaline also exhibits positive *dromotropic* (increased AV node conduction) and *bathmotropic* (increased myocyte excitability) effects.

There are a number of important potential adverse effects associated with adrenaline therapy:

- Significantly increased myocardial work and O_2 consumption (positive chronotropy and inotropy).
- Potential myocardial ischaemia from coronary vasoconstriction.
- Pro-arrhythmogenic effects.
- Regional vasoconstriction, e.g. of splanchnic circulation.
- Increased lactic acid production: via stimulation of Emden–Meyerhof pathway via pyruvate: makes interpretation of lactate levels potentially challenging.

Adrenaline is not recommended for the routine treatment of acute heart failure, but is frequently used at low doses in patients with severe refractory haemodynamic instability. It remains widely used in anaphylaxis and as part of current Advanced Life Support (ALS) guidelines in the management of cardiac arrest.

Dopamine

Dopamine is a naturally occurring precursor of noradrenaline with varying receptor effects depending on dosage. At low doses (0.5–3mcg/kg/min) its predominant activity is on dopaminergic (DA_1 and DA_2) receptors, whilst at higher doses (3–10mcg/kg/min), β_1 effects predominate, with some β_2 mediated peripheral vasodilatation. Doses higher than these should be used with caution, as they are associated with an increasing risk of tachycardia, dysrhythmias, and α_1 stimulation resulting in increased SVR.

The routine use of dopamine remains contentious. It was thought that low-dose 'renal' dopamine to increase renal blood flow could be used to prevent renal failure, before a randomized clinical trial, comparing dopamine to placebo, demonstrated no difference in primary or secondary outcome. Nonetheless, in diuretic-resistant hypotensive chronic heart failure, dopamine (2.5mcg/kg/min) in conjunction with a furosemide infusion may optimize haemodynamics and renal perfusion sufficient to facilitate diuresis.

Adverse systemic effects of dopaminergic stimulation include confusion, nausea and vomiting, and altered immune regulation, which may also be associated with adverse outcomes.

Isoprenaline

Isoprenaline is a synthetic derivative of dopamine, with potent β_1 and β_2 effects. Chronotropic effects predominate, and it is rarely used as an inotrope. More frequently, it is used to provide a temporary increase in heart rate pending institution of definitive pacing. Isoprenaline may be useful in the presence of significant pulmonary hypertension where it acts both as an inotrope and a pulmonary vasodilator.

Dobutamine

Dobutamine is a synthetic derivative of isoprenaline, and an agonist at β_1 and β_2 receptors. It therefore increases cardiac output whilst also decreasing SVR. Current guidelines recommend using dobutamine in low-output states provided there is adequate blood pressure. Dobutamine may exacerbate tachycardia and tachyarrhythmias, and in the presence of hypovolaemia may result in profound hypotension. It is often used in combination with vasopressor agents, especially in refractory septic shock, where cardiogenic and vasodilatory shock may coexist.

Milrinone and enoximone

These agents are phosphodiesterase (III) inhibitors (PDEIs), and act as *inodilators* to cause:

- Increased stroke volume and cardiac output.
- Reduced PA pressure, PAOP, SVR, and PVR.

The haemodynamic effects of the PDEIs are similar to dobutamine, with some important differences:

- More potent peripheral and pulmonary vasodilatation.
- Less tachycardia and myocardial O_2 consumption.

Levosimendan

Levosimendan is a calcium sensitizer that exerts its inotropic effects through several important mechanisms:

- Binds to calcium saturated troponin-C in cardiac myocytes to cause a positive inotropic effect.
- Acts on ATP-sensitive potassium channels (KATP) on vascular smooth muscle causing vasodilatation.
- Exerts a cardioprotective effect via mitochondrial KATP channels.
- At high doses, has a mild PDEI action.

Overall these manifest as an increased cardiac output and stroke volume along with reduced pulmonary capillary wedge pressure and reduced SVR and PVR.

Initial studies produced conflicting results, with no improvement in overall survival, but these were performed in the context of chronic heart failure rather than haemodynamically compromised critically ill patients. More recent studies have supported its safety and efficacy in various patient populations.

Levosimendan would appear to be an ideal inotrope in the critically ill patient, increasing cardiac output without increasing oxygen requirements, and whilst exerting cardioprotective effects. Further studies are currently evaluating its potential applications.

Vasodilators

Vasodilator therapy is recommended early in the treatment of acute heart failure in the absence of hypotension (SBP <90mmHg) or severe obstructive valvular disease. The aim is to reduce both right- and left-sided filling pressures, and SVR, resulting in improved symptoms and haemodynamics.

Pulmonary vasodilators are indicated in right heart failure secondary to pulmonary hypertension (mean PAP >25mmHg).

There are numerous triggers for pulmonary hypertension during anaesthesia, surgery, and critical care. Hypoxia, hypercarbia, hypothermia, high airway pressures, acidosis, PEEP, hypovolaemia, and ischaemia can all contribute to acute increases in PAP or PVR, which if not recognized and corrected promptly, can result in a downward spiral of worsening pulmonary hypertension and decompensated heart failure. The failing right ventricle has little ability to compensate for acute changes in afterload. RV dilatation can in turn compromise *left* heart function and coronary perfusion.

Nitric oxide (NO) is an endogenous vasodilator produced by the vascular endothelium. NO donors form the mainstay of vasodilator therapies. These agents undergo biotransformation in smooth muscle cells to form NO, which produces venous and arterial vasodilatation via cyclic GMP. cGMP is broken down by phosphodiesterase (PDE) (in particular isoenzyme PDE-V). NO rapidly diffuses into the bloodstream and reacts with haemoglobin forming metabolites that are excreted in the urine. In heart failure, the resultant reduced systemic and pulmonary vascular venous tone, increased vascular compliance, and reduced afterload have the net effect of increasing cardiac output and reversing myocardial ischaemia.

Organic nitrates

The organic nitrates are systemic vasodilators that can be administered by a variety of routes (enteral, sublingual, subcutaneous, or intravenous). In the acute setting, nitrate therapy is usually titrated intravenously to the maximum tolerated dose without haemodynamic compromise. Limitations include the development of tolerance, with a marked attenuation of initial effects in up to 50% of patients.

Nitroprusside

Sodium (or potassium) nitroprusside is perhaps the gold standard against which other vasodilators are evaluated. It has a complex structure, containing a ferrous iron molecule bound to five cyanide molecules and nitric acid. Nitroprusside mediates its effects by decomposition to produce nitrosothiol on contact with red blood cells. Clearance is via hepatic metabolism to thiocyanate, which is then renally excreted with a half-life of 3–4 days. The main limitation of the drug relates to the toxicity of its metabolites. Suspected thiocyanate toxicity (lactic acidosis, confusion, and seizures) may require haemofiltration.

Inhaled nitric oxide

When administered by inhalation, NO diffuses rapidly across the alveolar capillary membrane into the smooth muscle cell causing local pulmonary vasodilatation. Other actions include bronchodilatation, anti-inflammatory, and antiproliferative effects. Compared to other agents, it also enhances ventilation-perfusion matching, since it increases blood flow only in well-ventilated lung areas.

It has a variety of clinical applications (Box 1.30).

Box 1.30 Clinical applications of inhaled nitric oxide

- Pulmonary hypertension of the newborn.
- Pulmonary vasoreactivity testing in cardiac catheterization.
- Preventing RV failure due to pulmonary hypertension after cardiac transplantation.
- Supporting RV function in the critically ill or after left ventricular assist device (LVAD) insertion.
- Treatment of ischaemia-reperfusion injury after lung transplantation.
- Improving oxygenation in severe acute respiratory distress syndrome (ARDS) or in chronic obstructive pulmonary disease (COPD).

Potential complications include toxicity due to the formation of nitrogen dioxide (causing pulmonary oedema) or methaemoglobinaemia (causing tissue hypoxia), although this is less likely at inhaled concentrations <80ppm.

Prostacyclin

Prostacyclin (prostaglandin I_2) is a naturally occurring vasodilator produced within endothelial cells from arachidonic acid. It also inhibits platelet aggregation and smooth muscle proliferation, and has anti-inflammatory effects. Synthetic analogues are epoprostenol (Flolan®), and iloprost, which are currently licensed for the treatment of New York Heart Association (NYHA) class III/IV pulmonary hypertension via specialized intravenous or aerosol devices. In the context of pulmonary hypertension and right heart failure in critically ill mechanically ventilated patients these agents have been found to be effective in decreasing pulmonary pressures without reducing systemic perfusion, and with minimal adverse effects. However, an effect on outcome has yet to be determined in clinical trials.

Phosphodiesterase inhibitors

Sildenafil is one of several phosphodiesterase V inhibitors used as a pulmonary vasodilator in the treatment of pulmonary hypertension. It can be administered orally, intravenously, or via inhalation. Only oral sildenafil is commercially available. It has been used effectively to treat RV dysfunction in transplant recipients and in weaning patients from NO therapy.

Other vasodilator agents

Neseritide is a recombinant DNA preparation of human ventricular brain natriuretic peptide (BNP). It binds to the guanylate cyclase receptor and converts GTP to cGMP, resulting in smooth muscle relaxation. Systemic hypotension limits its use.

L-Citrulline is metabolized to L-arginine in the pulmonary vascular endothelium. As a NO precursor, supplementation of citrulline is under evaluation in the prevention and treatment of pulmonary hypertension in children with congenital heart disease.

Bosentan is an antagonist at endothelin A and B receptors to inhibit endothelin-1 induced vasoconstriction. It produces pulmonary vasodilatation and improved haemodynamics in patients with chronic thromboembolic pulmonary hypertension.

Conivaptan is a vasopressin receptor antagonist. The vasoconstrictor effects of arginine vasopressin have led to development of antagonists proposed for the use in acute heart failure. Conivaptan reduces pulmonary capillary wedge pressure and right atrial pressure, with no significant change in other haemodynamic parameters.

Further reading

Hollenberg SM (2011). Vasoactive drugs in circulatory shock. *Am J Respir Crit Care Med*, 183(7):847–55. doi:10.1164/rccm.201006-0972CI.