

AQUA

**ANNUAL QUEENSTOWN
UPDATE IN ANAESTHESIA**

AQUA 2016

**Annual Queenstown
Update in Anaesthesia**

Programme and Abstracts

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International Faculty



Professor Bernhard Riedel

MB.ChB, FCA, FANZCA, FAHA, FASE, MMed, MBA, PhD

Bernhard is the current Director of the Department of Anaesthesia, Perioperative and Pain Medicine at the Peter MacCallum Cancer Centre and holds an honorary academic appointment at the University of Melbourne. Bernhard is an academic anaesthetist with a primary research interest that focuses on improving surgical outcomes, especially following cancer surgery. Previous appointments include: Professor and Deputy Chair in Anesthesiology and Intensive Care Medicine at The University of Texas M.D. Anderson Cancer Centre and Professor in Cardiac Anaesthesia at Vanderbilt University (USA).

New Zealand Faculty

Thomas Fernandez	Specialist Anaesthetist, Auckland City Hospital
Joanna Glengarry	Forensic Pathologist, Auckland City Hospital
Sheila Hart	Specialist Anaesthetist, Wellington Hospital
Kerry Holmes	Specialist Anaesthetist, North Shore Hospital
Chris Jephcott	Specialist Anaesthetist, Waikato Hospital
Jacob Munro	Orthopaedic Surgeon, Auckland City Hospital
Reza Nouraei	ORL Surgeon, Starship Children's Hospital
Kaye Ottaway	Specialist Anaesthetist, Anaesthesia Auckland
Karen Pedersen	Specialist Anaesthetist, Auckland City Hospital
Steve Watts	Specialist Anaesthetist, SCGH, Perth / Christchurch Hospital
Ken Whyte	Respiratory Physician, Auckland City Hospital
Paul Young	Specialist Intensivist, Wellington Hospital

Scientific Programme

FRIDAY, 19 AUGUST 2016

Session 1

0800	Onco-Anaesthesia: Can we make a difference?	Bernhard Riedel
0835	Update in Intensive Care Medicine	Paul Young
0905	Advanced Life Support Update	Sheila Hart
0930	Cough, spit, fat & snoring – do any of them ever change?	Ken Whyte

Session 2

1030	Update in Anaesthesia for Orthopaedic Surgery	Steve Watts
1055	Total Joint Replacement; making a good thing even better	Jacob Munro
1120	Recent Developments in Procedural Pain Management	Chris Jephcott

1300- 1500	Anaphylaxis Emergency Response Workshop <i>(Fully subscribed)</i>	Karen Pedersen
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SATURDAY, 20 AUGUST 2016

Session 3

0700	Behind the Scenes: A medicolegal forum <i>(Pre-registration required)</i>	Kaye Ottaway
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0800	Prehabilitation: Expanding the Role of Perioperative Medicine	Bernhard Riedel
0835	Advances in supplemental oxygen	Reza Nouraei
0905	Anaphylaxis Update	Karen Pedersen
0935	The Autopsy and You	Joanna Glengarry

Session 4

1035	Patients with liver disease undergoing non-hepatobiliary surgery	Thomas Fernandez
1105	AMREF Flying Doctors	Kerry Holmes
1135	Closing comments / Future meetings	Kerry Gunn

Onco-Anaesthesia: Can we make a difference?

Bernhard Riedel

Department of Anesthesia, Perioperative and Pain Medicine, Peter MacCallum Cancer Centre and University of Melbourne, Australia

Overview

The global burden of disease is changing at a rapid pace, with an exponential increase in the incidence of cancer, obesity and age-related morbidity. The World Health Organisation (WHO) predicts 22 million new cancer diagnoses per year globally by 2030. Of the current 15.2 million new cases of cancer (2015) an estimated 60-80% of cases will need surgery, some several times, for diagnostic, therapeutic, or palliative reasons.

It is increasingly recognized that anaesthetists have the opportunity to positively influence oncological outcomes, with potential for disease modification. This lecture will explore our current understanding of how the biological perturbations (neural-inflammatory-immunomodulating stress responses) that accompany surgery and how anaesthetic technique impact the susceptibility to perioperative tumor spread, including activation of micrometastatic disease. These pathophysiological processes impact tumour-stromal interaction, immune-editing, and genotypic plasticity and can be modulated by our choice of anaesthetic techniques, which include anaesthetic agents (e.g. volatiles [which are immunogenic], TIVA [which may have anti-inflammatory properties], neuraxial techniques [which block the adrenergic system]) and perioperative adjuncts (e.g. opioids, NSAIDs, β -blockers [which are anti-adrenergic and anti-inflammatory]). Whilst much of our understanding of these potential interactions comes from either in vitro cell line or xenograft models, there is increasing clinical data (albeit predominantly retrospective in nature) demonstrating an association with improved long-term survival for anaesthesia techniques that are underpinned by an anti-adrenergic-anti-inflammatory strategy. Until such time as adequately powered, randomized, controlled trials confirm or refute these findings we should place emphasis on such a strategy, which is easily delivered within our current armamentarium of regional (neuraxial) and intravenous anaesthetic techniques.

Additionally, it is recognized that postoperative morbidity negatively impacts on the ability of patients to return to their intended oncological treatment (RIOT; the cancer journey - with postoperative adjuvant therapy) with reduced cancer survival. As such, our focus should be on a comprehensive approach to patient care to facilitate optimal surgical outcomes, thereby ensuring timely access to such adjuvant therapies to potentially improve oncological outcomes by minimizing loco-regional recurrence and distant metastasis. Sedentary lifestyle choices, comorbid disease, and neoadjuvant cancer treatments adversely impact on the physiologic capacity (fitness) of patients, which increases postoperative morbidity. Well-coordinated perioperative care plans with optimization of co-existing diseases, prehabilitation with exercise, haematinic and nutritional optimization, implementation of evidence-based and outcome driven perioperative care pathways, a thorough understanding of the potential impact of anaesthetic technique on cancer biology, intensive postoperative surveillance to ensure early rescue from postoperative complications, and aggressive treatment of recurrent cancer are integral to achieving better cancer outcomes.

Discussion

The global burden of disease is changing at a rapid pace, with an exponential increase in the incidence of cancer, obesity and age-related morbidity. Cancer is currently the leading cause of death in developing nations and ranks next to cardiovascular diseases as the most common cause of death in the developed world. The WHO predicts that there will be 22 million new diagnoses of cancer per year globally by 2030. For many cancers, a diagnosis is no longer a terminal disease, but rather considered a chronic medical condition, often requiring increasingly complex surgical procedures with a curative intent. Of the 15.2 million new cases of cancer in 2015, an estimated 80% of cases will need surgery, some several times.¹ For the majority of patients with solid organ tumors, surgical resection still remains the cornerstone of intervention

for both curative as well as palliative measures. As such, as perioperative clinicians anaesthetists have an important role if effectively managing this global cancer 'tsunami'.

Surgery is a cost-effective intervention in terms of adjusted quality of life years gained by the patients. Importantly, lack of timely surgical access is estimated to equate to total welfare loss of ~17% of gross domestic product (GDP), with cancer and trauma accounting for more than 95% of macroeconomic loss in developing countries.² Improvements in early detection and effective new cancer treatment modalities will lead to a significant increase in the numbers of cancer survivors who will continue to need perioperative services for care of their primary tumors, disease recurrence, and non-oncological surgical care. As such, building surgical capacity should be a global health priority, with an urgent need for an improved understanding of the perioperative needs of the cancer surgery population and a thorough understanding of the implications of the biology of the disease process and cancer therapies on perioperative care and vice versa to ensure further improvement in cancer outcomes.

Within the 21st century a model of comprehensive cancer care, which is research driven, has resulted in lower rates of perioperative morbidity and mortality and improved oncological outcomes for a variety of solid tumours reported by high-volume centres.³⁻⁸ This benefit extends into long-term survival, with a significantly greater 5-year survival benefit from high-volume centres for oesophageal cancer surgery, with significant but lesser benefit also reported in gastric, pancreatic, and lung cancers. This observed correlation between hospital volume and late survival after cancer surgery is best explained by the differences in the quality of the initial surgery (including lymph node dissection and margin free resection) performed by high-volume and/or subspecialty trained surgeons and within the setting of an integrated multidisciplinary network of expertise, including medical oncology, pathology and radiology, anaesthesiology, perioperative and critical care medicine, and allied health services. Well-coordinated perioperative care plans with better optimization of co-existing diseases, implementation of evidence-based and outcome driven perioperative care pathways, a thorough understanding of the impact of anaesthetic agents on cancer biology, intensive postoperative surveillance with early rescue from postoperative complications,^{9,10} and aggressive treatment of recurrent cancer are integral to achieving better outcomes. Cancer patients and survivors present with increasingly complex medical co-morbidities, age-related conditions, disease specific challenges, including underlying causative risk factors, location of tumour, and side effects of increasingly complex cancer therapies (chemotherapy, immunotherapy and radiotherapy) with consequent alteration of local and distant organ function. In addition, our understanding of how the biological perturbations that accompany the perioperative surgical stress response and how our anaesthetic techniques impact susceptibility to perioperative tumor spread and control is rapidly evolving. As such, it is increasingly recognized that perioperative clinicians have the opportunity to positively influence oncological outcomes for cancer patients, with accumulating evidence for potential disease modification dependent upon anaesthetic technique and management of the perioperative period.¹²⁻¹⁵

Significant advances have been made with regards to understanding the pathophysiological processes (neural-inflammatory-immunomodulating stress response) of the perioperative period and their effects on tumour-stromal interaction, immune-editing, and genotypic plasticity and how we can modulate these effects within our current armamentarium of anaesthetic techniques, including anaesthetic agents (e.g. volatiles, TIVA, neuraxial techniques) and perioperative adjuncts (e.g. opioids, NSAIDs, β -blockers).¹²⁻¹⁸ Furthermore, cancer treatments can impair the physiologic reserve (functional capacity; fitness) of patients,^{19,20} with significant impact on the ability of patients to withstand surgery without morbidity.^{21,22} The ability to optimise patients to ensure optimal postoperative outcome is underpinned by the subsequent adverse impact of postoperative morbidity on the ability of patients to return to their intended oncological treatment (RIOT; postoperative adjuvant therapies) and the cancer care journey.^{15,23} Therefore, an in-depth knowledge of the adverse effects and toxicities associated with cancer therapies (chemotherapeutic agents, immunotherapy and radiotherapy) on the patient's overall functional status and timing of the surgical intervention to offer the patient the best chance for cancer control or cure is crucial. While we continue to undertake basic and translational research to better understand the perioperative biology in the context of cancer care, our aim and efforts should be focused on optimising the patient's preoperative condition (prehabilitation) to ensure the maximum benefits of surgery (neoadjuvant therapy when indicated, nutritional enhancement, physiological conditioning [strength and cardiovascular training], anaemia

management, and behavioral therapy for stress response reduction), minimize postoperative complications, and ensuring that the patient remains 'on track' to complete their cancer journey (adjuvant therapies).^{24,25}

Currently there are no prospective randomised controlled studies, which offer clear benefits of one anaesthetic technique (or perioperative strategy) over the other in terms of recurrence free survival or overall survival after cancer surgery. Published retrospective studies offer contradictory results and most of the studies have not taken the oncological factors (tumor stage and type, tumor burden, lympho-vascular space invasion, response to therapy, etc.), nutritional state, inflammatory burden and functional status into account.²⁸ Furthermore, one has to acknowledge the known shortcomings (bias in treatment allocation to the study groups) of a retrospective study despite the strengths of the clinical end points. In-vitro and animal data similarly cannot be correlated with or translated to clinical experience although they form the basis for future research models and can guide appropriate clinical protocols. Published literature from in-vitro and animal models usually involves studying the effects of individual cell lines in a controlled environment. We now also understand that the cancer biology for each of the tumors is different, and also that within each tumor there is phenotypic and genotypic heterogeneity and plasticity that explains the differences in response to therapy amongst individual patients and also the existence of circulating tumour cells (CTCs) often exacerbated by surgery.^{26,27} Our growing understanding of the concept of CTC release during surgery offers one possible explanation for the tenacity of some of the tumors in escaping the innate immunity of the host, with potential activation of the distant microenvironment for CTCs and that of undetected micrometastatic disease by the biologic perturbation that accompanies the perioperative surgical stress response. This potentially leads to loco-regional disease and distant clinical metastasis years after the primary therapeutic interventions with curative intent. This may explain the bimodal recurrence pattern observed after breast cancer surgery that is positively impacted in observational studies by perioperative NSAIDs.²⁸⁻³¹

To optimally care for the cancer surgery population, we need hypothesis driven protocols to evaluate if indeed these strategies are efficacious in improving long-term cancer outcomes. However, we should also marry lean methodology in our processes of care, with enhanced recovery programs that incorporate clinical strategies that target biologically plausible mechanisms (e.g. neural-inflammatory-immunomodulation) that may drive cancer recurrence to ensure optimal oncological outcomes. In the complex perioperative space, where key interventions to influence outcomes are frequently multimodal it will be difficult to show the efficacy of any one intervention (anti-adrenergic, anti-inflammatory strategies, avoiding volatile anesthesia, opioid-sparing strategies, goal directed fluid therapy and hemodynamic optimization, minimizing oxygen debt, etc.) singularly or as a unimodal intervention. It is therefore vital for anaesthetists and perioperative clinicians to collaborate with specialists in all areas of cancer care delivery (medical oncologists, immunologists, radiation oncologists, surgical oncologists, intensive care physicians, integrative medicine clinicians, and internal medicine physicians).

Contemporary surgical practice strategies focus on preoperative and perioperative optimisation to combat the morbidity inflicted by cancers and their treatments. Examples of these include prehabilitation with high protein nutrition, and exercise regimes to facilitate recovery from deconditioning associated with neoadjuvant therapies.²⁴ Some of this work has been incorporated into enhanced recovery packages, where opportunity presents for perioperative clinicians to be key advocates in initiating lifestyle changes in cancer patients—smoking cessation, exercise, and initiating discussions on advance care planning (ACP).

In summary, effective perioperative care of the cancer patient is increasingly complex and our knowledge of the biologic impact of the adrenergic-inflammatory-immune (surgical) stress response and anaesthetic techniques on cancer progression pathways, and thus long-term outcomes, is rapidly expanding. As such, anaesthesia and perioperative care for cancer patients should not simply be the prevention of awareness and administration of analgesia but rather an opportunity to minimise the biological perturbation of the surgical stress response and to adjust anaesthetic techniques to minimize activation of cancer progression pathways. More importantly, we should focus our perioperative strategies on reducing perioperative morbidity to ensure functional recovery after surgery that allows timely return to intended oncologic (adjuvant) therapies (RIOT).²³ It is this comprehensive approach to patient care that could

potentially influence oncological outcomes by minimizing loco-regional recurrence and distant metastasis. We require an ongoing concerted effort by scientists and clinicians, with focused research to improve our understanding of the impact of anaesthetic and perioperative strategies on long-term cancer outcomes to effectively confront the global cancer 'tsunami'.

Recommended Reading

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Update in Intensive Care Medicine

Paul Young

Intensive Care Unit, Wellington Hospital

It has been a big year for evidence-based intensive care. We have seen a number of important advances in our understanding of the management of critically ill patients. For this year's AQUA ICU update I have put together my *'top 10 papers of the recent past for the occasional intensivist'*. These are papers that address fundamental issues in the management of critically ill patients that are likely to be encountered by anyone who looks after critically ill adults in the ICU. Some are practice-changing, others are practice-informing, and some contain paradigm shifting ideas for the present and the future. Here are some summaries:

These are papers that are practice-informing:

Arabi et al. N Engl J Med. 2015; 372:2398-408.	
Patient population	Adults enterally fed within 48 hrs of ICU admission and expected to stay in ICU at least 72 hours
Intervention	Permissive underfeeding (40-60% of calculated caloric requirements)
Comparator	Standard care (70-100% of calculated caloric requirements)
1° outcome	90-day mortality
2° outcomes	ICU, hospital, 28-day, and 180-day mortality
Key findings	Permissive underfeeding patients received 46% of goal calories; standard care patients received 71% of goal calories. There was no difference in 90-day mortality
Bottom Line	Permissive underfeeding resulted in similar outcomes to standard care <i>but</i> patients in both treatment arms received substantially less than their calculated caloric requirements

Frat et al. N Engl J Med. 2015; 372:2185-96.	
Patient population	Patients with acute type 1 respiratory failure excluding those with neutropaenia, asthma, cardiogenic pulmonary oedema, shock, and type 2 respiratory failure
Intervention	Humidified high flow nasal prongs (HFNP) (50L/min) [intervention 1] Non-invasive ventilation (NIV) [intervention 2]
Comparator	Standard oxygen therapy (O ₂ via non-rebreather face mask)
1° outcome	Proportion of patients requiring intubation to day 28
2° outcomes	ICU and day 90 mortality, ventilator-free days, ICU LOS, dyspnoea and comfort
Key findings	Neither HFNP nor NIV reduced the rate of intubation compared with standard oxygen therapy. HFNP, as compared with standard oxygen therapy or NIV, was associated with reduced dyspnoea and respiratory discomfort as well as increased ventilator-free days, and reduced day 90 mortality.
Bottom Line	This study demonstrated no significant difference in the primary end point; however, secondary end points favoured HFNP over NIV or standard care. HFNP are in widespread use in NZ and these data suggest this therapeutic modality may be preferred to standard oxygen therapy or NIV in this patient population

Young et al. N Engl J Med. 2015; 373:2215-24.	
Patient population	Adults with fever and known (or suspected) infection
Intervention	1gm IV paracetamol Q6hrly until development of a contraindication, discharge from ICU, resolution of infection, or resolution of fever
Comparator	Placebo
1° outcome	Days alive and free from ICU (ICU-free days)
2° outcomes	Mortality at day 28 and day 90; body temperature; proportion of patients who discontinued study medication because of liver dysfunction
Key findings	No difference in ICU-free days or mortality. Paracetamol reduced body

	temperature by around 0.3°C. There was no difference in the number of patients who discontinued study treatment because of liver dysfunction.
Bottom Line	Using paracetamol to treat fever in patients with infections does not alter the number of days patients spend alive and outside ICU. Paracetamol is well tolerated in these patients but is only a weak antipyretic.

Young et al. JAMA. 2015; 314:1701-10.	
Patient population	Patients who required intravenous fluid therapy in ICU
Intervention	Plasma-Lyte® 148
Comparator	0.9% saline
1° outcome	Acute kidney injury or failure
2° outcomes	Proportion of patients who required RRT; serum creatinine levels in ICU; in-hospital mortality
Key findings	No difference in acute kidney injury or failure using Plasma-Lyte® instead of 0.9% saline. No difference in RRT requirements, serum creatinine, or in-hospital mortality
Bottom Line	For an all-comers ICU population saline and Plasma-Lyte® 148 result in similar renal outcomes.

These papers are game-changers:

Reade et al. JAMA. 2016; 315:1460-8.	
Patient population	Adults with agitated delirium that precludes extubation (excluding patients with traumatic brain injury or dementia)
Intervention	Dexmedetomidine by infusion at up to 1.5mcg/kg/hour
Comparator	Placebo
1° outcome	Dexmedetomidine increased ventilator-free time at 7 days by around a day compared with placebo
2° outcomes	Among the 21 a priori secondary outcomes, none were significantly worse with dexmedetomidine, and several showed statistically significant benefit, including reduced time to extubation and accelerated resolution of delirium.
Key findings	Dexmedetomidine lead to more rapid extubation and sped up resolution of delirium
Bottom Line	Dexmedetomidine is a highly effective treatment for agitated delirium. It is likely to be cost-effective.

Doig et al. Lancet Respir Med. 2015; 3:943-52.	
Patient population	Adults with feeding-related hypophosphataemia (serum phosphate <0.65 mmol/L within 72 h of starting nutritional support not explain by another major cause of low phosphate)
Intervention	Thiamine and electrolyte replacement PLUS a protocolised reduction in calorie delivery to 20 kcal/h for at least 2 days, then a slow increase in rate by around 20kcal/h every 24 hours until goal rate achieved with the proviso that if the phosphate dropped below 0.71 mmol/L at any time calorie delivery was immediately dropped to 20kcal/h before being slowly increased
Comparator	Thiamine and electrolyte replacement PLUS standard calorie delivery
1° outcome	Number of days alive after ICU discharge within 60 day follow-up
2° outcomes	Day 60 mortality and survival time to day 60
Key findings	No difference in the number of days alive and free from hospital to day 60 BUT more patients were alive at day 60 and overall survival time was increased with protocolised energy restriction
Bottom Line	If you encounter a low phosphate you should reduce enteral calorie delivery

Baharoglu et al. Lancet. 2016 25; 387:2605-13.	
Patient population	Adults within 6 h or supratentorial intracerebral haemorrhage symptom onset who had used antiplatelet therapy within 7 days and had a CGS of ≥ 8
Intervention	Platelet transfusion
Comparator	Standard care
1° outcome	Proportion of patients with death or dependence at 3 months
2° outcomes	Survival to 3 months, haematoma expansion after 24 h, platelet transfusion complications
Key findings	Administering platelet transfusions to patients with ICH who are taking antiplatelet therapy increases the risk of death or dependence at 3 months, is associated with an increased risk of transfusion-related complications, and does not reduce haematoma expansion
Bottom Line	Platelet transfusion for patients on antiplatelet agents with ICH are a really bad idea

These papers contain bright ideas that may change practice in the future:

Eastwood et al. Resuscitation. 2016; 104:83-90.	
Patient population	Patients mechanically ventilated in ICU after non-traumatic cardiac arrest
Intervention	Mild therapeutic hypercapnia (PaCO ₂ 50–55 mmHg) for 24 h during mechanical ventilation
Comparator	Normocapnia (PaCO ₂ 35–45 mmHg)
1° outcome	Neurone specific enolase and S100B levels
2° outcomes	Glasgow Outcome Scale Extended (GOSE) at 6 months
Key findings	NSE levels were lower in patients allocated to therapeutic hypercapnia. S100b concentrations decreased over time in the therapeutic hypercapnia group but not in the normocapnia group.
Bottom Line	Mild therapeutic hypercapnia is a promising novel intervention for neuroprotection in patients with hypoxic ischaemic encephalopathy.

Hodgson et al. Crit Care Med. 2016;44:1145-52.	
Patient population	Mechanically ventilated adults expected to be ventilated the day after tomorrow
Intervention	Early goal directed mobilisation (active exercise at the highest level possible as soon as possible for 1 h per day)
Comparator	Standard Care
1° outcome	Highest maximal level of exercise achieved in ICU & increased duration of exercise in ICU
2° outcomes	Time from admission to first mobilisation, duration of MV, ICU and hospital LOS, adverse events, physical function
Key findings	Higher levels of activity and a longer duration of activity in ICU for intervention patients than control patients
Bottom Line	Active mobilisation of intubated and ventilated ICU patients can be done; at present we don't know if it should be done

Singer et al. Sepsis 3.0.	
Objective	To evaluate and update definitions for sepsis and septic shock
Process	Task force of 19 experts decided what sepsis should be and then sent their recommendations to 31 societies requesting peer review and endorsement
Identified limitations of previous definition	1. Inadequate specificity and sensitivity of the SIRS criteria. 2. The use of the various terms sepsis, septic shock, and organ dysfunction lead to discrepancies in reported incidence and observed mortality
Definitions & outcomes	<i>Sepsis</i> is now defined as 'life-threatening organ dysfunction caused by a dysregulated host response to infection' and is associated with an in-hospital mortality of >10%. <i>Septic shock</i> is now defined as 'a subset of sepsis with profound circulatory, cellular and metabolic abnormalities' and is associated with an in-hospital mortality >40%.
Diagnostic criteria	Life threatening organ dysfunction is formally defined as an increase in the sequential organ failure assessment (SOFA) score of 2 or more points. However, patients with suspected infection who are likely to have the poor outcomes typical of sepsis can be identified if they have at least 2 of the following quick SOFA (qSOFA) criteria: (i) RR≥22/min; (ii) altered mentation; or, (iii) SBP 100mmHg or less. Septic shock can be identified by a vasopressor requirement to maintain a MAP of 65mmHg or greater and a lactate >2mmol/L in the absence of hypovolaemia.
Bottom Line	These are the new sepsis and septic shock definitions (according to an all male panel with no representatives from any discipline other than critical care and no representatives from outside high income countries 😊)

Advanced Life Support Update

Sheila Hart

Department of Anaesthesia, Wellington Hospital

The International Liaison Committee on Resuscitation (ILCOR) was formed in 1993 and it has identified the following mission: 'to identify and review international science and information relevant to cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) and to offer consensus on treatment recommendations'.

Representatives from the American Heart Association (AHA), the European Resuscitation Council (ERC), the Heart and Stroke Foundation of Canada, the Australian and New Zealand Committee on Resuscitation (ANZCOR), the Resuscitation Council of Southern Africa, the Inter-American Heart Foundation, and the Resuscitation Council of Asia currently sit on ILCOR.

The first ILCOR conference was held in 1999 and initial guidelines produced in 2000, with subsequent re-evaluation on a 5 yearly cycle. The most recent meeting was held in Dallas in February 2015 with Consensus on Science and Treatment Recommendations (CoSTR) statements produced in October 2015.

The following areas in ALS were reviewed as part of the 2015 review process:

Defibrillation Strategies for Ventricular Fibrillation (VF) or Pulseless Ventricular Tachycardia (pVT)

- Biphasic waveform (ALS 470)
- Pulsed biphasic waveform (ALS 470)
- First-shock energy (ALS 470)
- Single shock versus stacked shocks (ALS 470)
- Fixed versus escalating defibrillation energy levels (ALS 470)
- Recurrent VF (ALS 470)

Airway, Oxygenation, and Ventilation

- Oxygen dose during CPR (ALS 889)
- Basic versus advanced airway (ALS 783)
- Supraglottic airways (SGAs) versus tracheal intubation (ALS 714)
- Confirmation of correct tracheal tube placement (ALS 469)
- Ventilation rate during continuous chest compressions (ALS 808)

Circulatory Support During CPR

- Impedance threshold device (ITD) (ALS 579)
- Mechanical CPR devices (ALS 782)
- Extracorporeal CPR (ECPR) versus manual or mechanical CPR (ALS 723)

Physiological Monitoring During CPR

- End-tidal carbon dioxide (ETCO₂) to predict outcome of cardiac arrest (ALS 459)
- Monitoring physiological parameters during CPR (ALS 656)
- Ultrasound during CPR (ALS 658)

Drugs During CPR

- Epinephrine versus placebo (ALS 788)
- Epinephrine versus vasopressin (ALS 659)
- Epinephrine versus vasopressin in combination with epinephrine (ALS 789)

- Standard-dose epinephrine (SDE) versus high-dose epinephrine (HDE) (ALS 778)
- Timing of administration of epinephrine (ALS 784)
- Steroids for cardiac arrest (ALS 433)
- Antiarrhythmic drugs for cardiac arrest (ALS 428)

Cardiac Arrest in Special Circumstances

- Cardiac arrest during pregnancy (ALS 436)
- Lipid therapy for cardiac arrest (ALS 834)
- Opioid toxicity (ALS 441)
- Cardiac arrest associated with pulmonary embolism (PE) (ALS 435)
- Cardiac arrest during coronary catheterization (ALS 479)

Post resuscitation Care

- Oxygen dose after return of spontaneous circulation (ROSC) in adults (ALS 448)
- Post resuscitation ventilation strategy (ALS 571)
- Post resuscitation hemodynamic support (ALS 570)
- Post resuscitation antiarrhythmic drugs (ALS 493)
- Targeted temperature management (ALS 790)
- Timing of induced hypothermia (ALS 802)
- Prevention of fever after cardiac arrest (ALS 879)
- Post resuscitation seizure prophylaxis (ALS 431)
- Seizure treatment (ALS 868)
- Glucose control after resuscitation (ALS 580)
- Prognostication in comatose patients treated with hypothermic targeted temperature management (TTM) (ALS 450)
- Prognostication in the absence of TTM (ALS 713)
- Organ donation (ALS 449)

Each area had a PICO (population, intervention, comparator, outcome) question generated with identification and prioritisation of the outcomes to be reported. For example, for Antiarrhythmic drugs for cardiac arrest, the PICO question is:

‘Among adults who are in cardiac arrest in any setting (P), does administration of antiarrhythmic drugs (e.g., amiodarone, lidocaine, other) (I), compared with not using antiarrhythmic drugs (no drug or placebo) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?’

Following this there was literature review, written summary of the evidence for each outcome and development of the Consensus on Science statement. Whenever possible, consensus-based treatment recommendations were then created. The number in brackets represents the unique PICO identifier.

The quality of evidence available in relation to CPR and ECC is low to very low, really only allowing for weak recommendations based on evidence. However, there will still be some strong recommendations in the guidelines, especially where consensus opinion was that not following the recommendation could potentially result in harm.

These CoSTR statements are then used by ILCOR member organisations to update their national resuscitation guidelines, taking into account local factors, but with a commitment to minimise international differences in resuscitation practice. The Australian and New Zealand Committee for Resuscitation (ANZCOR) released their updated guidelines in January of 2016, with 47 updated guidelines out of their 75.

So what is new in our guidelines? The good news is that there are no major changes, and relatively few minor ones, so very little impact on current ALS practice. The majority of new recommendations in ALS relate to the post resuscitation phase of care. So this will be a recap of ALS with emphasis on the minor changes.

Basic life support



Just a brief mention of the BLS algorithm. The importance of early access and cardiac arrest prevention again highlighted, with early, high quality CPR. There is recognition of the emergency dispatcher coordinating the activity of bystander CPR whilst awaiting the arrival of the ambulance to facilitate early intervention. Of course, early defibrillation is a priority, with survival rates for out of hospital cardiac arrest (OHCA) of up to 50-70% if defibrillation is achieved in 3-5 mins. Still using the

DRS ABCD approach. CPR in a 30:2 ratio, compressions at 100-120 per minute (so an increase on previous recommendations), depth 1/3 of chest depth, duty cycle of 50%. ILCOR recommends at least 5cm, but not more than 6cm depth of chest compression. ANZCOR feel that it is impossible to tell the difference between 5 and 6cm and that too shallow a compression is more of an issue than too deep. They have not specified an upper limit for compression depth for this reason.

Compression only CPR if unwilling/unable to do mouth-to-mouth ventilation, results in better outcomes than no CPR. If doing ventilation, do not interrupt compressions for more than 10 seconds for breaths.

In an unwitnessed arrest, commencing compressions and allowing a short period of compressions whilst awaiting defibrillation may enhance the chance of successful defibrillation. In practice, the algorithm ensures this happens, with its focus on commencing compressions early, whilst awaiting arrival of the defib/AED/emergency services. ANZCOR recommends defibrillation as soon as the pads are attached if it is a shockable rhythm.

Public access programs and availability of AEDs essential if we are to improve outcomes from OHCA.

Advanced Life Support

There is a continued emphasis on recognition of the sick and deteriorating patient, with use of early warning systems and patient at risk teams recommended, to identify inpatients who are a risk of degenerating into cardiac arrest and implementing treatment before this occurs (or deciding resuscitation is not indicated).

Advanced Life Support for Adults

```

graph TD
    StartCPR[Start CPR  
30 compressions : 2 breaths  
Minimise Interruptions] --> Attach[Attach  
Defibrillator / Monitor]
    Attach --> AssessRhythm[Assess Rhythm]
    AssessRhythm --> Shockable[Shockable]
    AssessRhythm --> ReturnCirc[Return of Spontaneous Circulation?]
    AssessRhythm --> NonShockable[Non Shockable]
    Shockable --> Shock[Shock]
    Shock --> CPR1[CPR for 2 minutes]
    CPR1 --> AssessRhythm
    ReturnCirc --> PostResusc[Post Resuscitation Care]
    NonShockable --> CPR2[CPR for 2 minutes]
    CPR2 --> AssessRhythm
    
```

During CPR

- Airway adjuncts (LMA / ETT)
- Oxygen
- Waveform capnography
- IV / IO access
- Plan actions before interrupting compressions (e.g. charge manual defibrillator)

Drugs

Shockable

- * Adrenaline 1 mg after 2nd shock (then every 2nd loop)
- * Amiodarone 300mg after 3 shocks

Non Shockable

- * Adrenaline 1 mg immediately (then every 2nd loop)

Consider and Correct

- Hypoxia
- Hypovolaemia
- Hyper / hypokalaemia / metabolic disorders
- Hypothermia / hyperthermia
- Tension pneumothorax
- Tamponade
- Toxins
- Thrombosis (pulmonary / coronary)

Post Resuscitation Care

- Re-evaluate ABCDE
- 12 lead ECG
- Treat precipitating causes
- Aim for: SpO2 94-98%, normocapnia and normoglycaemia
- Targeted temperature management

January 2016

The 2015 areas of review were (***bold italic are changes***):

1. Defibrillation strategies for pulseless VT and VF

- a. No major developments since 2010.
- b. The precordial thump may be considered for patients with monitored, pulseless ventricular tachycardia if a defibrillator is not immediately available (but evidence for success of this is weak and this should not delay defibrillation).
- c. All new machines deliver a shock using a biphasic waveform and the recommendation remains to use a defibrillator with a biphasic waveform (truncated exponential (BTE) or rectilinear biphasic (RLB) waveforms) where possible.
- d. ILCOR suggests an initial biphasic shock energy of 150J or greater for BTE waveforms, 120J or greater for RLB waveforms and 360 J if monophasic (although no longer manufactured, still in use in some places). ANZCOR have kept it simple, recommending 200J as the default for any biphasic machine, irrespective of waveform, with the caveat that other energy levels may be used providing there is relevant clinical data for a specific defibrillator that suggests that an alternative energy level provides adequate shock success (e.g. Usually greater than 90%). 
- e. ***If the 1st shock is not successful and you are not at the maximum energy of the defibrillator, then you can increase the energy level for the next shock.***
- f. Single shock recommended rather than a stack of 3
 - i. A sequence of up to 3 stacked shocks can be considered in patients with a perfusing rhythm who develop a shockable rhythm where the setting is:
 1. a witnessed and monitored setting and 
 2. the defibrillator is immediately available (e.g. first shock able to be delivered within 20 seconds and
 3. the time required for rhythm recognition and for recharging the defibrillator is short (i.e. <10 seconds).
- g. Pads better than paddles
 - i. Decreases the amount of hands off time as pads can be charged during CPR and reduces risk of arcing if paddles elevated from the chest.
 - ii. 8cm away from any PPM ideally
- h. Hands off time for defibrillation should be < 5 seconds.

2. Airway, oxygenation and ventilation

- a. Concern around the routine use of oxygen has been expressed.
- b. 100% FiO₂ should be used during CPR, titrated to saturations in the post resuscitation phase.
- c. ***The evidence (weak, observational studies) do not suggest superiority of an advanced airway technique over BMV, or for a SGA vs ETT.*** These studies have many limitations and bias and so there is no recommendation to change current practice. Intervention should be based on a stepwise approach, taking into account patient factors and airway operator skill level.
- d. ***Waveform capnography recommended to confirm ETT position both initially and ongoing during CPR.***

3. Circulatory support during CPR

- a. No evidence that CPR feedback devices improve outcomes in cardiac arrest, but may be useful in training to improve technique.
- b. ***Impedance threshold devices not recommended.***
- c. ***Automated compression devices not recommended*** unless unable to perform high quality CPR, or this puts the rescuer at risk. For example, CPR during cath lab procedures, where this will put the rescuer at risk of radiation exposure.
- d. ***Extracorporeal CPR is indicated in selected patients*** when standard ALS has failed (for example arrest in the cath lab), but this is not readily available in most centres in New Zealand.

4. Physiological monitoring

a. Recommend waveform capnography

- i. Where this is not available other means of detecting CO₂/oesophageal intubation.
- ii. Recommend against using ETCO₂ values as a predictor of mortality and therefore to aid decision to stop the resus.

b. Cardiac USS

- i. Recommend use to rule out potential reversible cause of the arrest.
- ii. Must not interfere with standard ALS (for e.g. do not stop compressions to perform scan).

5. Drugs

a. Standard dose adrenaline recommended (1mg)

- i. There is evidence of benefit in short term outcomes (ROSC and admission to hospital).
- ii. Unclear in terms of longer term outcomes e.g. survival to discharge and neurological outcomes.

b. Amiodarone 300mg in VF or pVT recommended

- i. improves ROSC rates, again unclear if any longer term benefit.

c. Adding Vasopressin to adrenaline is not recommended. However, in places where vasopressin is already being used in place of adrenaline this may continue.

d. Other drugs, including calcium, lignocaine, magnesium, potassium, sodium bicarbonate (and other buffers) may be considered to help manage particular conditions that are associated with patients who have arrested, but routine use not recommended.

e. Fibrinolytics should not be used routinely in cardiac arrest, but may be considered when pulmonary embolus is the suspected/known cause of cardiac arrest.

f. Data on the drugs used in ALS is very limited, with no real evidence that any drug administration improves long term survival, but no changes are recommended to current practice until there is high quality evidence on long term outcomes.

6. Cardiac arrest in special circumstances and special populations

a. ILCOR ALS Task Force prioritised 5 topics for review in 2015:

i. Cardiac arrest during pregnancy

1. Uterine displacement
2. Early ALS and delivery
3. Limited evidence for any interventions in obstetric arrest but still a strong recommendation

ii. Lipid therapy for cardiac arrest associated with overdose

1. Routine lipid emulsion use in LA toxicity, TCA OD and other
2. No evidence available so unable to make any recommendations based on evidence, but ILCOR dose then say 'despite the paucity of data, we do not wish to discourage the use of an antidote with some theoretical basis in a dire clinical situation'

iii. Opioid toxicity

1. Use naloxone in opioid induced resp arrest with standard ALS for cardiac arrest

iv. Cardiac arrest caused by PE

1. Thrombolysis may be indicated (and prolonged CPR)

v. Cardiac arrest during coronary catheterization

1. If pVT or VF give 3 stacked shocks immediately prior to starting compressions
2. Mechanical compression device may be appropriate to reduce radiation exposure to staff
3. Extracorporeal CPR may be indicated

b. Other special circumstances include, but are not limited to:

- i. Avalanches

1. Criteria to reduce futile extracorporeal life support
- ii. Arrest post-sternotomy and cardiac surgery
 1. Chest reopening
 2. Early defib even more of a priority to reduce compression time and risk of cardiac injury. Stack of 3 shocks considered if defib immediately available and can give first shock in 20s
- iii. Anaphylaxis
 1. Peri arrest algorithm
 2. Routine ALS and adrenaline once in cardiac arrest
 3. Large volumes of fluids may be needed
- iv. Asthma
 1. Arrest in Asthma linked to
 - a. severe bronchospasm and mucous plugging leading to asphyxia
 - b. cardiac arrhythmias due to hypoxia, stimulant drugs (e.g. β -adrenergic agonists, aminophylline) or electrolyte abnormalities
 - c. dynamic hyperinflation, i.e. auto-positive end-expiratory pressure (auto-PEEP), can occur in mechanically ventilated asthmatics
 - d. tension pneumothorax (often bilateral)
 2. Standard ALS with early ETT (disconnection of circuit may be needed, with chest squeeze, to relieve gas trapping and subsequent impairment of venous return)

7. Post resuscitation care

- a. **Avoid hypoxia and hyperoxia**
- b. Use highest FiO₂ during CPR until oxygen can be measured reliably post ROSC
- c. Maintain normocarbia
- d. Haemodynamic goals should be incorporated into any post resuscitation bundle of care
- e. **Targeted Temperature management (TTM)**
 - i. 32-36°C (previously 32-34°C)
 - ii. for 24 hours
 - iii. Recommended for:
 1. Out of hospital cardiac arrest (OHCA) with VF/VT as initial rhythm and remain unconscious after ROSC
 - iv. Suggested for:
 1. OHCA with unshockable rhythm and remain unconscious after ROSC
 2. In hospital cardiac arrest (IHCA) and unconscious after ROSC irrespective of initial rhythm
 - v. Recommend against prehospital cooling with cold IV fluids after ROSC
 - vi. Treat fever that develops after period of TTM
- f. Cath lab and PCI in those with OHCA and evidence of ischaemia (ST elevation or new LBBB), or no evidence of ischaemia but cardiac most likely cause even if remain comatose. Okay to proceed during TTM phase.
- g. Treat seizures appropriately, but routine seizure prophylaxis not recommended
- h. Standard glucose management protocols, treat if glucose > 10mmol/l
- i. **In those treated with TTM, 72 hours post ROSC should be the earliest to start prognostication about outcome, and longer if any residual sedation/paralysis. Multiple modalities should be used.**
- j. If subsequent brain death occurs after arrest and ROSC, discussion of potential organ donation should occur

So, in summary, the changes in ANZCOR ALS guidelines produced in January 2016 following on from the 2015 ILCOR review are:

1. If the first shock is not successful and you are not at the maximum energy the machine can deliver, increase the energy.
2. There is equipoise between the basic and advanced airway techniques
3. Use of waveform capnography emphasised
4. Impedance threshold device not recommended
5. Automated compression devices not recommended

6. Cardiac ultrasound may be useful to rule out reversible causes
7. In the post resus phase
 - a. Avoid hypoxia or hyperoxia, maintain normocarbia
 - b. TTM recommendations, treat fever.
 - c. No routine seizure prophylaxis
 - d. Prognostication suggestions and organ donation

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Cough, spit, fat & snoring – do any of them ever change?

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So what is new & what is old in the airway that you need to know about?

Ageing lung: With age we eat into our biological reserve and our vulnerability increases leading eventually to frailty, sarcopenia & imminent death. As our population ages Anaesthesia & Geriatrics are increasingly inter-twining specialties and understanding the ageing lung and the resultant mechanical changes in the lung moves centre stage.

COPD: There appears to be an epidemic of COPD though prevalence is very influenced by the diagnostic criteria. We run a risk of increasing over diagnosis as the dividing line between COPD and ageing blurs. COPD sufferers are increasingly co-morbid and that is compounded by the fact they are an increasingly older cohort. They are also vulnerable to a variety of diseases requiring surgical management – how do we assess their peri-operative risk?

In COPD patients having major elective surgery are we able to prognosticate in terms of longevity and functionality accurately and what options are available to minimize their peri-operative risk?

Broader assessment tools such as frailty, functional measures such as modified shuttle tests can identify high risk groups but in complex comorbid patients their interpretation can be challenging and hard evidence for reliable “prognostication” in terms of surgical outcomes is debatable.

BODE, DECAF, B-AE-D etc – prognostic scores for Africa exist but their role in the individual stable patient requiring anaesthesia remains unproven. The other side of prognosis is “uncertainty” and determining when an operative procedure is futile is something we have not been trained to do well. What new therapies are available to influence the anaesthetic risk of the COPD patient undergoing elective surgery? A host of new inhalers have arrived for the treatment of COPD but have they altered the management and do they alter risks?

Bacterial colonization & bronchiectasis – *do they matter?* The respiratory biome – evidence is beginning to accumulate that we have a complex degree of respiratory colonization in the lung in health and with advances in our understanding of innate immunity there is a hint of how those interact to protect us from the billion litres of toxic gas (air) we breathe in a lifetime.

As CT scanners multiply like rabbits and scans follow, we are identifying an increasing burden of bronchiectasis in patients with limited respiratory symptoms, often mild COPD. To what extent does the presence of bronchiectasis alter the risks of anaesthesia and surgery? Should inhalational anaesthesia be avoided if at all possible in such patients?

Obesity, snoring & breathing or lack of breathing – is the fog clearing?

We angst about obstructive sleep apnoea and the epidemiology of sleep disordered breathing steadily looks bleaker and bleaker. It may be a disease of gender and age!

However, we often miss the elephant in the corner which is obesity hypoventilation syndrome (OHS). OHS probably carries a very significantly increased anaesthetic risk but is often missed even after peri-operative problems. What clues moves a fat snorer into a potential patient with obesity hypoventilation?

AQUA 2016 – Respiratory pot-pourri

Respiratory infections, anaesthetics and surgery

Respiratory Biome

Ageing and lung mechanics – implications for anaesthesia?

Cilia and inhalational anaesthetics +/- respiratory mechanics +/- abdominal muscles

Bronchiectasis epidemic

Obstructive airways disease, breathing and ageing

Epidemiology – non-smokers increasingly recognized/ageing lung

Walking co-morbidity?

New treatments?

Pharmacological treatments:

Inhalers for Africa but no great advances;

PDE4 inhibitors (son of theophylline)

Personalised medicine

Pulmonary rehabilitation

Assessing severity in Anaesthetic pre-admit clinics BODE, B-AE-D or B-AE-C etc.

Obesity & breathing

OSA – epidemiology & its implications/who to focus on?

OHS – the elephant in the corner

Update in Anaesthesia for Orthopaedic Surgery

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Introduction

Orthopaedic surgery makes up a significant amount of the daily throughput of most operating suites. Exposure is both elective and acute, with an escalating demand for care, exacerbated by an ageing population. Most tertiary centres now provide at least one extra dedicated orthopaedic theatre just to manage the fractured neck of femur population. Combined with upper and lower limb fractures, these orthopaedic injuries account for 3 of the top 5 presentations for unplanned surgery in Australia.

Elective orthopaedics is dominated by shoulder and knee arthroscopic surgery, and major joint arthroplasty. Many of these procedures are being performed in the private sector, supported by third party insurers.

This update on anaesthesia for orthopaedic surgery will focus on clinical innovations I feel are most likely to influence the future direction of anaesthesia services for orthopaedics, with special emphasis on interventions that produce meaningful outcomes.

Arthroscopic Surgery

Knees

The majority of lower limb arthroscopic surgery involves correction of chondral or meniscal lesions of the knee. These are low-acuity cases, mostly with fit patients and carried out on a day-stay basis. Procedures are quick and complications rare. There is little evidence to support moving away from balanced general anaesthesia for these cases. Morphine injected into the intra-articular space provides no additional analgesia when compared to placebo. Routinely performing peripheral nerve blocks (PNB) is also not supported. Neuraxial blockade should be reserved for more complex patients for whom GA is less desirable. Low-dose intrathecal bupivacaine (heavy 5-8 mg) mixed with fentanyl or clonidine (20-25mcg), inserted in the lateral position with a 15 minute "set time", will produce reliable surgical anaesthesia without adversely influencing turnover or delaying same-day discharge.

Shoulders

Shoulder arthroscopy is different. Acromioplasty, cuff repair and shoulder stabilisation are commonly associated with high levels of patient discomfort postoperatively. It can be difficult to manage these cases in the ambulatory setting unless a reliable analgesia plan is in place. In the absence of plexus blockade there can be considerable variation in opioid requirements between patients, and predicting who will (or wont) do well is difficult.

There is no doubt that interscalene nerve block (ISB), either with or without GA, will improve pain scores, decrease rescue opioid requirements and improve patient satisfaction when compared to systemic analgesia. This improvement will become less detectable beyond 18-24 hrs. It is important to both anticipate and manage the block wear-off period. Effective regional analgesia can be extended by using a continuous nerve block technique. Maintenance dose requirement with Ropivacaine 0.2% is low (~5ml/hr). A lower background rate (2ml/hr) with an intermittent 5ml bolus capability is associated with low pain scores and avoidance of motor blockade. Disposable, patient-controlled devices have been successfully used with low-risk in the outpatient setting for this purpose. Attention to asepsis and line fixation is mandatory if complications are to be avoided. The first dose down the catheter should always be administered in a monitored setting, and practitioners are advised to review ANZCA PS3 (regional anaesthesia) prior to instituting a block program.

Use of ultrasound to guide placement of nerve blocks is well-supported and should be considered a standard of care when performing Peripheral Nerve Blocks (PNB). Ultrasound guidance is superior to

other nerve localisation techniques with respect to block success, performance time, onset time, needle passes and complications. Access to a well-stocked regional anaesthesia trolley with appropriate echogenic needles, will improve the integration of PNB into routine practice. Traditional dose-related side effects of interscalene brachial plexus block (Horner's syndrome, hoarseness, dyspnoea and motor weakness) are largely avoided when using modern ultrasound techniques with low volumes. Contemporary audit databases confirm a low rate of complications with little difference in outcomes between ISB placed awake, sedated or under GA. Patients prefer to be asleep.

Other analgesic techniques commonly associated with shoulder surgery include local infiltration, subacromial injection/infusion and suprascapular nerve block. All provide some benefit with respect to early postoperative pain scores but are inferior to ISB. Concerns about LA-mediated chondrotoxicity have led to a decline in the utilisation of subacromial and intra-articular infusion techniques, and they are no longer recommended by the American Academy of Orthopaedic Surgeons.

Fractured neck of femur (#NOF)

The biggest change in the management of the patient with a fractured NOF, in my career, is the introduction of the fast-track pathway. The whole approach to these patients is now more holistic and multi-disciplinary, with a focus on the best mechanism to achieve return to home or care facility. Effectively patients are now managed under geriatric medicine, with a brief orthopaedic episode of care within the admission. All patients should be approached systematically, commencing in ED on arrival. Pathways should include routine blood workup, iron studies, ECG, early non-opioid analgesia, bladder management, dietary assessment, medication rationalisation and correction of coagulation abnormalities. Early intervention for correctable abnormalities should be initiated. Optimally a Consultant-lead operating service, a dedicated theatre and a radiography team should also be part of the process.

Many patients with #NOF are high-risk, there are few non-operative options for management and best practice advocates early fixation (< 48 hrs). While every effort should be made to optimise patients prior to surgery, delays for additional tests or specialist consultation should be avoided unless the outcome is critical to the management.

Perioperative morbidity is high. Hypoxia (17%), post-operative delirium (25%), transfusion (28%), congestive cardiac failure (14%), acute renal impairment (12%) and myocardial infarction (4%). Mortality at 30 days is 12-15%.

Integrated ortho-geriatric care systems for fractured NOF have been associated with reduced 1-year mortality, earlier hospital discharge, increased return to same place of residence, and higher functional levels (ADLs) than standard-care models. If your hospital does not have a NOF pathway then it is overdue.

How does anaesthesia contribute to #NOF management?

Provision of effective regional analgesia as soon after admission as possible is recommended. Both fascia iliaca (FIB) and femoral nerve blocks (FNB) have been shown to be advantageous in this setting. Catheter-based techniques are probably the gold standard for pre-operative analgesia, as they provide ongoing pain relief with minimal systemic effects. The approach used at SCGH is to insert a CFNB in ED, commence an overnight infusion and top-up the block prior to removal of the catheter at the time of surgery.

There is good evidence supporting the use of supplementary PNBs for #NOF analgesia, prior to surgery and combined with spinal or GA.

Choice of Anaesthesia for #NOF

In many centres, there is a tendency to favour neuraxial anaesthesia for fractured NOF. Single-centre randomised and cohort studies support this choice, but are limited somewhat by size or study design. Recent reviews and meta-analyses, combining multiple publications, have been unable to demonstrate a difference in 30-day mortality between neuraxial block and general anaesthesia. There is only a subtle trend towards improved 1-yr outcomes favouring the neuraxial group. My feeling is that

the difficulty in producing solid evidence in favour of one technique versus another is multi-factorial. Combining studies increases the heterogeneity in a population that is already difficult to enrol in randomised studies. They are acute admissions, often with cognitive impairment and they have multiple other problems that may skew outcomes. Of significance is the fact that not all fractured NOFs undergo the same operative treatment. This is probably the most important factor limiting the ability to detect differences in outcome when comparing interventions.

It makes sense to consider percutaneous fixation (pin and plate / proximal nail) as a totally different procedure to hemi-arthroplasty. Proximal fixation is minimally invasive with little or no femoral reaming. General anaesthesia supplemented by FNB is safe and effective for these procedures. Conversely hemi-arthroplasty is a major insult, with similar physiological stressors to hip replacement, including the risk of bone cement implant syndrome.

Registry database analysis favours regional anaesthesia over general anaesthesia for hip replacement (odds ratio 1.31). Incidence of adverse cardiac and respiratory events is lower with RA, transfusion risk is lower and RA patients go home quicker.

So for hemi-arthroplasty, my preference is to utilise neuraxial blockade as the default technique. Frequently this will be in association with invasive monitoring and pressor infusions in higher risk patients.

Adductor canal block (ACB)

This block is what's trending in orthopaedic anaesthesia. Most knee arthroplasty centres are utilising a locally-modified ERAS program to promote early mobility and discharge after knee replacement. Regimes vary between centres, but most involve surgeon-administered local anaesthesia infusion (LIA) and multi-modal analgesia. Addition of standard femoral or sciatic nerve blocks will improve the quality of analgesia after knee replacement, but have the potential to delay early mobilisation. Recent experience with continuous adductor canal blockade looks promising. Studies show that analgesia is improved compared to LIA alone and ambulation is better. Our experience is that there is improved capacity to rescue patients who are limited by breakthrough pain. This block is effectively a sub-sartorial femoral block, below the level of the motor innervation of the quadriceps. Analgesia of the anterior knee without weakness is the aim. It is easy to perform with ultrasound assistance and has no significant complications.

Summary

This update in anaesthesia for orthopaedics has selectively targeted arthroscopy, fractured NOF and knee arthroplasty; all procedures common to the specialty but without a clear consensus as to which anaesthesia techniques will produce the best outcomes. Balanced general anaesthesia should be viewed as the default option for the majority of orthopaedic procedures. Addition of single-shot or continuous ISB has clear benefits for shoulder surgery and incorporation into daily practice is encouraged.

Anaesthesia for percutaneous fixation of fractured NOF should be considered a different challenge to arthroplasty for the same condition. Both GA and RA have equivalent outcomes for standard fixation. Neuraxial block is the better option for hip replacement or hemi-arthroplasty.

Adductor canal blockade as a supplementary technique for analgesia after total knee replacement is recommended.

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Total Joint Replacement; making a good thing even better

Jacob Munro

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Hip and knee replacement are among the most successful surgeries performed. Increasing demand, broadening indications and elevated patient expectations have brought new innovations to maximise outcomes and make best use of health resources. This talk will address changes in system flow, the management of obese patients and the use of emerging technology to achieve these aims,

Recent developments in procedural pain management

Chris Jephcott

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In the ward-based environment, the provision of adequate and safe analgesia to allow procedures such as burns dressings changes and wound debridements to be undertaken, can be a challenge.

Reports from our nursing staff, that patients seem to be suffering during these procedures led us to introduce a ketamine and midazolam PCA regimen to our burns ward. This was based on the model that had previously been developed in Western Australia to facilitate burn-related procedures for the large number of patients admitted after the 2002 Bali bombing.

Using this technique, procedures that were previously taking 2-3 hours could be completed more thoroughly in 30-45 minutes while patients remained comfortable and cooperative. Patients had little memory of the procedures and did not require the prolonged period of fasting that would have been required for general anaesthesia. Side effects were tolerable in nature and frequency.

Whilst this approach had major advantages over the options previously available, over time some limitations became apparent: specifically, after the procedure had been completed on the ward, patients could remain sedated for a number of hours. During this time, they were less inclined to eat or take part in their rehabilitation.

We addressed this by introducing a novel therapy that had recently become available in New Zealand based around methoxyflurane. Methoxyflurane is an anaesthetic vapour in common use for the maintenance of general anaesthesia prior to the 1970's. Subsequently its use declined after it was found that prolonged exposure to the drug could be associated with vasopressin-resistant renal failure. This is thought to be a dose-related effect.

Methoxyflurane has been reintroduced in Australasia for use as an inhaled analgesic. A dose of methoxyflurane well below the threshold reported to be toxic is administered via the Pentrox inhaler: a patient-utilised hand-held device. Methoxyflurane has a rapidly titratable analgesic effect at sub-anaesthetic concentrations.

The Pentrox inhaler has been widely used for analgesia in Australasia by paramedics and the military in the pre-hospital setting and in over 5 million uses to date, there have been very few reported clinically significant adverse effects providing the dose recommendations have been followed.

As far as we could determine the use of the Pentrox inhaler for burns procedures had not been reported, so with ethics committee approval we set up a prospective randomised crossover trial investigating its role in this context compared to ketamine/ midazolam. Strict inclusion criteria led to only small numbers being recruited but the results of this small trial demonstrated that for these patients, Pentrox was able to offer analgesia equivalent to that of the ketamine/ midazolam regimen with the advantage of minimal sedation following the procedure.

We have developed a protocol for the use of Pentrox on surgical wards at Waikato Hospital. Apart from burns procedures, it is currently being used successfully for other ward-based procedures including vacuum-assisted wound dressing changes and the removal of brachytherapy rods following prostatic radiotherapy.

We have introduced an in-house training package by which key personnel (including non-anaesthetist doctors and nurses) undergo training and certification in the use of the drug and in the technique of its administration. These procedures can then be carried out on the ward autonomously without the necessity of an anaesthetist to supervise. Patient safety is a key focus of the training and of the procedures so far undertaken, there have been no patient safety issues identified.

As an acute care hospital serving a large population, we are at times in the position of admitting more acute cases for emergency surgery than we have the resources to treat. This can lead to elective surgery being cancelled to allow the backlog of emergency cases to be cleared.

In an attempt to improve theatre efficiency, we reviewed all acute admissions over the 4-month period during 2009. Of these, we are identified cases that came to acute operating theatres for surgery under general anaesthesia that we anticipated could have been undertaken using a Pentrox-based sedation technique.

We predicted that between 30 and 40 cases a month could be amenable to this technique. Of these 90% were general surgical - mostly abscesses requiring drainage. This represented just over one quarter of the total number of general surgical acute operations performed each month.

Abscess drainage has traditionally been considered to be too painful to be performed under local anaesthesia alone and patients are consequently booked for a general anaesthetic in an acute operating theatre. As the pathology is unlikely to be life threatening, they are triaged as low urgency and often spend a protracted period of time in hospital until either a space in theatre becomes available or their pathology worsens to the extent that the surgery is deemed more urgent.

We have developed a technique for the use of Pentrox to allow the incision and drainage of abscesses without the requirement for general anaesthesia. This involves a combination of topically applied and subcutaneously administered local anaesthesia as well as the use of the Pentrox inhaler to provide supplemental analgesia and sedation.

We anticipate performing these procedures in a procedural room on the general surgical ward with the Pentrox administration being supervised by a trained and certified nurse. This allows the patient to have their procedure completed within a few hours of admission rather than the 1-4 nights they currently wait in hospital for an acute operating theatre to become available.

Apart from improved convenience to the patient, this process should offload up to 8% of the cases we currently process through the acute operating theatres, thus reducing the likelihood of elective surgery needing to be cancelled. It should also save approximately 700 acute inpatient bed days per year.

We have recently published a case series of 173 procedures undertaken using Pentrox for the provision of analgesia. 97% of these were successful and clinically significant adverse effects were rare and self-limiting.

Apart from our case series, there are an increasing number of published papers that support the efficacy and safety of analgesic doses of methoxyflurane for a variety of procedures including bone marrow biopsies, colonoscopies and the management of interventions in the emergency department.

Interestingly, the Pentrox inhaler has recently been approved for use in the UK, Europe and parts of Asia, so it seems likely that the use of this drug and its applications will continue to expand Worldwide over the coming years.

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Prehabilitation: Expanding the Role of Perioperative Medicine

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Introduction

Technical advances in the fields of anaesthesia and surgery in combination with our aging population has led to an expanding volume of complex surgery being performed on older patients. Patients often present for surgery with reduced functional capacity mediated by the biological effect of their surgical disease e.g. cancer, the associated therapies e.g. neoadjuvant chemoradiation therapy, their underlying comorbid disease and/or through their lifestyle choices e.g. inactivity. These factors combine to accelerate a 'deconditioning storm' with reduced functional capacity, with reduced ability of the body to deliver and/or utilize oxygen (O₂) leading to reduced exercise capacity, impaired health related quality of life, and reduced ability to withstand major stressors such as complex surgery. As such, decreased functional capacity associates with an increased incidence of post-operative morbidity and mortality, length of hospital stay, healthcare expenditure, reduced quality of life, and reduced longevity. This provides the impetus for prehabilitation—the optimisation of functional capacity following diagnosis and prior to elective major surgery.

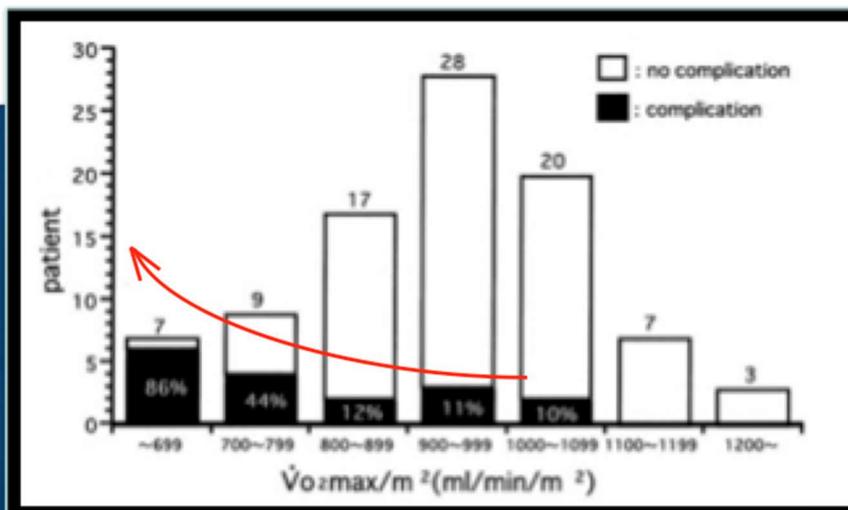
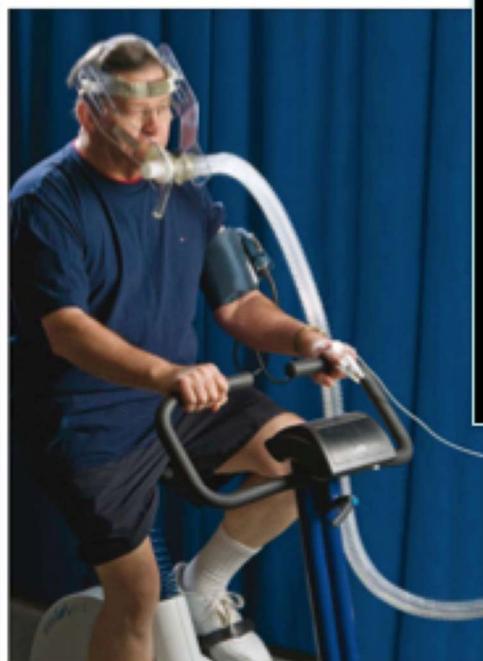
Risk Stratification

Perioperative morbidity represents a major public health challenge. It is estimated that 12.3% of surgeries are performed on high-risk patients (expected mortality >5%), with an estimated risk of postoperative morbidity between 7%-50% and accounting for 80% of all deaths following surgery. The presence of a single post-operative complication increases the risk of mortality for up to 8 years after surgery, independent of baseline comorbidities.

Patient-centred risk assessment and cardiopulmonary exercise testing (CPET or CPX), using gas exchange-derived variables such as oxygen consumption at Anaerobic Threshold (AT) and oxygen consumption at peak exercise (pVO₂), allows for objective measurement of functional capacity and is used to guide surgical risk assessment and perioperative strategies for patient optimisation to reduce postoperative morbidity and mortality. These gas exchange derived variables reflect the integrative capacity of components in the O₂ cascade. Lack of sufficient tissue O₂ supply reduces exercise capacity and physical function, leading to impairments in abilities to participate in activities of daily living and increased risk of postoperative complications. Other benefits of improved functional capacity may be mediated through improved anti-inflammatory and microcirculatory function mediated by signaling via the endothelial-nitric oxide pathways during exercise.

Impaired functional status of surgical patients has been consistently shown to predict adverse postoperative outcomes and mortality (Figure 1) and increasing levels of evidence suggest that CPET is a suitable and effective method for objective quantifying of surgical risk. For rectal surgery West et al estimated that AT and pVO₂ gave an area under the ROC curve of 0.87 (95 per cent confidence interval 0.78 to 0.95; P<0.001) and 0.85 (0.77 to 0.93; P<0.001) respectively, indicating that they can help discriminate patients at risk of postoperative morbidity. The optimal cut-off points identified were 10.6 and 18.6 ml/kg/min for VO₂ at AT and at peak, respectively.

CPET and Objective Perioperative Risk Stratification



Declining VO₂ max associates with ↑ postop complications

Nagamatsu et al – J Thorac Cardiovasc Surg, 121: 1064-8, 2001

Peter Mac

Figure 1. Objective risk stratification with cardiopulmonary exercise testing (CPET). A decline in functional capacity, as measured by VO₂ max, shows an increase in postoperative complications (black shaded columns).

In a more recent study and specific to colorectal surgery, West et al., exploring the relationship between CPET-derived parameters and in-hospital morbidity, showed that using multivariable logistic regression selected CPET variables associated significantly with increased odds of in-hospital morbidity (AT <11.1 ml/kg/min; OR = 7.56 [95 %CI 4.44 to 12.86]; P <0.001) and pVO₂ <18.2 ml/kg/min; OR 2.15 [95%CI 1.01 to 4.57]; P = 0.047).

In a recent systematic review Moran et al. (2016) confirmed the utility of CPET as a preoperative risk-stratification tool with ability to predict postoperative outcome following major intra-abdominal surgery. Cardiopulmonary exercise testing-derived cut-points for AT and pVO₂ predicted: intensive care unit admission (AT <9.9-11 ml/kg/min) and 90 day - 3 year survival (AT 9-11 ml/kg/min) after hepatic resection and transplant, morbidity and length of stay after pancreatic surgery (AT <10-10.1 ml/kg/min), and mortality and morbidity after intra-abdominal surgery (AT 10.9 and <10.1 ml/kg/min, respectively).

Declining Physiologic Capacity after Preoperative n-CRT

While less invasive and arguably less accurate means of assessing functional status include the Eastern Cooperative Oncology Group (ECOG) performance status, incremental shuttle walk test and six minute walk test, there is an extensive body of evidence that supports the use of CPET for risk stratification of cancer patients. CPET is the logical choice of assessment in patients with cancer because of the effects of disease, loco-regional and systemic treatments on multiple stages of the O₂ cascade (cardiovascular system, respiratory system, anaemia, autonomic dysfunction and skeletal myopathy).

Neoadjuvant chemoradiation therapy (n-CRT) adversely affects functional capacity, with 10-15% decline in AT and pVO₂. As such, previously relatively 'fit' patients (AT >11 ml/kg/min) may now fall below this threshold (10-11 ml/kg/min) and are thus at increased risk for adverse postoperative

outcomes. These reductions in turn are significant predictors of postoperative morbidity and one year mortality. To this end, CPET derived parameters can guide postponement of surgery until functional capacity has recovered or preferably guide the implementation of a prehabilitation exercise program to expedite recovery after n-CRT. West et al (2015) reported the feasibility of a 6-week structured responsive exercise-training program in rectal cancer patients receiving neoadjuvant therapy, with return to baseline exercise capacity in the treated group but not in the control group.

Adoption and Accreditation of CPET in Perioperative Medicine

Given that CPET is an integrated, dynamic test of the cardio-respiratory-metabolic systems and is considered the gold standard in assessing cardio-respiratory functional reserves it is increasingly adopted in the preoperative assessment of patients scheduled for major surgery. A survey conducted in 2011 by Huddart et al. (2013) reported that an estimated 32% of all adult anesthetic departments in England had access to preoperative CPET services. Five years on, it is expected that more than half of all hospitals in the UK will now have access to such services. Importantly, this survey highlighted that there was a lack of consistency in the way tests are reported and utilized. As the uptake of CPET services continue to expand, and as the evidence expands that prehabilitation programs (with exercise as a pivotal component) before and after surgery may improve fitness and thus reduce complications and death after surgery, it is essential that testing is of high quality and is reproducible if it is to benefit patient care. As a result, the Perioperative Exercise Testing and Training Society (POETTS), established in the UK in 2016, has set out to introduce guidelines for perioperative CPET, with standardized education and accreditation for practitioners. The society will also provide educational resources, an opportunity to identify local mentors for training, and facilitate collaborative research for CPET, including the establishment of a national CPET database, housed in the Health Services Research Centre (HSRC) at the Royal College of Anaesthetists, to establish valid risk thresholds and to identify the best variable or combination of variables to predict surgical outcome. POETTS will likely also expand to have an international role in CPET training, education and research.

The POETTS website (<http://poetts.co.uk/home>) provides a useful resource with links to current evidence (majority of published single centre cohorts, systematic reviews etc.), accreditation and mentoring pathways, and a link to recommended exercise training programs.

Prehabilitation

The evidence is now irrefutable that exercise has significant physiological and psychological benefits and a pivotal role in preventing many cancers within the general population. An increasing body of evidence supports the fundamental notion that **functional capacity is an attractive modifiable therapeutic target** and thus exercise forms a central component of emerging prehabilitation programs prior to major surgery. Exercise training especially interval training has a long-term anti-inflammatory response that may offset the systemic inflammatory response associated with major surgery. Thus exercise training prior to and following major surgery may modify the inflammatory response and may be of benefit. This supports what a lot of clinicians already believe; high-risk, deconditioned patients, when given the opportunity to improve their physical function and activity before and after treatment, through a structured multidisciplinary bundled program, that also includes haematologic optimisation, nutritional optimisation, pain management, pharmacist review, smoking and alcohol cessation programs to improve their functional state, will suffer fewer postoperative complications, leave hospital quicker after major surgery, and return to their baseline functional capacity earlier (or even better).

Prehabilitation is defined as the process of enhancing the functional capacity of the individual to enable him or her to withstand a stressful event and reduce complication risk (Figure 2). As such, one of the top 10 (from 92) most important research questions identified for perioperative medicine, in a survey conducted by Boney et al. (2015) for the Royal College of Anaesthetists/James Lind Alliance in the UK, was *"How can preoperative exercise or fitness training, including physiotherapy, improve outcomes after surgery"*.

The Role of Prehab and Rehab in the Cancer Surgical Patient's Survivorship Journey

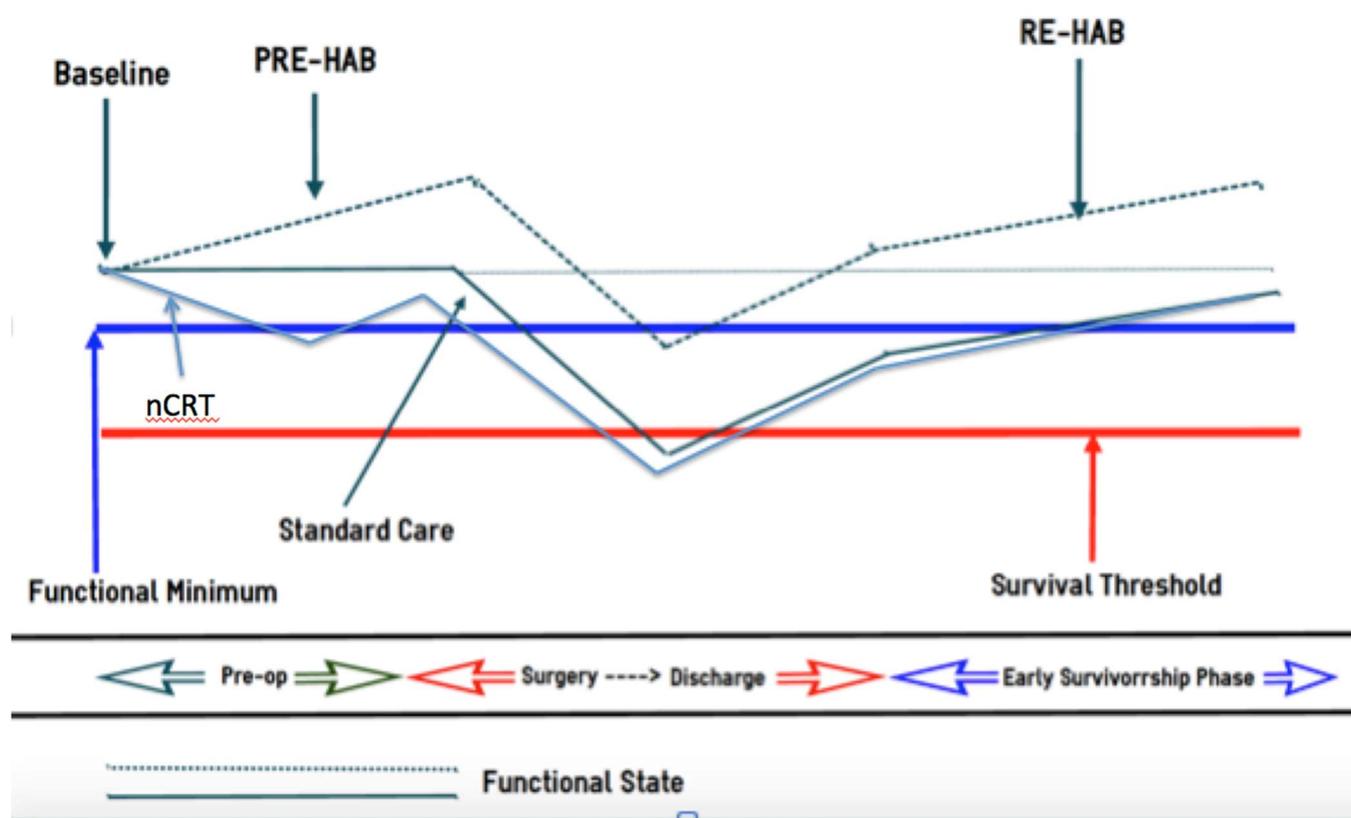


Figure 2. Schematic representing the role of prehabilitation and rehabilitation in improving perioperative outcomes for major surgery. *Timely intervention with 'prehabilitation' (and rehabilitation) is aimed at ensuring patients do not descend below the theoretical physiological threshold to ensure an uncomplicated recovery (blue line).*

At Peter MacCallum Cancer Centre in Melbourne we have integrated CPET facilities into the preoperative workup of patients scheduled for major cancer surgery, with utility in identifying the high-risk surgical patient who would benefit from prehabilitation. Once risk stratified, high-risk patients scheduled for major surgery are optimised through multidisciplinary preoperative 'prehabilitation'. Their CPET derived data provides a validated guide to formulating patient specific exercise prescriptions. In addition to exercise therapy, prehabilitation is also tailored to include perioperative interventions such as haematinic optimisation, (immuno)nutritional optimisation, abstinence of smoking and alcohol, and psychological therapy to improve postoperative outcomes. Additionally, high risk patients may have their surgical procedures adjusted to reduce risk of surgical complications, and be stratified for postoperative care in high acuity areas (e.g. HDU / ICU) and if needed also scheduled for post-operative 'rehabilitation'.

Our 'prehabilitation' program has been able to train over 100 patients in the last 24 months prior to their major cancer surgery. In a retrospective cohort study (Huang et al; 2015) of prehabilitation in patients with cancer having major colorectal, oesophagogastrectomy, or lung resection surgery we reported a significant overall increase in pV_{O_2} , with 'responders' to our prehabilitation program suffering fewer major postoperative complications. The optimal exercise-training program follows traditional guidelines consisting of either supervised and/or home-based endurance (aerobic) training combined with resistance training to induce skeletal muscle adaptation, prescribed at a moderate intensity (60-85% of a predetermined physiological parameter such as heart rate).

Prehabilitation is not a new concept; it is utilized successfully to improve patient outcomes in cardiac, colorectal and lung cancer surgery with positive outcomes achieved within short preoperative time

frames. Prehabilitation has been shown to be feasible and safe, increasing the AT and pVO₂ within 4-6 weeks, as well as offering improvements in function and quality of life. Ongoing research will explore the role of high intensity training programs in achieving optimization in a shorter period prior to scheduled surgery. Li et al (2013) demonstrated that 81% (cf. 40% in the control group) returned to baseline functional capacity at 8 weeks after surgery. This has significant implications, with earlier return to baseline but also significant implications for the cancer patient who suffer less postoperative morbidity and who return to intended oncologic (adjuvant) therapy (RIOT – the cancer journey) in a timely manner. The introduction of neoadjuvant cancer treatment in the surgical pathway may provide a window of opportunity to intervene with exercise training before, during and after cancer treatments to ameliorate or reverse the harmful effects on physical fitness.

Prehabilitation leverages the ‘teachable moment’ of impending major surgery, with patients often more compliant due to being in better physical condition without acute post operative pain, and also ensures the advantageous use of surgery waiting time, especially when neoadjuvant therapies are needed or patients are on surgical waiting lists within the public healthcare systems. Large, prospective studies are required to evaluate the impact of these interventions, the optimal type of training program and the optimal timing through further research.

Useful information on current modalities of exercise programs can be found on the POETTS website: <https://rayzume.com/POETTS/Interval-Exercise-Training-Programme>.

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Advances in supplemental oxygen

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Anaphylaxis Update

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My credentials for giving this talk are that I am an anaesthetist and I work in the Anaesthetic Allergy Clinic (along with Dr Peter Cooke and in close collaboration with the immunologists at ADHB) where we investigate about 60 cases of suspected perioperative anaphylaxis every year. I am also a member of ANZAAG (Australia New Zealand Anaesthetic Allergy Group) and I am on the steering group developing the ANZCA Online Anaphylaxis Emergency Management Module.

There is a lot of ground to cover and only a limited amount of time so I have decided to focus on a few areas that fulfil at least some of the following criteria – new, interesting, clinically important and poorly understood. I have used a small number of references which are all well worth reading.

ANZAAG/ANZCA updated perioperative anaphylaxis management guidelines

These guidelines were released at the ANZCA ASM in May this year. I would highly recommend that you familiarise yourself with the management cards and take the time to read the management guidelines and the background paper. These are all available on the ANZCA website but are easier to find on the ANZAAG home page (www.anzaag.com – look under the Anaphylaxis Management tab).

Interpretation of serum tryptase results in suspected cases of anaphylaxis

Laboratory guidelines are misleading. It is vital that the clinical presentation and timings of samples in relation to symptoms are taken into account. Changes from baseline (rather than absolute values) are what count. A “negative” tryptase in no way excludes a diagnosis of anaphylaxis.

Chlorhexidine

The incidence of anaphylaxis to chlorhexidine is increasing worldwide. It is now in the top 3 causes of perioperative anaphylaxis at the Auckland Anaesthetic Allergy Clinic (along with antibiotics and muscle relaxants). It is ubiquitous in the healthcare environment and avoiding re exposure of allergic individuals is a big problem. ANZCA has recently released a Chlorhexidine Policy Document PS60 which, along with the background paper, is well worth a read. They can be found on the ANZCA website ([ANZCA 2015 Anaphylaxis Guidelines](#)). The Danish Anaesthetic Allergy group have published a comprehensive review of the subject (IgE-mediated allergy to chlorhexidine, Lene Heise Garvey et al, J Allergy Clin Immunol Volume 120 number 2 pages 409-415). I will also present some data about 14 patients seen at our clinic during the period January 2012 to December 2015 who were skin test positive for chlorhexidine.

Rocuronium and Suggamadex

Rocuronium does cause more anaphylaxis than any of the other muscle relaxants except for suxamethonium (Anaphylaxis is more common with Rocuronium and succinylcholine than with Atracurium, JI Reddy, PJ Cooke et al, Anesthesiology 2015; 122: 39-45). The paper referenced uses data from the Auckland Anaesthetic Allergy Clinic with the denominator being derived from Safersleep records. Suggamadex is not recommended as a treatment for suspected anaphylaxis to Rocuronium. All the evidence is well laid out in this review (Sugammadex and rocuronium-induced anaphylaxis, Takazawa, T., Mitsuhata, H. & Mertes, P.M. J Anesth (2016) 30: 290. doi:10.1007/s00540-015-2105-x) Also, it is expensive and it's use might result in an unwanted pregnancy! (Dalton, J. and Van Hasselt, G. (2016), Sugammadex – time of onset: nine months. Anaesthesia, 71: 115-116. doi: 10.1111/anae.13356).

New receptors

The receptor which Atracurium binds to on the mast cell to cause degranulation has been discovered (Identification of a mast-cell-specific receptor crucial for pseudo-allergic drug reactions, Benjamin D. McNeil et al, Nature 519, 237-241, 12 March 2015, doi:10.1038/nature14022)

PEGs

Polyethylene glycols (PEGs) or macrogols are polyether compounds widely used in medical and household products. Although generally considered biologically inert, cases of mild to life-threatening immediate-type PEG hypersensitivity are reported with increasing frequency. Awareness of PEG's allergenic potential remains low. These patients commonly present with a history of repeated, severe reactions to a range of unrelated products in hospital and at home. (Immediate-type hypersensitivity to polyethylene glycols: a review, E. Wenande and L. H. Garvey, *Clinical & Experimental Allergy*, 46, 907-922, 2016)

The Autopsy and You

Joanna Glengarry

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Examination of the human body after death, variably described as post-mortem examination, autopsy or necropsy, is recognised as a valuable part of the medicolegal investigation of death. It may be used for forensic purposes, medical purposes, civil purposes or for education and teaching.

The earliest known forensic autopsy took place in the thirteenth century in Italy at the University of Bologna and post-mortem examinations were used for forensic purposes and anatomical discovery long before medicine developed concepts of pathogenesis of disease and cellular pathology (Rokitansky and Virchow in the 19th century), after which it was seen to be a valuable source of learning regarding anatomy, pathology and disease.

In modern times, the overall autopsy rates for the diagnosis of disease are declining as the overall population health improves, with the ready availability of advanced diagnostic tools and with an increasing societal and medical unease with the autopsy process. However, medicolegal or forensic autopsies remain static and the investigation of criminal and unnatural deaths has remained unchanged and is perhaps increasing in complexity, with greater expectations of the Courts and Police.

Today an autopsy is a medical procedure that is carried out by forensic pathologists and some anatomic pathologists in order to investigate the medical factors involved in a death. An autopsy seeks to discover the cause of death, nature and extent of any injuries, seek medical information to assist in reconstructing the circumstances surrounding the death and delineating patterns of injury and death within the community that could be prevented.

The autopsy provides information regarding patterns and trends in death and injury to Coroners who evaluate the broader social and legal issues and often make recommendations that are aimed at preventing similar deaths in the future.

The Coroner must balance a number of competing interests in making the decision whether to (a) accept jurisdiction over a death and (b) order a post-mortem examination on the deceased. The decision making process is somewhat of a quadrumvirate comprising:

1. Legal obligations of the Coroner: preventing further similar deaths, determining cause of death, establishing identity of the deceased and manner or circumstances of death
2. Police: detecting death related to criminal acts
3. Medical desire for an autopsy
4. The wishes of the deceased's family/whanau.

Medical learning, feedback and the ability to critically review processes and systems in how we treat people is but one element of this and one might argue that it is sometimes ranked by the Coroner as the least of the four. Whilst the Coroner's Act empowers the Coroner to overrule a next of kin objection to a post-mortem examination, this is exceptionally rare in practise.

So, what is a possible solution to the dilemma of medical desire to seek information about a patient's death when the Coroner declines jurisdiction? As a clinician, we are used to free discourse about morbidity and mortality, in fact it is an essential part of responsible and professional, critically evaluative practise. One solution offered is the process known as a Hospital Autopsy. This is a non-Coroner's autopsy used as a diagnostic tool to elucidate and clarify purely medical issues. The report is prepared for the treating clinicians and is available in the medical record once completed. This investigation is used when the cause of death is known (because if the cause of death is unknown, it mandates referral to the Coroner) but addresses issues such as stage or extent of disease, response to treatment or clarification of complex medical issues. A common request we receive is for the definitive diagnosis of complex neurodegenerative diseases. On an annual basis, Hospital Autopsies are rare, with less than a dozen annually performed in forensic centres. Often the step that limits this investigation is that consent from the family/whanau is essential. Many families/whanau are actively engaged in the process and seek further answers, however many wish to commence their grieving process and prefer to end their contact with healthcare services.

It is often a source of frustration to hospital clinicians that, when a case is accepted by the Coroner, little or no feedback is received regarding the autopsy findings. How do we remedy this?

1. It is permissible under the Coroner's Act for "a doctor who attended the person concerned before death" to attend the autopsy examination. So if the demands of clinics, theatre lists and the like allow, give us a call and you will be made welcome to observe the autopsy.
2. Accessing the Autopsy Report is regrettably difficult. Our report is prepared for the Coroner and therefore must be sent to the same. We do not have the discretion to send it to other parties.
3. However, the Coroners have indicated that they are happy for us to talk to you about the findings, so again, give us a call.
4. Register as an interested party with the Coroner's Office. When the death is referred to Coroner and jurisdiction accepted, send an email to NIIO (niiio@justice.govt.nz) to advise you want a copy of the final report. It won't guarantee receipt of the report (human error and movement of case files). Don't expect a report until at least weeks to months have passed.
 - a. The report takes weeks to months to prepare as it is a complex medicolegal document written for a wide audience – the Coroner, doctors, juries, police, families and lawyers. Forensic Pathologists are often expected to comment on how death relates to the medical and social history, circumstances, witness statements, scene and death environment, injury patterns and causation, pathologic disease processes, the results of specimen analysis, genetic and inheritable factors, biomechanical factors and medicolegal concepts.
5. In the case of deaths that occur whilst the person was undergoing an anaesthetic, or that appear to have been a result of it, we absolutely rely on your expertise in the complex issues that may arise around anaesthesia.
 - a. Deaths due to an anaesthetic are complex and should be performed by a forensic pathologist, not by a hospital anatomical pathologist. They require a greater level of investigation and expertise. This does not mean all post-op deaths from every cause should be referred to us however!
 - b. There are deaths in this setting that may not be able to be diagnosed by the autopsy. There are some biochemical or metabolic abnormalities that, by virtue of post-mortem artefact, cannot be diagnosed – hyperkalaemia, hypoxia, hypercapnia and hypoglycaemia are classic examples. The process of death and the loss of ATP and cellular metabolic processes means everyone who dies irrespective of cause is hypoxic, hypercapnic, hypoglycaemic and hyperkalaemic.
 - c. Post-mortem toxicological analysis is an entirely different beast to toxicology during life. There is no standard "therapeutic range" after death, as practitioners generally do not prescribe to the deceased! Post-mortem redistribution and the production or destruction of drugs after death means that comparing antemortem and post-mortem drug levels can be problematic.
 - d. Diseases without structural abnormalities, such as the cardiac channelopathies and some cases of epilepsy, are well-recognised causes of a "negative" post-mortem examination. We sit on the Cardiac Inherited Diseases Group to aid in the diagnosis of these through the use of the "molecular autopsy".
 - e. It is likely that we will receive any report for the Coroner prepared by you. In return we are absolutely in favour of a multidisciplinary, team based and collaborative approach to these cases and best practice would suggest we meet to discuss the death before our autopsy report is signed and sent to the Coroner.

Forensic Pathologists are Fellows of the Royal College of Pathologists of Australasia and in New Zealand, operate under the banner of the National Forensic Pathology Service of NZ. We are located in:

- Auckland: Drs Simon Stables, Paul Morrow and Joanna Glengarry
- Palmerston North: Dr Kate White
- Wellington: Dr Amy Spark
- Christchurch: Dr Martin Sage

There are currently 5.5 FTE nationally although an ideal workforce of at least 8 nationally is recommended. We have recently created two registrar training positions. We perform about 1800-2000 autopsies nationally and of those, approximately 200 are suspicious deaths or homicides. We are involved in the medical investigation of all deaths referred to the Coroner: sudden or unexpected deaths due to natural disease, suicides, accidents and homicides. We operate a 24/7 on-call roster for the Police to attend scenes of death and perform these cases. We provide medicolegal advice to hospitals, the Courts, Police, Coroner and HDC and advisory committees and regularly appear as expert witnesses. In the event of a mass disaster, we are key professionals involved in the Disaster Victim Identification process.

Patients with liver disease undergoing non-hepatobiliary surgery

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Patients with liver disease undergoing non-hepatobiliary surgery have an increased risk of morbidity directly associated with their underlying liver dysfunction. They have greater transfusion requirements, higher infection risk, greater potential for organ dysfunction and experience longer hospital stays with higher mortality.

The prevalence of liver disease is rising in New Zealand. 10% of the New Zealand population have chronic liver disease with 10% of these patients having cirrhosis (1). The largest causes in New Zealand are Hepatitis B and C and Alcoholic and Non Alcoholic Fatty Liver Disease (1). Anaesthetists will see an increase in non-hepatobiliary surgery for cirrhotic patients due to longer term survivals, an increasing disease burden and an aging affected population. Operative risk correlates with the severity of the underlying liver disease and the nature of the surgical procedure.

Knowledge of the perioperative implications for anaesthetising these patients is of relevance to prevent morbidity and mortality and enable improved outcomes.

Pre-operative Assessment

Assessment of the patient with liver disease presenting for non-hepatobiliary surgery should involve elucidation of the cause and nature of their disease. Disease severity should be assessed along with the presence of cirrhosis, portal hypertension, related complications and associated organ dysfunction.

It is important to risk stratify these patients before their surgery. Historically the Childs Pugh Scoring system was used to assess perioperative risk following hepatic and non-hepatobiliary surgery. The score comprises five variables and stratified into groups A (<7), B (7 to 9) and C (10-15) based on increasing severity (2).

Child-Pugh classification of severity of cirrhosis

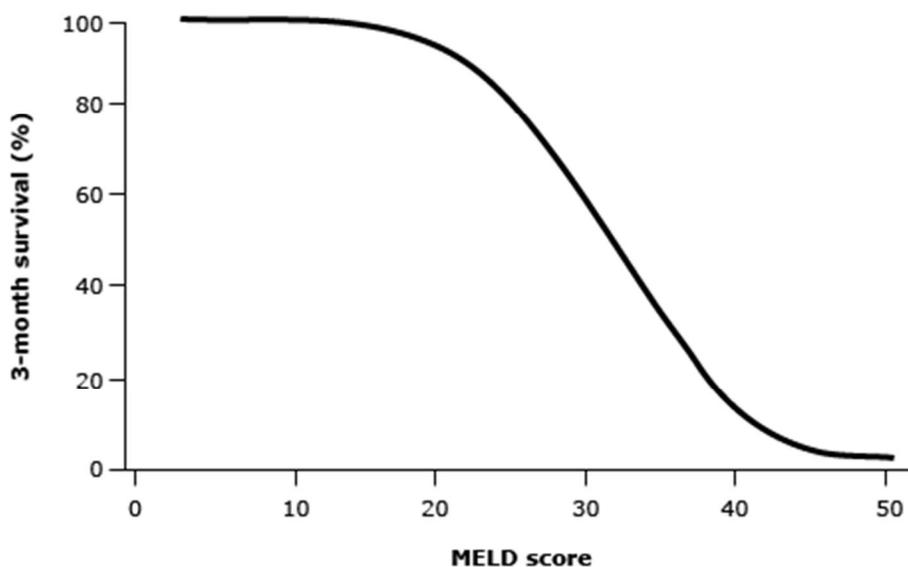
Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/L)	2 to 3 mg/dL (34.2 to 51.3 micromol/L)	>3 mg/dL (>51.3 micromol/L)
Albumin	>3.5 g/dL (35 g/L)	2.8 to 3.5 g/dL (28 to 35 g/L)	<2.8 g/dL (<28 g/L)
Prothrombin time			
Seconds over control	<4	4 to 6	>6
INR	<1.7	1.7 to 2.3	>2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

The Child-Pugh classes correlate with one- and two- year patient survival of:

- Class A: 100 and 85%
- Class B: 80 and 60%
- Class C: 45 and 35%

The Child-Pugh score has been superseded by the more objective and accurate Model for End Stage Liver Disease (MELD) score which predicts post-operative mortality independent of the type of surgery. A higher MELD score is associated with a higher mortality and patients with MELD >15 should avoid elective non-essential surgery where possible (3). Most patients with MELD scores above 25 will die in hospital regardless of treatment and 3 month survival decreased exponentially beyond this (2), (4).

Estimated 3-month survival as a function of the MELD score in patients with cirrhosis



MELD: model for end-stage liver disease.

Thorough assessment of liver synthetic function, potential organ dysfunction and disease related complications is essential to ensure a stable intraoperative course and avoid perioperative morbidity. This is particularly important in the presence of portal hypertension where renal dysfunction, porto-pulmonary hypertension and hepato-pulmonary syndrome may be present increasing the likelihood of post-operative decompensation. Patients having acute or emergency surgery and those undergoing intra-abdominal surgery are at even higher risk independent of their underlying liver dysfunction.

Optimisation of coagulopathy and fluid and electrolyte abnormalities is important preoperatively to ensure a more stable intraoperative course. Nutritional assessment is very important and correction of protein-calorie malnutrition with nutritional support is beneficial.

Intraoperative Management

As with any patient, the choice of anaesthetic and level of monitoring should be tailored to the nature of surgery and overall patient assessment. The use of regional anaesthesia where possible allows a decrease in patient exposure to opioid analgesia avoiding possible respiratory depression and potential for worsening delirium or encephalopathy. When opioids are required fentanyl should be utilized preferentially as it's metabolism is not affected by hepatic dysfunction. Certain Benzodiazepines such as midazolam or diazepam should be avoided or used with caution due to the potential for increased duration of action and worsening CNS depression/encephalopathy.

Tense ascites may reduce the Functional Residual Capacity (FRC), complicate ventilation and increase the risk of aspiration. Rapid Sequence Induction (RSI) may be indicated and drainage of ascites will aid ventilation. Severe liver disease is associated with reduced plasma cholinesterase activity and prolonged neuromuscular block following suxamethonium is possible, though rarely a problem clinically. Atracurium and cisatracurium are the muscle relaxants of choice in liver disease due to metabolism through Hoffman's degradation. Rocuronium onset time is longer with a prolonged recovery time in cirrhotic patients. A number of small studies have shown Sugammadex can safely reverse neuromuscular blockade after rocuronium in patients with liver dysfunction however, appropriate dosing is necessary and reversal may not be as rapid as in patients with normal liver function (5), (6).

The presence of clinical coagulopathy may warrant preoperative correction and acquisition of blood and component products depending on severity, nature of surgery and anticipated blood loss. The preoperative INR has no predictive value and point-of-care testing with thromboelastography is useful for guidance of component therapy. This should always be used in conjunction with clinical findings. Thrombocytopenia is common in portal hypertension due to sequestration and decreased thrombopoietin production. Platelet function should be assessed as thrombocytopenia alone is not an indication for platelet therapy. In situations of severe thrombocytopenia with associated dysfunction treatment options include platelet transfusions, splenic embolisation and splenectomy. Recombinant thrombopoietin and other thrombopoietic agents are currently under investigation in clinical trials. Prevention of hypothermia is especially important in patients with liver disease to prevent coagulopathy. The operating room temperature should be increased and patient and fluid-warming devices should be used.

Intraoperative haemodynamic stability can be challenging due to underlying low systemic vascular resistance, blunted chronotropic and inotropic responses in cirrhotics and challenging fluid status arising from hypoproteinaemia and resultant decreased effective plasma volume. Hepatic blood flow decreases during anaesthesia and is normally compensated with increased hepatic arterial flow. Cirrhotic patients have decreased ability to increase hepatic arterial flow. Their liver perfusion and oxygenation rely on stable haemodynamics which must be preserved to avoid worsening liver dysfunction. Vasodilatory hypotension should be treated with appropriate intravascular volume expansion and administration of a vasoconstrictor. 4% Albumin is an acceptable volume expander particularly given the underlying hypoalbuminaemic states of many of these patients. Fluid resuscitation can be challenging as excessive administration can lead to increased cardiac filling pressures leading to hepatic congestion, pulmonary oedema, and resulting respiratory failure. Renal perfusion should be optimised as these patients are high risk for concomitant renal dysfunction which greatly increases morbidity and further complicates fluid balance.

Intraoperatively strict attention must be paid to monitoring glucose levels. Multiple factors affect glucose levels, including the inflammatory response to surgery, steroid administration, hepatic dysfunction, altered glycogen stores, and insulin resistance in liver failure. Hyponatraemia is often present and must be corrected to ensure prevention of encephalopathy. Rapid correction should be avoided to prevent central pontine myelinolysis.

Post-operative Care

The postoperative care of patients with liver disease begins with appropriate placement. This is determined by the severity of the patient's disease, associated co-morbidities and the nature and course of surgery. Admission to a High Dependency Unit or Intensive Care Unit should be considered for any high risk or high MELD patient even in the setting of uneventful surgery. Where encephalopathy and altered GCS is present preoperatively, a period of post-operative ventilation should be considered due to potential for lack of airway protection.

Where possible a multidisciplinary team approach should be adopted to postoperative care with involvement of gastrointestinal physicians for ongoing follow up and monitoring of liver function. Attention should be paid to the potential for specific manifestations of liver disease including encephalopathy, renal dysfunction, wound infections and sepsis especially in the presence of ascites and malnutrition. Ongoing monitoring for postoperative coagulopathy is essential with bleeding possible not only from surgical sites but gastrointestinal sources also. Hypoxia and hypotension

should be avoided and are poorly tolerated, contributing to worsening liver and neurological dysfunction.

Dietician involvement with maintenance of caloric and low protein nutrition is important. The pre-emptive use of laxatives / enemas and avoidance of hypovolemia or hyponatraemia will minimise potential for encephalopathy.

Analgesia should be provided with regional and simple analgesics where feasible. Opiates are generally tolerated in patients with compensated liver disease but must be used with caution in patients with hepatic dysfunction due to risk of respiratory depression and possible encephalopathy arising from accumulation and prolonged effects. When necessary, opioid analgesia should preferentially be in the form of fentanyl due to its renal excretion. Oral opiates if required should be administered at reduced doses or with increased time intervals to prevent accumulation. NSAIDs should be avoided due to risk of nephrotoxicity, gastrointestinal bleeding and platelet dysfunction.

Antiviral therapy

Antiviral therapy is now halting the progression of hepatitis C and B liver cirrhosis and saving a number of patients from transplant. Patients who present for elective surgery with undiagnosed cirrhosis secondary to hepatitis should have surgery deferred and be referred to hepatologists for consideration of antiviral therapy prior to surgery. This will markedly improve their liver synthetic reserve and reduce their in-hospital morbidity and mortality. Hepatitis B requires four weeks treatment (Entecavir) whilst hepatitis C requires 12 weeks (Viekira Pak/Harvoni). Whilst hepatitis B antiviral therapy suppresses viral disease new antiviral treatments are available that cure hepatitis C. In both diseases antivirals can be utilised for treatment of decompensated cirrhosis, even resulting in reversal of cirrhosis and improvement in portal hypertension (7), (8).

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AMREF Flying Doctors

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The African Medical Research and Education Fund, or AMREF, mainly draws fundraising from Europe and the UK. It's largely unheard of in NZ, despite one of the original founders being Sir Archie McIndoe, surely a candidate for most shamefully under-recognised New Zealander. AMREF itself is a large organisation which concerns itself mainly with training local healthcare workers and addressing public health matters in East Africa. The Flying Doctors are a small component of it and have a rotating cast of volunteer doctors from all over the world.

The Flying Doctors retrieve and transport tourists and locals from Africa to all over the world. With the money made from this (usually insurance payments) they fund surgical teams and charity retrievals. Any profit left over goes to the parent body for their services. The volunteer physician program provides the Flying Doctors with free labour for the retrievals that is then billed out to clients providing a large payment to the organisation.

When I was here for two months in 2007 I flew the equivalent of twice around the world in the back of little turboprop and jet aircraft. Apart from going to a large number of countries in Africa I also repatriated people to Italy, Pakistan, Israel, England and the Canary Islands. I picked up people from bush rollovers, a priest who had been shot by the Lords Resistance Army, and a man attacked by a lion and hyenas.

When I returned in February 2015 the workload was less intense. February is always quiet apparently, but still an adventure. I travelled in police motorcades in Mombasa and Nairobi, with the traffic through the middle of Mombasa stopped for us to hurtle through. I spent a weekend in Nigeria, which was much nicer than expected, and I flew into Somalia on several occasions. I saw gunshots, psychosis and some extremely third world medicine. I had VIPs having seizures in our little cramped cabin, and I intubated a young student on the runway of Kilimanjaro International Airport after he was delivered by two doctors with GCS 3 and no airway. In my down time I also managed to do a couple of day trips around Nairobi and spent a day visiting a local hospital's theatre complex to watch some obstetric anaesthesia.

The volunteer program is open to anyone with Anaesthetic and ICU experience, and they will accept applications from anyone in Advanced Training onwards. It certainly is an amazing experience, and provides an easy, short-term way to do some very gentrified aid work. People tend to come for a month at a time and AMREF have a calendar on their website (www.flydoc.org) that lets you see which months are still available, but they tend to fill quickly. It is extremely easy to organise as the Flying Doctors take care of the local registration. The whole process was orders of magnitude easier than trying to get Australian registration, for example.

The work itself isn't hugely different from other retrieval organisations, and is usually at a lower level of intensity. But the environment it is conducted in is unique. Having the organisation based here, and with local pilots and nurses means people have a very good sense of what's safe and what's not. The Volunteer Physician is the only outsider in the organisation, and so for a month you get an amazing view from the Kenyan perspective. Africa is not without its troubles, and it's really interesting to talk to people who have insider knowledge of events.

As with everything in life there are negative aspects, and these are worth considering before volunteering.

Since I was there in 2007 the Flying Doctors had become a company, and there is a definite flavour of profit maximisation coming through. The profits still go to the parent AMREF organisation, but volunteering this time hasn't felt as 'aid workery' as in 2007. This might be an important consideration for you if you do want to feel like you are contributing more directly. Also, they are not like the Red Cross in that they have definitely 'taken sides'. Part of the flying is to pick up Kenyan soldiers injured in or near Somalia by al-Shabaab, you would need to be comfortable with this lack of impartiality.

As with any retrieval job there is a lot of downtime. This can feel quite restrictive as it's not completely safe to just wander around Nairobi. I would recommend coming later in the year when it's much busier.

Volunteering abroad is never an inexpensive exercise. Flights to Nairobi have to be paid for, though day-to-day living can be done quite cheaply and you are provided bed and breakfast.

Working here is not as safe as working in a theatre in NZ, but it wouldn't be an adventure if it were. The day-to-day safety is fine, as the free accommodation is in a good area only a 10 minute walk from the airport. The planes are very good quality and are well maintained. For the aviation buffs these include a fleet of Cessna Caravans, King Airs and Citation Bravo jets. Flying into Somalia has been the only truly scary experience this time, mainly because of the low, fast approach from the sea to make the plane a smaller target to any bored AK-47 toting individual nearby. However, it is at the Volunteer's discretion as to what flights they are prepared to go on. If you don't want to see the lovely beachside real estate of Mogadishu, the Flying Doctors have a pool of locum doctors which they will call on. These locums also allow you to take time out to see some of Kenya. Taking time off is as simple as saying that you are not available for those few days. Volunteer Physicians apparently sometimes bring family along and head away on safari from time to time.

Overall it's an amazing experience, and one I can definitely recommend. If you're happy with the drawbacks of the job then it will provide you with a month unlike any you're likely to find anywhere else.

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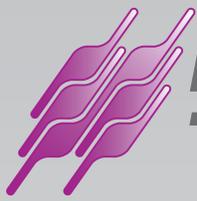
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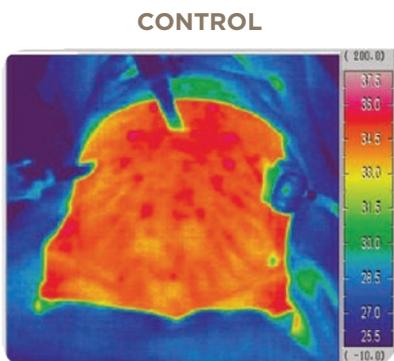
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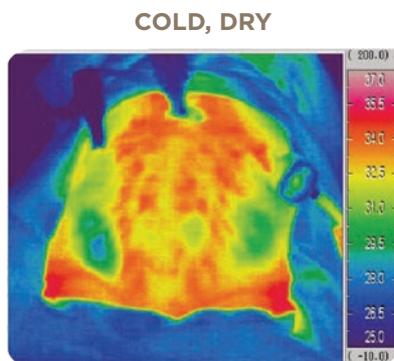
F&P **HumiGard™**

Humidify to Protect

TEMPERATURE MAINTENANCE



AT THE START OF INSUFFLATION



AFTER TWO HOURS OF INSUFFLATION

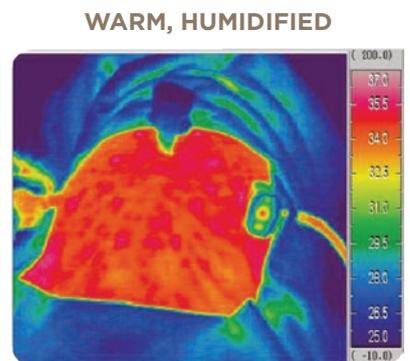


Image courtesy of Matsuda et al., 2002.

1. Patel A & Nouraei S. *Anaesthesia*. 2015
2. Miguel-Montanes R. et al. *Crit Care Med*. 2015
3. Badiger S. et al. *BJA*. 2015

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Two steps in the right direction
for effective post-operative pain relief^{1,2}

Start *Dynastat*¹
(parecoxib sodium for injection)

Continue with
*CELEBREX*²
(celecoxib)



References:1. Dynastat Data Sheet. 2 Celebrex Data Sheet.

Minimum Data Sheet. DYNASTAT® (parecoxib sodium) 40mg solution for injection Indications: single peri-operative dose for management of post-operative pain. Assess individual patients' overall risks and benefit/risk profile of alternative parenteral therapies before prescribing DYNASTAT. Use lowest effective daily dose for shortest duration possible. **Contraindications:** hypersensitivity to ingredients; allergic-type reactions to sulphonamides, aspirin, NSAIDs or COX-2 specific inhibitors; severe hepatic impairment; cardiac or major vascular surgery; previous MI or stroke. **Precautions:** Not for administration other than IV or IM. Increased risk of CV/thromboembolic events, deep surgical infections, or sternal wound healing complications following CABG surgery. Consider potential benefit/risk in patients with significant risk factors for, or history of, CV disease. May mask fevers; history of GI ulcer disease or GI bleeding; aspirin triad, asthma; renal or hepatic impairment or disease; use of ACE inhibitors, angiotensin receptor antagonists, diuretics, beta blockers, NSAIDs, corticosteroids, SSRIs, oral anticoagulants, cyclosporin or methotrexate; not a substitute for aspirin for CV prophylaxis; dehydration; fluid retention; oedema; hypertension; severe hypotension; heart failure; signs of serious skin reactions including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis; sulfonamide allergy; pregnancy & lactation; children; elderly. See Data Sheet for details. **Adverse Effects:** nausea, abdominal pain, vomiting, oedema peripheral, alveolar osteitis, hypoaesthesia, oliguria, respiratory insufficiency, sweating increased, pruritus, mouth dry, flatulence, pharyngitis, back pain, rash, hypertension, hypotension, circulatory collapse, acute renal failure, dizziness, dyspepsia, constipation, hypokalaemia, ecchymosis, agitation, insomnia, postoperative anaemia, aggravated hypertension, abnormal sternal serous wound drainage, respiratory insufficiency, wound infection, gastroduodenal ulceration, bradycardia, hyperglycaemia, AST increased, ALT increased, BUN increased, thrombocytopenia, cerebrovascular disorders, rare cases of Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, jaundice, hepatomegaly and hepatic failure. See Data Sheet for details. **Dosage and Administration:** single 40mg IV or IM injection. **Medicine Classification:** prescription medicine. V11014.

Minimum Data Sheet. CELEBREX® (celecoxib) 100mg and 200mg capsules Indications: symptomatic treatment of pain & inflammation in osteoarthritis, rheumatoid arthritis & ankylosing spondylitis, management of acute pain & treatment of primary dysmenorrhoea. **Contraindications:** hypersensitivity to celecoxib or other excipients; allergy, asthma or urticaria with sulphonamides, aspirin, NSAIDs or COX-2 specific inhibitors; concomitant use of other NSAIDs; peri-operative use in cardiac or major vascular surgery; unstable/significant established IHD, PAD or cerebrovascular disease; active peptic ulceration; GI bleeding; estimated creatinine clearance <30 mL/min; CHF; severe hepatic impairment. See Data Sheet for details. **Warnings and Precautions:** known CV disease or risk factors; history of CV disease; history of, or at risk of, GI ulcer disease or bleeding; asthma and rhinitis, with or without nasal polyps; renal and liver dysfunction; dehydration; serious skin reactions including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis; concomitant use with ACE inhibitors, angiotensin receptor antagonists, diuretics, beta blockers, corticosteroids, oral anticoagulants, cyclosporin or methotrexate; fluid retention & oedema; hypertension; cardiac failure; may mask fevers; reversible infertility, pregnancy (spontaneous abortion) & lactation; children. Discontinue at first appearance of skin rash, mucosal lesions or any sign of hypersensitivity. See Data Sheet for details. **Adverse Effects:** More common: headache, dyspepsia, URTI, diarrhoea, sinusitis, abdominal pain, nausea. Rarely: drug rash with eosinophilia and systemic symptoms (DRESS, or hypersensitivity syndrome), syncope, CHF, ventricular fibrillation, pulmonary embolism, cerebrovascular accident, MI, GI perforation, GI bleeding, pancreatitis, liver failure, thrombocytopenia, agranulocytosis, aplastic anaemia, pancytopenia, hypoglycaemia, suicide, aggravated epilepsy, acute renal failure, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, sepsis, sudden death, angioedema, anaphylactoid reaction. See Data Sheet for details. **Dosage and Administration:** use lowest effective dose for shortest duration possible. 200-400 mg daily. Maximum recommended dose is 400 mg per day. See Data Sheet for details. **Medicines Classification:** prescription medicine. V10815

Before prescribing, please review Data Sheet available from Medsafe (www.medsafe.govt.nz) or Pfizer New Zealand Limited (www.pfizer.co.nz) or call 0800 736 363. ®Registered trademark PF8183 DA 1645DW PP-CEL-NZL-0029 08/16.



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