Objectives

- Examine impact of perioperative renal failure, and discuss structure and function of kidney
- Explore strategies for periop fluid management
- Discuss possible future directions for intra-operative decision making aids
Renal failure

- Increased risk of CKD
- Increased mortality
- Independent risk factor for cardiovascular complications
- Much higher cost of care and resource utilization
- Risk adjusted $16,000 increase in cost of care
Question

Is a small bump in creatinine an issue?
Bihorac et al - 2013

- Looked at various poor outcomes, including death

- Attempt to find degree of renal failure that matters
Bihorac et al - 2013

• Found that rises in serum Creatinine of 0.2mg/dl or greater, or 10% changes from baseline were associated with increased mortality and morbidity

• Not causative
Why are the kidneys so sensitive to changes in circulating volume?
The kidneys, unlike the lungs, do not have a dual blood supply
Renal blood supply

1. Filtration
2. Reabsorption
3. Secretion
4. Excretion

Excretion = Filtration – Reabsorption + Secretion
Renal blood supply

- Primary function is to maintain filtration fraction
- With decrease in incoming blood efferent arteriole must constrict
- See ACE inhibitor and renal artery stenosis
Prediction

What kind of patients get significant renal failure?
Prediction of renal failure

- Kheterpal, Tremper et al 2009
- Used NSQIP definition of renal failure – an increase of 2.0mg/dl creatinine
- Renal failure rate of 1%
- From NSQIP database
Pre-operative predictors

- Age > 56
- Male
- Emergent surgery
- High risk surgery
- Diabetes
- Acute heart failure
- Ascites
- Hypertension
- Pre-op mild/moderate renal failure
Kheterpal et al 2007

- Single center, included intra-operative data also

- Renal failure defined as drop below 50ml/min

- Rate of 0.8%
Kheterpal et al 2007

Pre-op risk factors

- Age, emergent surgery, liver disease, BMI, high risk surgery, PVOD and COPD

Intra-op risk factors

- Total vasopressor dose, use of vasopressor infusion, administration of diuretic

- ARF associated with increased mortality at 30, 60 and 365 days
Strategies

Wet vs dry
Shoemaker et al 1988

- Cardiac index >4.5L/min/m²
- $\text{DO}_2 > 600\text{ml/min/m}^2$
- $\text{VO}_2 > 170\text{ml/min/m}^2$

- ‘Supra-max’
- Achieved with fluids, blood, vasodilators, inotropes
- Reduced mortality – 21% vs 38%
Goal Directed Therapy

• Optimizing stroke volume and cardiac output – ‘supramax lite’

• Requires a monitor and an intervention

• Initially PA Catheter, followed by EDM
• Then pulse contour analysis (calibrated and un-calibrated)
• Includes PPV/SPV from art line
Goal Directed Therapy

- Considerable heterogeneity in clinical trials

- Mainly compared to standard therapy – this has changed a lot over the years
OPTIMISE trial – Pearse et al 2014 JAMA

- Large UK based, multi-center
- 734 patients
- Major general surgery

- Usual care vs cardiac output guided algorithm

- Primary outcome 30 day composite mortality and morbidity
OPTIMISE

• Used LiDCO pulse contour analysis device
• Give 250cc bolus of colloid over 5 mins
• Stop when SV fails to rise by at least 10%
• Also ran infusion of dopexamine until 6 hours post op
OPTIMISE

• Overall fluid volumes given similar

• No significant difference in primary outcome

• Or outcomes for length of stay, ICU days, 30 or 180 day mortality
OPTIMISE - Meta-analysis

- Reduced post-op infection
- Reduced length of stay
- But not 30 day mortality
GDT - conclusion

• Popular – easy to do

• Evidence inconclusive

• Doesn’t alter overall amount of fluid given

• May reduce immediate complications

• No mortality effect
GDT - conclusions

• Evidence weaker when used inside an Enhanced Recovery After Surgery program

• Patients optimized better prior to surgery?

• Less bowel prep, better hydrated at presentation
Zero balance

• Idea to keep patient ‘net zero’ at end of surgery

• Change in mindset
Brandstrup et al 2003

- Aiming at ‘unchanged body weight’ in elective colorectal surgery
- Randomized, observer blinded
- 141 patients
- Average BMI 25
- 98% patients ASA 1 or 2
- Significant difference in fluid admin – 2740ml vs 5388
Brandstrup et al 2003

- Reduced cardiopulmonary complications – 7% vs 24%
- Reduced wound healing complications – 16% vs 31%
- Renal failure not significantly different in the two groups
Conflicting approaches

- One where we measure every variable possible and despatch the kitchen sink to attain a goal

- Another where we don’t measure so much and stick to plan A – zero balance
Myles et al NEJM 2018

- Multi-center, international, randomized
- 3000 high risk patients
- Restrictive vs liberal iv fluid regime during and up to 24 hours following surgery

- RELIEF trial

- Australia and Canada 75% total
RELIEF trial

- 1490 vs 1493 patients
- Mainly ASA 3 and 4 (62% vs 62.4%)

- Criteria – Age >70, or presence of heart disease, diabetes, renal impairment or morbid obesity
- Major abdominal surgery, but liver resection excluded
RELIEF trial

- Liberal regime
- 10ml/kg crystalloid on induction
- Followed by 8ml/kg/hr through surgery
- 1.5ml/kg/hr following that
- At 24hrs – median 6146ml total fluid given
- Median weight gain 1.6kg
RELIEF trial

- Restrictive regime
- Max 5ml/kg at induction
- No other iv fluids to given unless indicated by a goal-directed device (EDM or pulse contour analysis)
- Crystalloid at 5ml/kg/hr through surgery
- Followed by 0.8ml/kg/hr post-op
RELIEF trial

- At 24 hours – median fluid 3671ml
- Weight gain 0.3kg
RELIEF trial - outcomes

- 1 year disability free survival – restrictive 81.9% vs 82.3%
- AKI: 8.6% vs 5.0% (P<0.001)
- Septic complications or death 21.8% vs 19.8% (P=0.19)
- Surgical site infection 16.5% v 13.6% and RRT 0.9% vs 0.3% were higher but not significantly so
RELIEF trial

• Problematic

• Did the pendulum swing too far (again)?

• Editorial (Brandstrup) ‘...a modestly liberal fluid is safer than a truly restrictive regime’
RELIEF trial

- Surgery performed is much different
- Minimally invasive

- Patient profile has changed
- More co-existing disease

- More likely to have renal perfusion at the margin
BJA 2006 – editorial

• Titled – Wet, dry or something else?

• ‘The great fluid debate continues to rage’
‘Wet, dry or something else’-
BJA 2015 – Minto and Mythen

• Science, art or random chaos?

• Editorial accompanying study by Lilot et al
Lilot et al

- Retrospective analysis
- 5912 patients, UC Irvine and Vanderbilt
- Intra-abdominal surgery, minimal blood loss

- Regression analysis favored strongly personnel over patient factors
Minimal effect

- Minimum or median MAP
- Median heart rate
- EBL
- Surgical approach

- A patient undergoing a 4h procedure, weighing 75kg could receive between 700 and 4500ml crystalloid, depending on their anesthesia provider
Subgroup

• Prostatectomies removed due to specific protocol at UC Irvine

• However when data analyzed separately this group had lowest infusion rate and smallest range of variability

• Provider effect eliminated by a protocol
Minto and Mythen

Do you really know how much fluid you give?
Summary

What we know

What we don't know

The sweet spot
Summary

• Clear sense of incorrect approaches

• Evidence against for ‘one size fits all’
Strategies – initial plan

• History and physical

• Assessment of fluid deficit prior to induction of anesthesia

• Procedure specific goals

• Clear plan and goals

• Incorporate data gained at induction into assessment
Strategies

• Use of dynamic monitoring
• Careful assessment of EBL, insensible loss

• SPV, PPV from art line
• EDM

• Understanding of limitations
Strategies - data

• Individual data
• Process
• Outcome
Strategies

• Decision support software

• AlertWatch is one example of this

• At least – ensuring attention directed to fluid administration
Future directions

Better analysis of available data

Better data (monitors and markers – blood and urine)
Markers

Gleeson et al - Feb 2019

Renin as a marker of Tissue-Perfusion and Prognosis in Critically Ill Patients
Gleeson et al 2019

• Outperformed lactate as a predictor of ICU mortality
• Not affected by RRT
• Under investigation
Other markers

• Cystatin C – a better creatinine?

• L-FABP – released by kidneys into urine under oxidative stress

• No ‘ideal marker yet found’
Future directions

Predicting Blood Pressure Response to Fluid Bolus Therapy Using Attention-Based Neural Networks for Clinical Interpretability

Girkar et al Dec 2018 (pre-print)
MIT Computer Science Lab
Machine learning

• Model developed for administration of fluid bolus

• Then test model on remaining data and assess its predictive value – in this case it was 85%
Machine learning

• You can then look into the algorithm

• Five most important features – respiratory rate, diastolic BP, temperature, bicarb and base excess
Machine learning

• Not causative

• Data dependent

• Machine algorithm will cheat – fracture prediction without using image
Machine learning

- May be of great utility in future
- Simple things can be implemented immediately
Discussion

Questions?