Faculty of
Health Sciences

Fakulteit Gesondheidswetenskappe
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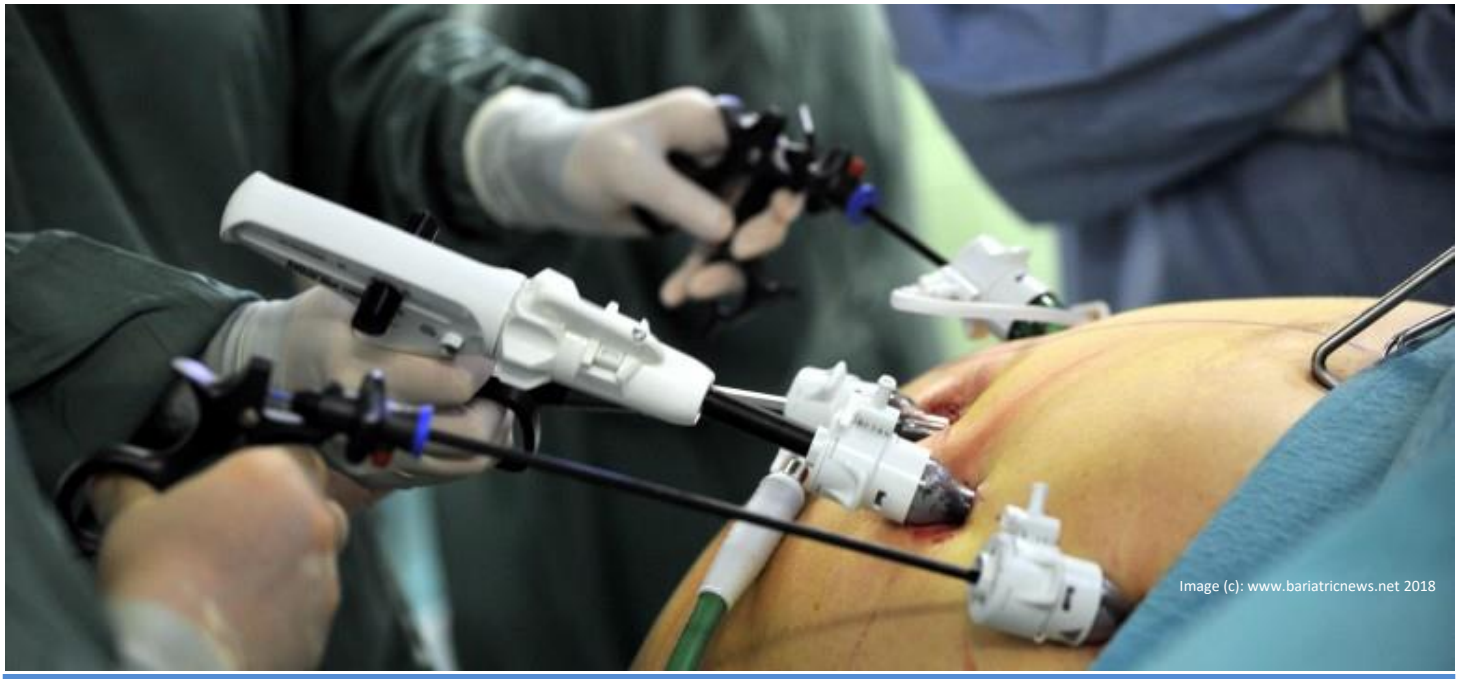

23rd. Annual Controversies and Problems in Surgery Symposium 2019

04-05 October 2019

SURGERY IN HIGH RISK POPULATION

Venue: University of Pretoria, Hatfield Campus, Sanlam Auditorium

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23RD ANNUAL CONTROVERSIES AND PROBLEMS IN SURGERY SYMPOSIUM 2019
DATE: 04-05 OCTOBER 2019 VENUE: SANLAM CENTRE, UNIVERSITY OF PRETORIA MAIN CAMPUS
THEME: SURGERY IN HIGH RISK POPULATION

DAY 1 (04 OCTOBER 2019)

TIME	*TOPIC*	*NAME*
07h00-08h00	**REGISTRATION AND TEA**	
	CHAIR: PROF MULAUDZI/PROF PEARCE	
08h30-08h40	**WELCOME NOTE**	PROF MONTWEDI
08h40-08h55	Opening address by Deanery Faculty of Health Science	PROF T DE JAGER
09h00-09h20	Operative risk in elderly patients with cardiovascular dysfunction	DR MAAKAMEDI
09h20-09h40	Timing of major surgery in relation to an acute ischaemic cardiac event, what are the problems and how to ameliorate those problems	DR MOTSHABI
09h40-10h00	Drug and antibiotic treatment in critically ill surgical patients, what are the considerations	PROF PARUK
10h00-10h20	Preparation of the elderly patients for emergency surgery	DR MOTILALL
10h30-11h00	**TEA AND VISIT TO THE EXHIBITION**	
	CHAIR: PROF KOTO	
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11h20-11h40	Challenges of haemodialysis in obese patients	PROF MULAUDZI
11h40-12h00	Essentials in pre-operative assessment of the super-obese for elective bariatric surgery	DR LUBBE
12h00-12h20	Surgical risk in the severely morbidly obese patients	PROF VAN DER WALT
	CHAIR: PROF LUVHENGO	
12h20-12h40	Management of hypercalcaemia in the elderly	DR BULABULA
12h40-13h00	Management of graves' disease in pregnancy	PROF MOLAOA
13h00-13h20	Management of phaeochromocytoma or Cushing disease in pregnancy	DR CAIRNCROSS
13h30-14h20	**LUNCH**	

CHAIR: PROF MOLAOA		
14h20-14h40	Challenges of breast cancer in pregnancy	DR NIETZ
14h40-15h00	Breast cancer in elderly patients	DR MOKONE
15h00-15h20	Major GIT cancer surgery in the elderly	PROF MONTWEDI
15h20-15h40	Fertility issues in young colorectal cancer patients	DR OYOMNO
15h40-17:30	**AFTERNOON TEA**	
18:00-19:00	**DINNER**	
DAY 2 (05 OCTOBER 2019)		
07:30-08:00	**REGISTRATION AND TEA**	
	CHAIR: DR SIKHOSANA	
08h00-08h30	Elective surgery in cirrhotic patients, when to operate, when to manage conservatively	PROF BRAND
08h30-09h00	Approach and challenges to surgery in HIV infected patients	DR JACKSON
09h00-09h30	Preparation and management of patients on anti-coagulation or anti-platelet therapy for elective or emergency surgery	PROF PEARCE
09h30-10h00	Challenges of laparoscopic surgery in the elderly frail patients	MR MAHARAJ
	CHAIR: DR TSHIFULARO	
10h00-10h30	Management of major abdominal trauma in pregnancy	DR MOTHABENG
10h30-11h00	Challenges of severe trauma in children	PROF SHAIK
11h00-11h30	Surgical care in-transition from paediatrics to adulthood	DR MULLER
11h30-12h00	Challenges in surgery for preterm babies	PROF LOVELAND
12h00-12h30	(CHALLENGES IN) Management of burns in children	PROF SHAIK
12h30-13h30	**Brunch**	
	CHAIR:MR MOTHABENG	
13h40	**ETHICS TOPIC: ETHICAL CONSIDERATION OF BARIATRIC SURGERY IN A DEVELOPING COUNTRY:**	PROF ROSSOUW DR LUBBE

WELCOME NOTE

I have great pleasure in welcoming you to the 23r^{d} Annual Controversies and Problems in Surgery Symposium.

We trust that the theme for this year “Surgery in special populations” will provoke interesting and challenging thoughts to presenters and attendees alike.

I urge you to debate robustly and constructively with each other on these matters.

I thank the speakers from far and near who gave off of their time to be part of this symposium. Your dedication and commitment to the course is highly appreciated. We welcome the delegates, new and old who choose us over other competing matters of interest. I hope we will meet your high level of academic expectations.

The trade has been and still is an important integral part of our meetings, thank you for your continued support.

The success of this congress is made possible by a team of hard working members of the Department of Surgery who put the entire program and all logistics in place, Thank you for your hard work.

I wish you all a pleasant and memorable symposium.

Yours sincerely

Welcome to the 23rd Annual Controversies and Problems in Surgery Symposium 2019

Dear colleagues and guests

On behalf of the organizing committee and the Faculty of Health Sciences, it is our great pleasure to welcome you to the 23rd Annual Controversies and Problems in Surgery Symposium 2019 hosted at the University of Pretoria.

The Faculty of Health Sciences is recognized internationally through its provision of teaching and learning and research opportunities aimed at producing graduates in the professional health disciplines. The Faculty is home to 5500 undergraduate and 1500 postgraduate students who want to positively impact lives in communities and society in more than 40 disciplines.

This year's theme focuses on Surgery in High Risk Population and we hope that the knowledge acquired from this conference will add value to the world of surgery. To the Surgical Research Society of Southern Africa and the Department of Surgery at the Faculty of Health Sciences thank you for continuously promoting the science and practice of surgery, creating platforms for surgery experts to share knowledge and information in Southern Africa. We also would like to thank the sponsors for their significant contribution and for supporting research, innovation and development in the surgical disciplines.

THE UP WAY is what we believe makes UP one of the top universities in the country and the world. It reflects our brand that lives in the hearts and minds of our staff, students and alumni. We teach, learn innovate, impact and live the UP way, because success matters.

We hope you will have an insightful, collaborative and impactful symposium that will help change lives. #LifeChangers

Prof. C (Tiaan) de Jager
Dean: Faculty of Health Sciences

Operative risk in elderly patients with cardiovascular dysfunction

Background

Older people are the fastest growing cohort of individuals undergoing surgery. The latest mid-year population estimates produced by Statistics South Africa (Stats SA) show that South Africa's population is estimated at 56, 5 million people. The estimates indicate that the proportion of elderly (60 years and older) in South Africa is growing, reaching 8,1 % in 2017. According to the estimates, there are 4, 6 million people in South Africa over the age of 60. Most of these patients will present for surgery at some point in their lives.

There is no precise definition of 'the aged', 'the elderly' or 'advanced age'. Ageing does not occur abruptly but represents a continuum. Nevertheless, data analysis by age quintiles supports the clinical relevance of usually defining patients aged >64 years as the elderly cohort.

Aging is a physiologic process where the structure and functional capacity of organs and tissue progressively degenerates over time. Age-related cardiovascular changes insidious and precede cardiovascular diseases associated with aging.

The cardiovascular phenotype of the elderly can be summarised as follows:

Systolic hypertension and widened pulse pressure

One of the cost common phenotypes of vascular aging is increased arterial stiffness which occurs as a result of increased vascular collagen and reduced elastin content. Aortic pulse wave velocity and pulse pressure also increase ultimately leading to increased systolic pressure and reduced diastolic pressure plus a widened pulse pressure.

Atherosclerosis

The aging process is associated with a chronic low-grade inflammation that predisposes the vasculature to atherosclerosis and endothelial dysfunction.

Arrhythmias

Pacemaker cells are progressively lost with advancing age which leads to sinus node dysfunction and ultimately **sick sinus syndrome**. Also, atrial tissue is replaced by fibrosis and there's associated atrial enlargement due to reduced ventricular compliance. Both these factors predispose elderly patients to **atrial fibrillation**. The incidence of atrial fibrillation increases with age such that it is present in 10% of those over 80. **Heart block** and **ventricular ectopy** are examples of other arrhythmias prevalent in older patients.

Autonomic nervous system

Ageing is accompanied by a variety of neurohumoral changes. Increased basal sympathetic outflow and norepinephrine plasma concentrations suggest an upregulation of sympathetic outflow. Alpha (α-) and beta (β-) adrenergic receptor sensitivity is reduced. Impaired response to stress associated with exercise, anaesthesia and surgery. Also, the response to fluid changes during surgery is poorly tolerated.

Valvular heart disease

The prevalence of valvular heart disease (VHD) increases with age, with degenerative valve disease thought to be the most common VHD in the elderly. **Aortic valve (AV)**

sclerosis is the most common valvular abnormality associated with increased aging. Aortic sclerosis usually progresses to calcific or degenerative **aortic stenosis**. The tri-leaflet aortic valve undergoes calcification and thickening without obstruction to ventricular outflow. Of adults aged ≥ 65 years, up to 29% present with age-related aortic sclerosis. It is also associated with coronary artery atherosclerosis and endothelial dysfunction.

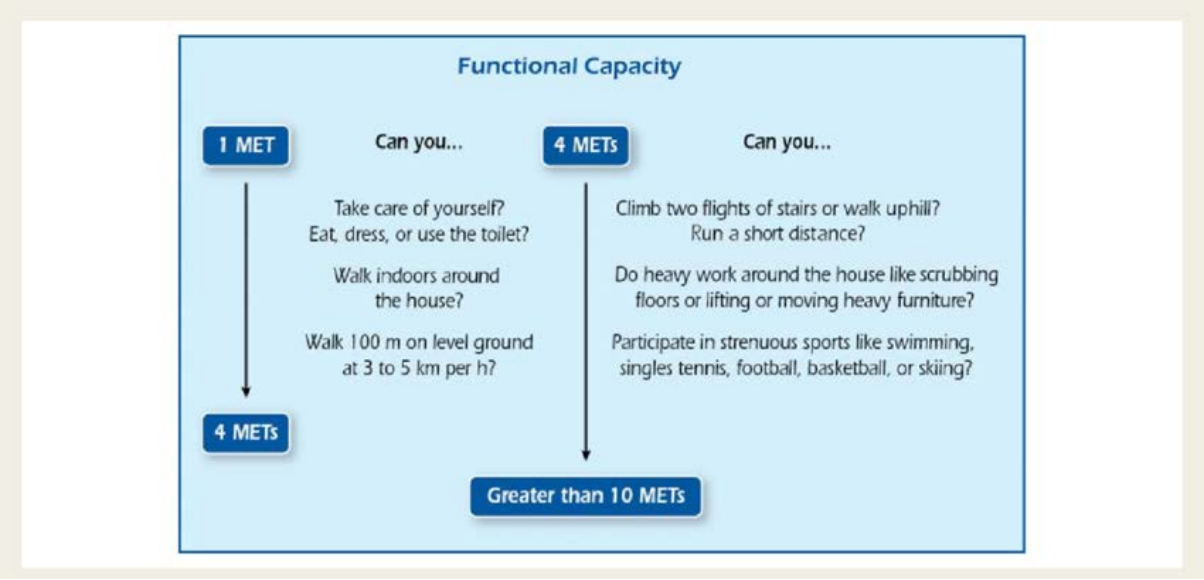
Cardiac risk stratification in elderly patients

Several multivariate studies have shown that the primary pre-operative risk factor for poor post-operative outcome is not age but co-morbidity. Cor-morbid diseases increases with aging for reasons mentioned already. Cardiac disease, in particular ischaemic heart disease, heart failure and arrhythmia, and reduced physiological reserve are the strongest predictors of post-operative **major adverse cardiac events (MACE)**, namely: cardiac death, non-fatal myocardial infarction, congestive cardiac failure and pulmonary oedema.

Post –operative complications can be predicted using several risk markers, i.e. functional capacity, clinical and surgical risk markers and more recently introduced, biomarkers of cardiac risk. These are discussed in the following section.

Functional capacity

In clinical practice, exercise tolerance in daily life ('medical' or 'physical fitness') best reflects the 'quality' of biological age. It is one of the most important predictors of perioperative outcome in the elderly surgical patient.



Functional status can be expressed in metabolic equivalents (METS) levels. One MET corresponds to the oxygen consumption *(Vo_2)* of a 70 kg, 40 year old man in a resting state, which is approximately 3.5 $ml.kg^{-1}.min^{-1}$. Functional capacity is assessed by recording activities of daily living, and has been classified as **excellent** (>10 METS), **good** (7-10 METs), **moderate** (4-6 METs), **poor** (< 4 METs) or **unknown**.

Patients unable to perform **4 METS** during most normal daily activities have increased perioperative short-term and long-term cardiac risk. The accurate assessment of functional capacity may be difficult in the geriatric population because many elderly patients

may have comorbid conditions or chronic pain, which limits their functional capacity. Some studies have demonstrated that perioperative cardiovascular events are more common in patients who had the inability to walk 4 blocks or climb 2 flights of stairs.

Clinical markers

Clinical markers of increased perioperative cardiovascular risk for myocardial infarction, congestive heart failure and death can be placed in three categories: major, intermediate and minor predictors. These have been derived from the **Revised Cardiac Risk Index (RCRI),** developed by Lee et al in 1999. These clinical risks include a history of ischemic heart disease, history of congestive heart failure, history of cerebrovascular disease, use of insulin therapy for diabetes, preoperative serum creatinine > 177 µmol/l.

Major	
	Recent myocardial infarction (<30d)
	Unstable or severe angina
	Decompensated congestive heart failure
	High-grade atrioventricular block
	Symptomatic ventricular arrhythmias in the presence of underlying heart disease
	Supraventricular arrhythmias with uncontrolled ventricular rate
	Severe valvular disease
Intermediate	
	Mild angina pectoris
	Prior myocardial infarction by history or pathological Q waves
	Compensated or prior congestive heart failure
	Diabetes mellitus
Minor	
	Advanced age
	Abnormal ECG
	Rhythm other than sinus
	Low functional capacity
	History of stroke
	Uncontrolled systemic hypertension

Advanced age

Advanced age does, in fact, present an independent predictor of perioperative cardiac outcome although by itself, is considered only one of the minor clinical predictors. Diseases such as diabetes mellitus, renal insufficiency, and compensated congestive heart failure, are more likely to occur in the older population. Age-related physiological decline, multi-morbidity and frailty are independently associated with increased perioperative risk.

Surgery-specific risk

Different surgical procedures would be associated with different cardiac risk and outcomes. Surgery-specific cardiac risk is related to two factors: type of surgery and degree of haemodynamic cardiac stress associated with a particular surgical procedure.

Risk of procedure	
High Risk (>5%)	Emergent major operations Aortic and other major vascular surgery Peripheral vascular surgery Anticipated prolonged procedure with large fluid shifts
Intermediate (1-5%)	Carotid endarterectomy Head and neck procedures Intraperitoneal and intrathoracic surgery Orthopaedic surgery Prostate surgery
Low risk (<1%)	Endoscopic procedures Superficial procedure Cataract surgery Breast surgery

Surgery-specific risk is classified as high-risk (combined perioperative incidence of myocardial infarction and/or death ≥ 5%), intermediate-risk (cardiac risk generally <5%)) and low-risk (cardiac risk generally <1%))

Risk scoring tools available

Over the years, several risk scoring systems have been developed to better predict cardiac risk in patients presenting for non-cardiac surgery, namely:

• 1999 – RCRI score by Lee and Goldman
• 2011 – **M**yocardial **I**nfarction and **C**ardiac **A**rrest (MICA) risk calculator by Gupta et al
• 2013 – ACS NSQIP risk calculator

RCRI (Revised Cardiac Risk Index)

In 1999, Lee et al developed and validated an index (Lee's Revised risk Index) for predicting cardiac risk in a prospective cohort study of 4315 patients aged ≥ 50 years of age undergoing elective noncardiac surgery.

Variable	**Points**
History of ischemic heart disease	1
History of congestive heart failure	1
History of cerebrovascular disease	1
Use of insulin therapy for diabetes	1
Preoperative serum creatinine > 177 μmol/l	1
High-risk surgery	1

The Revised Cardiac Risk Index (RCRI) is, perhaps, the most well-known and simplest tool. It consists of 6 predictors of risk, including: high-risk surgery (defined as intraperitoneal, intrathoracic, or suprainguinal vascular); history of ischemic heart disease; history of congestive HF, history of cerebrovascular disease; preoperative treatment with insulin; and pre-operative creatinine > 177 μmol/l

Total RCRI points	Risk estimate, %	99% CI for the risk estimate
0	3.9	2.8%-5.4%
1	6.0	4.9%-7.4%
2	10.1	8.1%-12.6%
≥3	15	11.1%-20.0%

NSQIP MICA (National Surgical Quality Improvement Program)

This cardiac risk calculator was derived from a 2007 National Surgical Quality Improvement Program (NSQIP) database, a multicenter prospective database of 211 410 patients from over 250 hospitals. It provides a risk estimate of perioperative **M**yocardial **I**nfarction or **C**ardiac **A**rrest (MICA). Five (5) predictors of perioperative myocardial infarction or cardiac arrest were identified: type of surgery, dependent functional status, abnormal creatinine, American Society of Anesthesiologists' class, and increasing age.

Its predictive value exceeds that of the RCRI. However, its limitation is that it only predicts two cardiac complications, i.e. myocardial infarction and cardiac arrest. The NSQIP MICA adjusts odds ratios depending upon the surgical site and predicts the risk for cardiac arrest or MI only.

ACS NSQIP risk calculator (American College of Surgeons)

The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) surgical risk calculator was developed from data of 1.4 million cases from 393 hospitals that took part in the ACS NSQIP program in the United States.

A web-based tool consisting of 21 patient-related factors and eight surgical procedures is used to calculate the risk of MACE and eight other outcomes individualized to the patient with excellent performance in predicting outcome.

Guidelines

Anaesthesia societies across the world have well developed cardiovascular guidelines based on evidence available for peri-operative management of patients with cardiovascular diseases presenting for non-cardiac procedures. The most commonly referenced guidelines which were recently updated include:

• 2014 – ACC/AHA and ESC Guidelines
• 2017 – Canadian Cardiovascular Society (CCS) Guidelines

Biomarkers

1. **Brain natriuretic peptide (BNP)**

Brain natriuretic peptide (**BNP)** is a 32-amino acid polypeptide hormone secreted by the cardiomyocytes attached to its N-terminal fragment (76 amino acids) of pro-BNP (**NT-pro-BNP)** which is biologically inactive are released from the myocardium in response to

various stimuli such as myocardial stretch, cardiac failure and ischemia/infarction. Their main biological effects are natriuresis/diuresis, vasodilation and inhibition of renin-aldosterone production.

Several studies have shown that preoperative natriuretic peptides are useful predictors of postoperative major adverse cardiac events (MACE) within 30-days after noncardiac surgery. Major adverse cardiac events include cardiac death, non-fatal myocardial infarction, or cardiac arrest.

A meta-analysis of by Rodseth et al of 2179 patients from 18 studies showed that a preoperative NT-proBNP/BNP measurement was independently associated with the primary outcome of death or nonfatal myocardial infarction at 30 days after noncardiac surgery.

Preoperative NT-proBNP/BNP when combined with risk scoring systems, improves risk prediction. Values ≥ 300 ng/L for NT-proBNP and ≥ 92 mg/L for BNP were identified as significant thresholds associated with an increased risk of the primary outcome. When combined with preoperative cardiac Troponin (cTnI), these biomarkers provide more prognostic information than when used individually.

2. Cardiac Troponin I

Most myocardial infarctions (MI) and myocardial injuries after non cardiac surgery (MINS) occur within the first 24 – 72 hours, especially in patients receiving analgesia that often masks ischemic symptoms. It is for this reason that 65% perioperative myocardial infarctions are asymptomatic. Without cardiac troponin monitoring, most of these myocardial infarctions go unnoticed and are associated with an increased 30-day mortality. Among patients undergoing noncardiac surgery, the peak postoperative TnT measurement during the first 3 days after surgery was significantly associated with 30-day mortality.

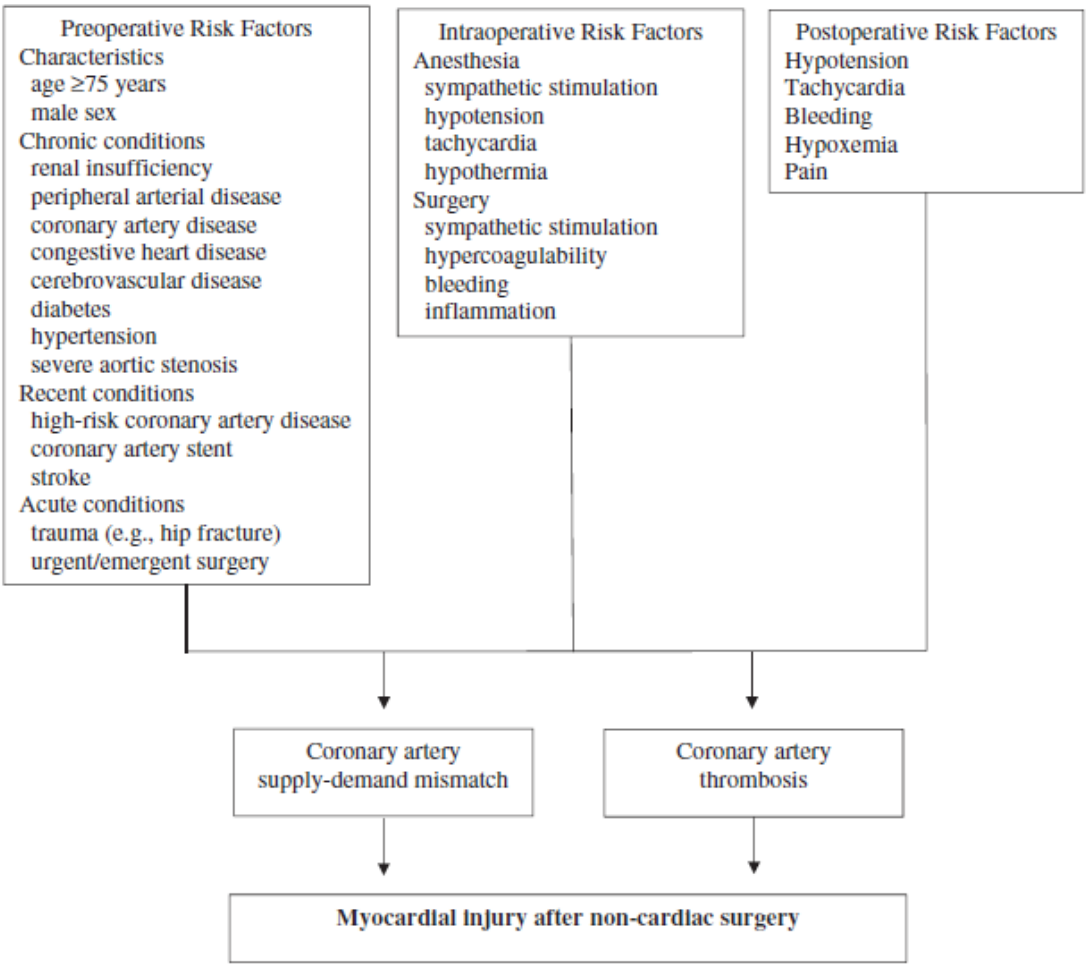
According to a large multinational prospective cohort study (VISION study, n=15 133 patients) in 2012, an elevated troponin T level in the after noncardiac surgery was the strongest predictor of mortality within 30 days. This study was preceded by a systematic review and metanalysis of 14 studies (n=3,318 patients) in 2011 that showed that an elevated troponin level after noncardiac surgery independently predicted mortality (OR, 6.7; 95% CI, 4.1-10.9) within 1-year.

Therefore, high-risk patients as identified by risk scoring tools, should have Troponin T surveillance on days 1, 2, and 3 after surgery while the patient is in hospital to avoid missing >90% of MINS.

Post-operative complications

Elderly patients with cardiovascular dysfunction presenting for surgery are at risk for **M**ajor **A**dverse **C**ardiac **E**vents (MACE) and **M**yocardial **I**njury after **N**on-cardiac **S**urgery (MINS) which is defined as an elevated post-operative troponin T measurement judged as resulting from myocardial ischaemia but not fulfilling the definition of Myocardial Infarction. About 82–93% of MINS occur without any ischaemic symptoms and would go unrecognized without troponin T monitoring.

A composite of factors (preoperative, intraoperative and post-operative) are responsible for MACE and MINS as demonstrated below. Some of these are either avoidable, modifiable or treatable, whereas others are not.



Strategies to Reduce Cardiac Risk

Medical Optimization

Patients with good functional capacity (≥ 4 METs) need not have exercise stress testing. The basis of performing preoperative cardiac risk stratification assumes the possibility that some or all of these risk factors identified may be modifiable with the ultimate goal of improving patients' outcomes.

Beta-blockers

Several studies have demonstrated the beneficial effects of beta-adrenergic blockers on peri-operative ischemia, arrhythmias and ultimately outcomes. Proposed mechanisms are multifactorial and include among others, reduced myocardial demands. Continuation of beta-blockers peri-operatively in patients on long-term beta-blocker therapy is a class I recommendation according to the AHA/ACC guidelines.

Modification or even discontinuation may be necessary in patients with hypotension, bradycardia, bleeding. Abrupt withdrawal of β-blocker therapy in perioperative period has shown to be harmful and is not recommended. In patients with preoperative testing suggestive of moderate- to high-risk myocardial ischemia, it is reasonable to begin perioperative β-blockers, if not contraindicated.

Statins

Lipid-lowering drugs, statins, are highly effective for primary and secondary prevention of major cardiac events perioperatively. Patients already on statin therapy long term should continue statin therapy perioperatively. This is a class I indication. For patients undergoing vascular surgery, it is reasonable to initiate statin therapy at least 2 weeks (Kristensen et al) before surgery and continue post-operatively.

Aspirin (acetyl salicylic acid - ASA)

Initiation and continuation of ASA for the purpose of preventing MACE is strongly not recommended with strong evidence, except in patients with recent coronary stents and those undergoing carotid endarterectomy. ASA should be stopped a minimum of 3 days (median 7) before surgery.

Angiotensin Converting Enzyme inhibitors (ACEI)

It is recommended that ACEI should be stopped 24 hrs prior to surgery to reduce risk of intraoperative hypotension which is an independent intraoperative predictor for MACE.

Conclusion

There is an increasing number of elderly patients with cardiovascular dysfunction presenting for surgical procedures. These patients are at risk of post-operative cardiac complications. Risk stratification tools allow physicians, surgeons and anesthesiologists to identify these high-risk patients. Even though available risk prediction tools are not ideal, their continued use improves outcomes and help develop guidelines as well as guide further research.

The use of cardiac biomarkers improve the predictive ability of risk prediction tools and should be considered in high risk elderly patients with cardiovascular disease.

Prevention of cardiac adverse outcomes requires a team approach consisting of cardiologists, surgeons, anaesthesiologists and intensivists knowledgeable in this area.

Timing of major surgery in relation to an acute ischaemic cardiac event what are the problems how to ameliorate those problems

Background

Coronary artery disease (CAD) is postulated to develop sub-clinically over a long period prior to overt presentation. It is a debilitating disease associated with increased morbidity, multi-organ dysfunction and death.

Cardiovascular disease (CVD) has been found to be a leading cause of death in the The Global Burden of Disease (GBD) study of the World Health Organization (WHO) reports cardiovascular disease as a leading cause of death in developed countries. CVD contributed 9.4%, 13.9% and 16.3% of mortality in low-, middle- and high-income countries, respectively. According to projections by the WHO, ischaemic heart disease will be the leading cause of death by 2030. It is estimated that in 2020, CAD will be responsible for approximately 11 million deaths globally.

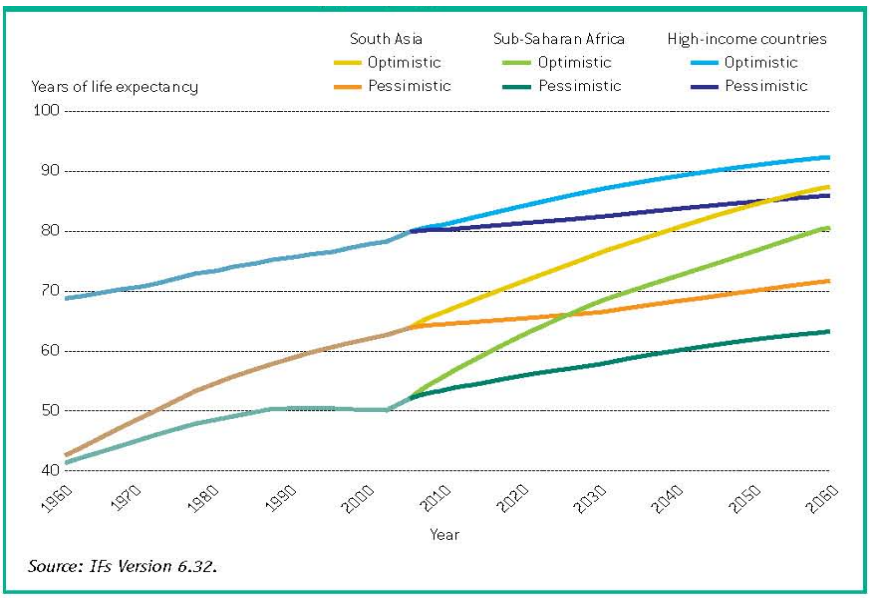


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Figure **Error! No text of specified style in document.**.1: Life expectancy in optimistic and pessimistic scenarios

Risk Factors for Acute Ischaemic Cardiac Events

The phrase "factors of risk" was coined by Dr William Kannel in 1961 to describe these predisposing conditions. The table below tabulates some of the risk factors associated with cardiac ischaemia.

Coronary Plaque Characteristics	Coronary Blood Flow Dynamics	Intrinsic Hemostasis Factors	Metabolic and Inflammatory Conditions	Neurohormonal Imbalance	Environmental Factors and Drugs
Plaque burden	Blood viscosity	Platelet function/volume	Diabetes mellitus	Stress	Smoking
Lumen encroachment	Shear stress	Circadian variation	Obesity	Catecholamine surges	Pollution
Lesion location	Reduced blood flow/low cardiac output	Factor V Leiden deficiency	Dyslipidemia	Depression	Climate
Plaque composition	Vascular tone and reactivity	Von Willebrand factor deficiency	Connective tissue diseases	Exertion	Legal drugs
Plaque biology	Arterial hypertension	Antiphospholipid syndrome	Infections	Autonomic dysfunction	Illegal drugs
Plaque configuration and remodeling			Renal disease	Endocrine imbalance	Diet
Endothelial dysfunction					Sedentary lifestyle

This table lists some of the established factors and conditions associated with increased acute coronary event risk. Note that there may be other, less well-established factors and unknown conditions that are not included.

Several cardiac risk indices [Davenport et al, Kheterpal et al, Gupta et al, Bilimoria et al, Alrzek et al, Lee et al, Kumar et al, Weber et al, Davis et al, Andersson et al, Kopec] have thus been developed over the years and include the commonly used revised cardiac risk index (RCRI) originally developed by Lee et al. A large cohort study including 782,969 patients, showed in-hospital mortality rates of 1.4% for RCRI of 0, 2.2% for RCRI of 1, 3.9% for RCRI of 2, 5.8% for RCRI of 3, and 7.4% for RCRI of 4 and greater.

RCRI risk score and associated Risk

Revised Cardiac Risk Index (RCRI)	Points
High-risk-type surgery (intraperitoneal, intrathoracic or supra-inguinal vascular)	1
Ischaemic heart disease	1
History of congestive heart failure	1
History of cerebrovascular disease Insulin therapy for diabetes	1
Preoperative serum creatinine >2.0 mg/dL (177 µmol/L)	1
Diabetes requiring insulin	1

RCRI = revised cardiac risk index; NT-proBNP = N-terminal probrain natriuretic peptide; BNP = brain natriuretic peptide; cTnT = cardiac troponin T; CI = confidence interval.

Final RCRI Score	Risk Group
0	Low Risk
1-2	Intermediate Risk
3-6	High Risk

Biomarkers in Risk Prediction

Biomarkers have been a subject of much interest particularly in diagnosing myocardial injury in the perioperative period. These include biomarkers representing a variety of pathophysiological pathways that promote atherogenesis or cardiac dysfunction such as markers of inflammation (CRP, interleukin-6), thrombosis (plasminogen activator inhibitor-1, D-dimer), endothelial dysfunction (homocysteine, urinary microalbuminuria), hemodynamic stress (natriuretic peptides), and myocardial injury (cardiac troponins). These biomarkers have formed the mainstay of diagnosis and surveillance of myocardial injury during the perioperative period, which may occur without evidence of clinical features of ischaemia.

Myocardial injury during non-cardiac surgery (MINS)

The conventional diagnostic criteria for acute myocardial ischaemia have not been created for the perioperative setting. Perioperative Myocardial Injury/Ischaemia in Non-cardiac Surgery is diagnosed by a postoperative peak high sensitivity troponin T of 0.03 ng/mL or greater due to myocardial ischaemia. It is independently associated with an increased the risk of 30-day mortality. Although a diagnosis of MINS has prognostic significance, the clinical utility is developing.

MINS is characterised by a rise in troponin, a biomarker of cardiac injury, with no symptoms and no evidence of myocardial ischemia on an electrocardiogram. It is diagnosed by elevation of cardiac troponin T (cTn) level where this troponin leak is not associated to non-cardiac ischaemic causes (eg, sepsis, pulmonary embolism, rapid atrial fibrillation, chronic troponin elevation). MINS is said to have a 30-day mortality rate of 10%.

MINS diagnostic criteria (only one required)

Any peak hs-cTnT ≥65 ng/L
An absolute increase in hs-cTnT of 5 ng/L
Peak cTnT 20 - 64 ng/L

The short-coming of hs-cTnT as a surveillance tool in patients at risk of MINS is that a nominal level of high-sensitivity troponin at baseline may be present in healthy subjects, and there is biological variability over time. Its changes could be due to circadian rhythm, seasonal changes or a random biological fluctuation around an inherent set point, specific to an individual. Use of multi-biomarkers panels in risk stratification have been investigated comprising of biomarkers such as BNP, high-sensitivity troponin I, and CRP. These have been tested against traditional risk scores. Some have subsequently been incorporated into risk scores with improvement of prediction. The Canadian guidelines recommend postoperative surveillance for MINS using cTn for 48 – 72 hours in patients with a baseline RCRI risk of >5% for MACE.

Criteria for daily postoperative cTnT surveillance for 48 - 72 hours (baseline risk >5% for perioperative MACE)

Elevated preoperative NT-proBNP or BNP measurement
Age 45 - 64 years, with significant cardiovascular disease and RCRI score ≥1
Age ≥65 years

Symptoms of ischaemia (such as pain in the chest, mandible, or upper extremity) may be absent in the perioperative setting where anaesthesia or strong analgesia has been administered. This is also true in patients with Diabetes Mellitus.

Diagnosis of Acute Myocardial Ischaemia (or Acute Coronary Syndrome)

Myocardial ischaemia is identified by a patient's symptoms and signs or from ECG abnormalities. ECG criteria to diagnose acute myocardial ischaemia require at least 2 anatomically contiguous lead with the following: i. ST elevation at the J point of at least 1mm

(depending on location) or ii. ST depression of at least 0.5 mm, and/or T wave inversion of at least 1 mm. It is diagnosed by a rise of cardiac biomarker value above the 99th percentile limit with at least 1 of the following: i. Symptoms of ischaemia, ii. New ST-segment T wave changes or new left bundle branch block, iii. New pathological Q waves, iv. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality v. Identification of an intracoronary thrombus by angiography or autopsy.

In patients with coronary ischaemia, the TIMI risk score, a simple prognostication scheme that categorizes a patient's risk of death and ischemic events and provides a basis for therapeutic decision making can be used. Although it is clear that patients with ischaemia should have either thrombolysis or percutaneous coronary intervention (PCI), and are already high risk for mortality, the TIMI Risk Score for STEMI provide risk stratification which helps treatment decisions after acute issues have been resolved.

TIMI Risk Score

Age ≥ 65	1
Aspirin use in the last 7 days (patient experiences chest pain despite ASA use in past 7 days)	1
At least 2 angina episodes within the last 24hrs	1
ST changes of at least 0.5mm in contiguous leads	1
Elevated serum cardiac biomarkers	1
Known Coronary Artery Disease (CAD) (coronary stenosis ≥ 50%)	1
At least 3 risk factors for CAD, such as: Hypertension -> 140/90 or on anti-hypertensives Current cigarette smoker Low HDL cholesterol (< 40 mg/dL) Diabetes mellitus Family history of premature CAD Male first-degree relative or father younger than 55 Female first-degree relative or mother younger than 65	1

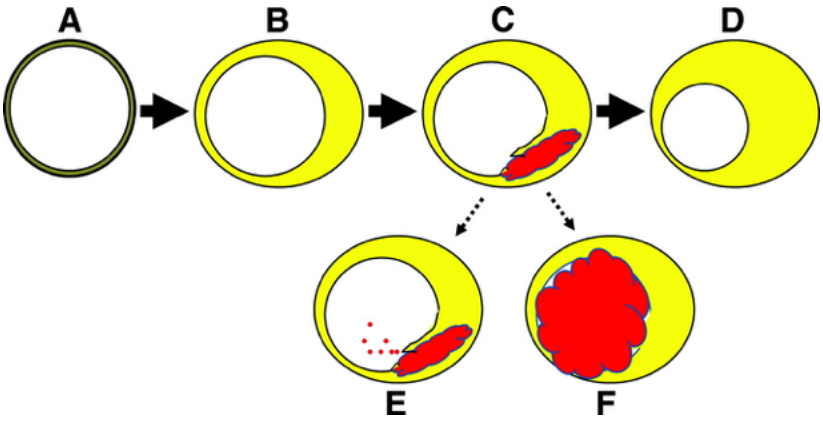
Score Interpretation

Score	Risk
0-1	4.7%
2	8.3%
3	13.2%
4	19.9%
5	26.2%
6-7	40.9%

% risk at 14 days of: all-cause mortality, new or recurrent MI,
or severe recurrent ischemia requiring urgent revascularization.

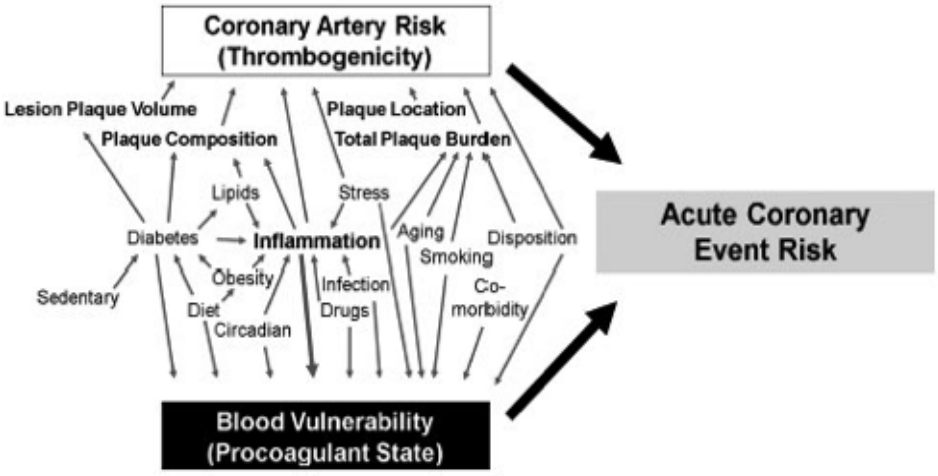
Acute Ischaemic Cardiac Events

Acute ischaemic events occur on the background of an early atherosclerotic process. During this period fatty infiltration occurs in the arterial wall. A necrotic core develops and increases in volume inflammatory processes. A thin-cap fibroatheroma is characterized by a large necrotic core covered by a thin layer of fibrous cap. The necrotic core is separated from the flowing blood by an ultrathin (mean thickness, 23 μm) layer of fibrous tissue that is depleted of smooth muscle cells, and is infiltrated by macrophages and T lymphocytes. Plaque growth, ongoing inflammation within the fibrous cap, external sheer stress, and other factors may particularly affect the thinnest region of the fibroatheroma, which may tear, exposing the highly thrombogenic material to the bloodstream



Armin Arbab-Zadeh, Circulation. Acute Coronary Events, Volume: 125, Issue: 9, Pages 1147-1156

Symptoms of ischaemia follow plague rupture and thrombus formation. Plaque rupture and thrombus formation may also occur in the vast majority of coronary arterial stenoses, ≥50% without symptoms of ischaemia. Factors influencing coagulation, inflammatory states, comorbidity, disposition, and environmental factors, together with "coronary" risk factors contribute to event occurrence.



Armin Arbab-Zadeh, Circulation. Acute Coronary Events, Volume: 125, Issue: 9, Pages 1147-1156

Progression of coronary atherosclerotic disease and reduction of the risk of acute coronary events is managed with lipid-lowering therapy and risk factor modification, decreasing the risk of coronary arterial thrombosis with antiplatelet therapy, and mitigating the effect on resulting ischemia.

In addition to these factors, patients with coronary artery disease may present with risk factors of thromboembolic events include: — atrial fibrillation (AF) associated with heart failure, hypertension, age ≥75 years, diabetes, stroke, and vascular disease. This would necessitate concomitant anticoagulation therapy.

Management of Acute Cardiac Events

Medical management of patients with coronary artery disease include Beta Blockers, Calcium channel Blockers, ACE Inhibitors, Statins, Antiplatelet therapy, Anticoagulant therapy. Patients with coronary artery stents are placed on dual antiplatelet therapy (DAPT) which includes Aspirin and a $P2Y_{12}$ agent. The duration of therapy differs between bare metal and drug eluting stents.

SAPT + NOAC SIHD + AF/DVT	Aspirin + Anti Xa / Direct Thrombin (IIa) Inhibitors
DAPT ACS + PCI/Stent	Aspirin + $P2Y_{12}$ / GP IIa/IIIb
DAPT + NOAC ACS + PCI/Stent + AF/DVT	Aspirin + $P2Y_{12}$ / GP IIa/IIIb + Anti Xa / Direct Thrombin (IIa) Inhibitors
DAPT + VKA ACS + PCI/Stent + Prosthetic valve	Aspirin + $P2Y_{12}$ / GP IIa/IIIb + Anti Xa + Warfarin

SAPS – single antiplatelet therapy, NOAC – non-vitamin K anticoagulants, VKA – vitamin K anticoagulants, ACS – acute coronary syndrome, PCI – percutaneous coronary intervention, SIHD – stable ischaemic heart disease

Perioperative Management for Elective Non-Cardiac surgery

Management of patents with ischaemic heart disease needs to be tailored to minimise risk of acute events. Planning and risk management has to take surgery risk into account. The following table classifies surgical risk.

Moderate to high risk	Low risk
> Neurosurgery	> Minor dermatological surgery, eg skin biopsy
> Spinal/epidural surgical procedures	> Cataract or glaucoma surgery
> Urologic surgery and procedures	> Dental procedures, eg simple extractions
> Vascular surgery	> Laparoscopic cholecystectomy
> GI surgery – major intra-abdominal	> Biopsy of a compressible site
> Orthopaedic joint surgery	> Joint aspiration/ injection
> Breast surgery	
> Thoracic surgery	
> Invasive ophthalmic surgery	
> Reconstructive plastic surgery	
> Pacemaker/ICD implantation	
> Liver biopsy	

ICD = Implantable cardioverter defibrillator; GI = gastrointestinal
Adapted with permission from Douketis *et al.*[33]

The importance of preventing even modest increases in heart rate cannot be overemphasized. Tachycardia, hypertension, hypotension, anemia, and pain should be treated aggressively. Treatment of tachycardia associated with hypotension is particularly challenging and requires an understanding of the patient's baseline and postoperative myocardial, valvular, and coronary physiology. Vasopressors to maintain blood pressure and β-blockers to slow heart rate while managing blood volume, postoperative pain, and respiratory function may be necessary.

Beta Blockers

The guidelines continue to recommend continuation of beta-blocker therapy in the perioperative period in patients currently receiving this medication. However, with regard to preoperative initiation of beta-blocker therapy the current ESC/ESA Guidelines have down-graded their recommendations. Preoperative start of beta-blockers may (rather than should) be considered in patients: 1) scheduled for high-risk surgery; 2) with ≥2 clinical risk factors or ASA physical status ≥3; and 3) with known ischemic heart disease (IHD) or myocardial ischemia. If the decision for preoperative initiation of oral beta-blocker therapy is made, atenolol or bisoprolol may be considered first choice. Neither the initiation of beta-blockers in patients undergoing low-risk surgery nor the initiation of high-dose beta-blocker therapy without titration is recommended.

Statins

Guidelines recommend perioperative continuation of chronic statin therapy with preference of statins with a long half-life or extended release formulation. Initiation of statin therapy should be considered preoperatively.

Antiplatelet therapy

In patients on Aspirin as a single antiplatelet therapy (SAPT), the decision for or against continuation during non-cardiac surgery must be based on individual weighing of the perioperative risk of bleeding against that of thrombotic complications. The decision should be made by a multidisciplinary team. Following BMS and DES implantation, dual antiplatelet therapy (DAPT) with Aspirin and $P2Y_{12}$-receptor antagonists for 4 weeks and 3-12 months, respectively, should be considered.

Anticoagulation

For patients receiving non-vitamin K antagonist direct oral anticoagulants (NOACs) it is recommended to discontinue NOACs for 2-3 times their respective half-lives before surgery with average risk of bleeding, and for 4-5 times their biological half-lives before surgery with high risk of bleeding. Depending on the type of VKA, it is recommended to stop therapy 3 - 5 days before surgery.

ACE Inhibitors

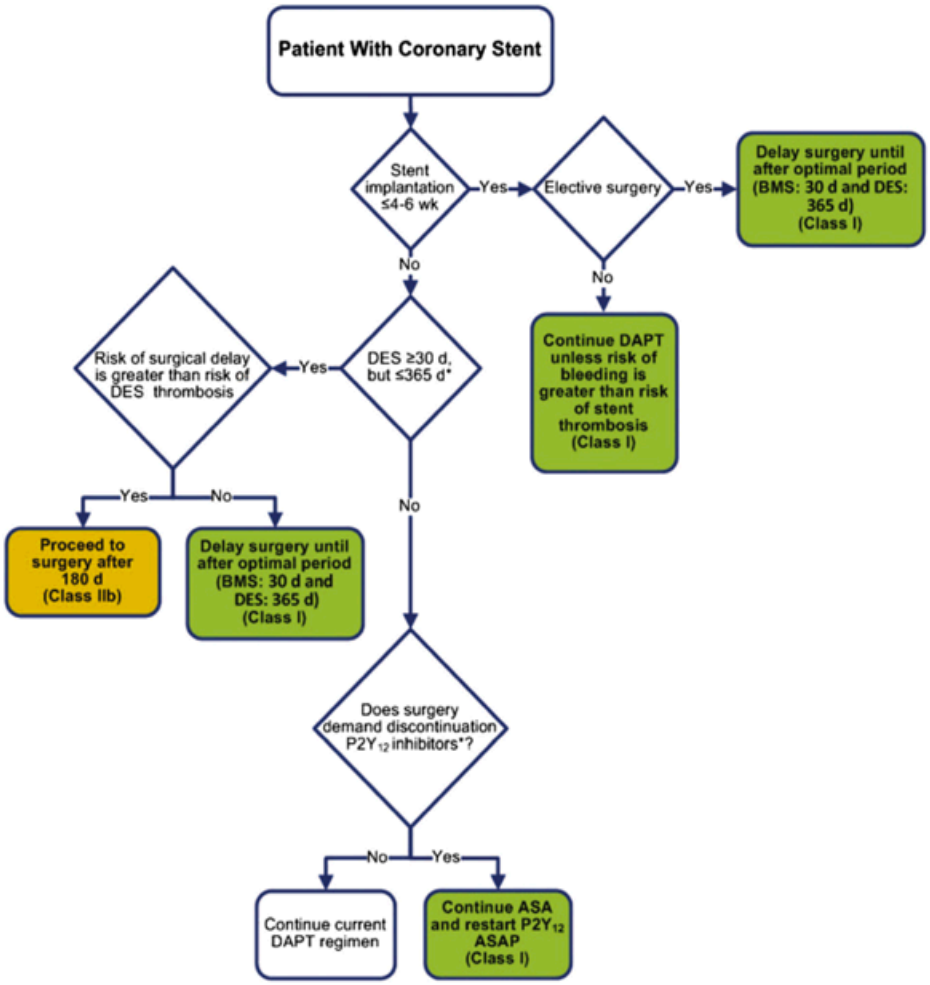
Guidelines take into account the proven benefit of ACEI or ARB therapy in medical patients with stable heart failure and left ventricular (LV) dysfunction, the lack of convincing evidence for a benefit of ACEI or ARB therapy on perioperative outcome, and the increased risk of severe hypotension during anaesthesia associated with such therapy.

Perioperative Management Of Patients With Coronary Stents

The respective recommended time intervals between PCI and subsequent elective non-cardiac surgery are listed. The Absorb bioresorbable vascular scaffold (Abbott Vascular, Abbott Park, IL), which has a higher propensity for stent thrombosis compared with second-generation

metallic DES, also produces DAPT management challenges in patients presenting for elective noncardiac surgery.

Due to the novelty of bioresorbable vascular scaffold therapy, there are no guidelines available for the management of patients undergoing elective noncardiac surgery. In some situations, DAPT is insufficient to abolish the residual risk of long-term recurrence of acute ischaemic events, , even with the use of more potent P2Y12 inhibitors. There is therefore clinical evidence for implementation of antithrombin strategies, targeting both attenuation of platelet activation and aggregation as well as suppression of thrombin generation and/or thrombin activity. Therefore, selective anticoagulants, direct thrombin inhibitors or factor Xa inhibitors, have been tested in the ACS population.



Perioperative management of antiplatelet drugs and anticoagulants

Management should follow a multidisciplinary team discussion to assess risk of bleeding against risk of acute ischaemic events.

Management during Emergent Surgery

During emergent surgery, there is not adequate time to stop DAPT and NOACS in patients at risk of acute ischaemic events. Reversal of these agents becomes important. The risk of clotting versus bleeding should be assessed. Long acting agents should be stopped, reversed where appropriate and bridged with short acting agents.

Groups	Receptor	Drug		Duration of action	Reversal
Antiplatelets	GP IIb/IIIa	Abciximab (ReoPro)		1 – 4 hours	Methyl Prednisone, DDAVP
		Eptifibatide (Intergrilin)		2.5 – 4 hours	
		Tirofiban (Aggrastat),		4 – 8 hours	
	ADP receptor / $P2Y_{12}$ Inhibitors	Thienopyridines	Clopidogel (Plavix), Prasugrel, Ticlopidine	3 – 7 days	Methyl Prednisone, DDAVP, Conjugated Estrogens
		Neocleoside Analogues	Ticagrelor (Brilinta), Elinogrel		
			Cangrelor,	60 – 90 min	
	Thromboxane	Synthase inhibitors	Aspirin	3 – 7 days	
	Phospodiesterase Inhibitors	Dipyridamole			
	Prostaglandin analoques	Iloprost, Prostacyclin			
	Other	Cloricromen, Ditazole, Vorapaxar			
Anticoagulants	Factor Xa Inhibitors	Heparins	LMWH, UFH	4, 24 hours	Protamine Sulphate, Ciraparantag (Ariparine)
		Oligosaccharides,	Fondaparinux (Arixtra),	24 – 72 hours	Ciraparantag (Ariparine), Andexanet Alfa (Andexxa)
		Heparinoids	Danaparoid		Protamine sulphate
		Direct Xa Inhibitors **(xabans)**	Rivaroxaban (Xarelto), Apixaban	18 – 36 hours	Andexanet Alfa (Andexxa)/ Ciraparantag (Ariparine)
	Direct Thrombin (IIa) Inhibitors	Bivalent	Hirudins : Bivalirudin (Angiomax)		Andexanet Alfa (Andexxa)/ Ciraparantag (Ariparine)
		Univalent **(gatrans)**	Dabigatran (Pradaxa),		Idarucizumab (Praxbind), Ciraparantag (Ariparine)
	VKA	Warfarin		3 – 7 days	PCC, Vit K
Thrombolytics / Antifibrinolytics	Alteplase, Streptokinase, Urokinase			30 – 100 min	TXA, Amicar

Reversal of antiplatelet therapy

Platelet transfusion is used for management of antiplatelet drugs in an emergency situation. This can be guided by use of the platelet aggregate test (VASP test). Methyl Prednisone, DDAVP, conjugated Estrogens have been shown to reduce bleeding from antiplatelet therapy.

Bridging for antiplatelet therapy

Intravenous short acting antiplatelet and anticoagulant agents are desirable due to their is short lived nature. Glycoprotein IIb/IIIa antagonists have for a long while presented themselves as an option for bridging therapy in the perioperative period. GPIIa/IIIb antiplatelet drugs have a short half-life and are ideal for bridging to avoid perioperative bleeding. The introduction of a neocleoside analogue P2Y12 antagonist Cangrelor has added to this drug armamentarium. This agent has an offset time of 30 – 60 minutes. These drugs can also be reversed using Methyl Prednisone, DDAVP, conjugated Estrogens.

Reversal of anticoagulant therapy

Prothrombin Complex Concentrates (PCC 25–50 units/kg in 10 minutes) are indicated for use in reversal of Warfarin related bleeding. They have been used off-label in the management of bleeding related to other direct anticoagulants (NOACS). Protamine Sulphate and can be used to reverse activity of heparins. Ciraparantag (Ariparine) can be used to reverse all NOACS whilst Andexanet Alfa (Andexxa) reverses Fondaparinux, Rivaroxaban, Dabigatran and Hirudins. A new drug Idarucizumab (Praxbind) has been developed to reverse Dabigatran (Pradaxa) related bleeding. Ciraparantag was found to be safe and well tolerated in healthy subjects, with minor non-dose limiting adverse events. Baseline haemostasis was restored from the anticoagulated state with doses of 100 to 300 mg within 10–30 minutes of administration and sustained for at least 24 hours.

Reduction in INR with vitamin K (IV or PO) will not be evident until approximately 18–24 hours after vitamin K administration, and large doses of vitamin K may lead to a hypercoaguable state which could last for a week or more, thereby increasing the risk of thrombosis in susceptible patients. Recombinant factor VIIa, although may also be used. rFVIIa has a short

duration of action (4 hours), and therefore may need to be administered multiple times to maintain the reduction in INR.

Bridging for anticoagulant therapy

Assessment of risk of thromboembolic phenomena emanating from atrial fibrillation can be assessed using the CHA_2DS_2-VASc score and the risk rate. Major guidelines have used the above fixed annual stroke risk as a guideline of starting anticoagulant treatment; where the ischemic stroke risk of more than 1% to 2% was used as an indication to start an anticoagulant therapy.

Preoperative bridging therapy with unfractionated heparin (UFH) or low molecular weight heparin (LMWH) is recommended in at risk patients. Bridging is accomplished by administration of the last dose of LMWH no later than 12 hours before surgery and that of UFH 4 hours preoperatively. Anticoagulation should be resumed when the risk of bleeding postoperatively is lower, after 6 hours.

The CHA2DS2-VASc score

CHA_2DS_2-VASc		
	Condition	**Points**
C	Congestive heart failure (or Left ventricular systolic dysfunction)	1
H	Hypertension: blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	1
A_2	Age ≥75 years	2
D	Diabetes Mellitus	1
S2	Prior Stroke or TIA or thromboembolism	2
V	Vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque)	1
A	Age 65 – 74 years	1
Sc	Sex Category (i.e. female sex)	1

Annual Stroke risk and the CHA2DS2-VASc score

Annual Stroke Risk	
CHA_2DS_2-VASc Score	**Stroke Risk %**
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	12.5

The HAS-BLED scoring system on the other hand is used to assess 1-year risk of major bleeding in patients taking anticoagulants with atrial fibrillation. This can be used to adjust therapy in the perioperative period to avoid major debilitating bleeding. A score of ≥3 indicates high risk.

HAS-BLED scoring system

	Condition	Points
H	Hypertension: (uncontrolled, >160 mmHg systolic)	1
A	Abnormal renal function: Dialysis, transplant, Cr >2.26 mg/dL or >200 µmol/L Abnormal liver function: Cirrhosis or Bilirubin >2x Normal or AST/ALT/AP >3x Normal	1 1
S	Stroke: Prior history of stroke	1
B	Bleeding: Prior Major Bleeding or Predisposition to Bleeding	1
L	Labile INR: (Unstable/high INR), Time in Therapeutic Range < 60%	1
E	Elderly: Age > 65 years	1
D	Prior Alcohol or Drug Usage History (≥ 8 drinks/week) Medication Usage Predisposing to Bleeding: (Antiplatelet agents, NSAIDs)	1 1

References on request.

Antibiotic treatment in critically ill surgical patients: What are the considerations

Fathima Paruk
Associate Professor and Head, Department of Critical Care, Steve Biko Academic Hospital, University of Pretoria

Critically ill patients in comparison to healthy individuals exhibit profound differences from a physiological, immunological and metabolic perspective. This has several implications in terms of our approach to prescribing drug therapy- and in particular antimicrobial therapy.

The following issues will be included in the lecture:

A. Choice of antimicrobial agent (empiric)

Antibiotics will not work unless there is source control. Their administration in the absence of source control will lead to treatment failure and also drive antibiotic resistance.

1. Community vs Nosocomial (72 hours in hospital) disctinction influences the initial choice of therapy.
2. Nosocomial pathogens
    i. ESCAPE (*VRE, MRSA, candida auris/Clostridium difficile/acinetobacter, pseudomonas, enterobacteriaceae* [*klebsiella, enterobacter species, E Coli, proteus, serratia*])
3. Always consider which of the following will need to be covered
    i. Anaerobes
    ii. Resistant gram positive (MRSA,VRE) pathogen
    iii. Resistant gram negative pathogen(s)(*acinetobacter, pseudomonas, enterobactaracea*)
    iv. Fungal infection

B. Directed therapy (De-escalation)

1. Important (preserves antibiotics, reduces resistance)
2. Only possible if appropriate specimens are taken for MCCS
    i. Intraoperative (a few mLs of pus or fluid in a container is far superior to a swab specimen)
    ii. CVP tip
    iii. A line tip
    iv. Blood culture
    v. Urine
    vi. ETA
    vii. Other – wound, CSF etc
3. Achieve within 72 hours
4. MICs are important for MRSA, CPEs,ESBLs
   Use another agent if
    i. carbapenems if the MIC >16 mg/L
    ii. colistin if the MIC exceeds > mg/L
    iii. vancomycin if the MIC > 1 mg/L
    iv. tigecycline if the MIC > 4mg/L

C. Dosing is difficult

1 Under-dosing is a risk due to
   i. ARC- augmented renal clearance
   ii. Hypo-proteinemia (increased clearance of free drug)
   iii. Shock (reduced perfusion)
   iv. Increased volume of distribution (hydrophilic antibiotics – Beta lactam antibiotics)

   This increases treatment failure and drives antibiotic resistance

2 Overdosing is a risk due to
   i. Renal dysfunction (renally excreted antibiotic)
   ii. Hepatic dysfunction(hepatic metabolism antibiotic)

3 Getting it right
   i. Loading dose vital (do not reduce even with renal failure)
   ii. Higher doses often required (see Table 1 for recommended doses)
   iii. Extended (carbepenems) or continuous infusions(Piperacillin-Tazobactam, Cefipime, Linezolid,Vancomycin) for time dependent antibiotics
   iv. Once daily dose –for concentration dependent antibiotics (aminoglycosides with trough monitoring)
   v. Therapeutic drug monitoring

D. Duration of treatment

1 If there is source control: Use clinical condition and biomarkers (PCT and CRP)
2 Site, organism and hardware also influence duration
3 Fungal – treat for 14 days after a negative culture

E. Adjunctive therapies

1 Quorum sensing inhibitors (biofilm)

F. Infection control

Table 1: Suggested dosing

Pipericillin – Tazobactam	**4.5g LD and then 18g over 24 hours**
Meropenem	**2g over 3 hours q8 (first 24-48 hours) then 1g over 3 hours every q8(8 hourly)**
Imipenem	**1g over 3 hours q6**
Ertapenem	**1g twice daily**
Cefipime	**2g LD and 6g over 24 hours**
Ceftazadime	**2g LD and 6g over 24 hours**
Tigecycline	**200mg LD and 100mg 12 hourly**
Gentamycin/Tobramycin	**5-7 mg/kg (trough < 1 µg/ml) (if >60 years or renal dysfunction- 5mg/kg)**
Amikacin	**20 mg/kg/day (trough < 5 µg/ml)**
Ciprofloxacin	**400mg TDS**
Colistin (combine with a second agent)	**12MU LD then 4.5 MU 12 hourly**

Aminoglycosides- troughs essential. With renal dysfunction the dosing interval – troughs will guide dosing interval as this will most likely increase to every 48-72 hours)
LD= loading dose
MU =million units

Preparation of the elderly patients for emergency surgery DR MOTILALL

Challenges of peritoneal dialysis in obese patients DR MALULEKE

Hemodialysis access in the Elderly and Obese

TV Mulaudzi

Does a fistula first approach work?

There is an increasing incidence of chronic kidney disease and end stage renal disease with age and diabetes mellitus. Construction of an autogenous arteriovenous fistula (AVF) as compared to prosthetic access offers the benefits of lower sepsis rates, lower mortality and better longevity(1).

In 2005, the Fistula First Breakthrough Initiative (FFBI) aimed to improve AVF access construction to 50% of all new hemodialysis patients (1, 2, 3).

A fistula first approach may however not be feasible in all patients. The Fistula First Catheter Last workgroup aimed to modify the efforts of the FFBI to individualize the type of access creation to benefit individual patients as opposed to a fistula at all cost approach (1, 4).

In the medical assessment of a dialysis candidate, certain factors may be associated with decreased arteriovenous fistula access patency rates. These include age, sex, obesity, diabetes mellitus, smoking, drugs, anaemia, hyperparathyroidism and peripheral vascular disease (1)

The aim of the article is to unpack the evidence guiding arteriovenous access in the elderly population and obese patients.

Elderly patients

A meta-analysis which included 13 retrospective and prospective observational studies was conducted to compare the primary patency of AVF access in elderly and non elderly patients (5). Subgroup analyses included differences in patency between prosthetic and autologous grafts and differences in outcome between proximal and distal AVF in elderly and non-elderly patients (5).

There was a statistically significant higher rate of radio-cephalic AVF failure in elderly patients compared to the non-elderly group, both at 12 months (OR= 1.525; p=0,001) and 24 months (OR = 1,357; p=0.019). Proximal brachiocephalic AVF had statistically significant better primary patency compared to distal radio-cephalic fistulas in elderly adults (5).

The above study suggests that strict adherence to the National Kidney Foundation- Kidney Disease Outcomes Quality Initiative guidelines in elderly

patients may be undesirable due to high failure rates especially when distal radio- cephalic AVFs are performed. However performing proximal AVF May increase the risk of steal in this patient subgroup(6).

Weaknesses of the study include the fact that no randomized studies were included in the meta-analysis. Furthermore, the definition of elderly was heterogeneous among the studies. There was no standardization of anatomic criteria used to select optimum sites for AVF construction, therefore it may be possible that poor veins were used in the elderly group (5).

A retrospective cohort study which included 1019 patients between 2007 and 2012 was conducted to assess AVF outcomes in octogenarians compared to non octogenarians (7). There was no difference in terms of primary outcome of failure to mature between the two groups (7). There was also no difference in incidence of steal and wound complications between the 2 cohorts. There was however a statistically significant lower overall survival in octogenarians compared to non octogenarians (7).

In a single centre retrospective study of elderly patients (>75 years) requiring dialysis, a comparison was made between AVF vs arteriovenous graft (AVG) for dialysis access. The primary fistula failure rate was higher in the AVF group (OR = 2,89; p= 0.008). The need for secondary intervention was also higher in the AVF group (p=0.03). The primary and secondary patency was similar between the groups and there was no difference in the all cause mortality (8).

Another retrospective analysis of prospectively collected data compared AVF vs AVG in > 65 years vs < 65 years dialysis requiring patients. The primary and secondary patency were the same in both groups. The incidence of failure to mature was however higher in the AVF group (9).

Obese Patients

Metabolic syndrome results in a pro- thrombotic state, associated with platelet dysfunction, endothelial dysfunction and a pro- inflammatory state characterized by increased levels of monocyte chemotactic protein 1(MCP), tumour necrosis factor alpha (TNF), IL 6, IL 8 and plasminogen activator inhibitor type 1. Patients with metabolic syndrome have been shown to have poor perioperative outcomes following cardiovascular and peripheral interventions. The outcomes of perioperative outcomes of patients with metabolic syndrome undergoing AVF access has not been adequately studied.

A single centre prospective observational study analyzed perivascular adipose tissue (adipose tissue surrounding vein 1cm from AV anastomosis) of 22 patients undergoing AVF access. The results revealed increased levels of MCP 1, IL6, IL 8, TNF, leptin, resistin and adiponectin in patients that had undergone negative vein remodeling (10).

Protack CD and colleagues conducted a single center retrospective review of patients undergoing hemodialysis access. Patients with metabolic syndrome were defined as those with a BMI of >30kg/ m^2 along with a BP> 130/90, HDL < 50mg/dl for women and < 40 mg/ dL for men, triglycerides > 150mg/ dl , and diabetes mellitus defined as a fasting glucose > 110 mg/ dl (11).

A total of 187 patients who underwent dialysis were enrolled in the study (115 with metabolic syndrome). Outcomes of survival, primary and secondary patency were compared between the 2 groups (mets vs no mets). The mean age of the patients was 66 and the time of follow up was up to 4.2 years. There was no difference in primary patency between the two groups, however there was a statistically significant difference in overall survival and secondary patency in favor of no metabolic syndrome (11).

In Summary

There is currently no level 1 evidence guiding the best practice approach in elderly patients. Current available evidence does however warrant caution when constructing AV access for octogenarians. Work up of the patient needs thorough investigation for anatomical suitability (arterial and venous). Risk of failure also needs to be balanced against the life expectancy of the patient. Furthermore, proximal AV access may be better than distal. In addition, AVG may have better overall patency than AVF due to poor veins in the elderly.

Metabolic syndrome and excess adipose tissue create a pro-thrombotic and pro inflammatory environment. The portion of the cephalic vein 1cm distal to the av anastomosis is most at risk for stenosis and subsequent thrombosis. Close surveillance in this patient group is warranted to asses wall remodeling and stenosis.

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Essentials in the pre-operative assessment of the super-obese for elective bariatric surgery

Body weight is classified according to body mass index (BMI) as:

BMI > 25 - Overweight

BMI > 30 - Class I Obesity

BMI > 35 - Class II Obesity

BMI > 40 - Class III Obesity

BMI > 50 - Super Obesity

The current accepted mortality after metabolic surgery (MS) ranges from 0.1% - 1% (depending on volumes performed). This mortality is the same as after cholecystectomy, knee replacement or hysterectomy. Risk factors contributing to complications and death after MS include Type II Dianbetes (T2D), BMI > 55 kg/m2 (main factor), obstructive sleep apnea (OSA), and cardiomyopathy. There is good evidence that perioperative morbidity and mortality is increased in patients with a BMI above 60 and age above 60 years. In the superobese population we also know that we will find a higher prevalence of psychiatric comorbid disease (Cleveland Clinic data). The preoperative workup of patients with obesity follows the standard guidelines followed in patients undergoing moderate risk surgical procedures. There are however certain specific risk factors and comorbidities that need to be taken into account, especially as BMI rises.

As with the work-up of all patients scheduled to undergo surgery, a comprehensive medical history, , physical examination (Fact Sheet. Metabolic & Bariatric Surgery.) and appropriate laboratory testing should be performed to assess surgical risk. In the obese population in general, special time is also spent on the psychosocial history. This review will focus on the specific comorbidities found in patients with superobesity and highlight the essentials in preoperative assessment in this patient population.

Cardiopulmonary Disease

In patients suffering from super obesity, three distinct cardiorespiratory comorbidities that have to be taken into account include obstructive sleep apnoea (OSA), obesity hypoventilation syndrome (OHS) and obesity cardiomyopathy, and lastly the difficult airway.

Obstructive Sleep Apnoea (OSA)

OSA is a syndrome characterized by periodic, partial, or complete obstruction in the upper airway during sleep. This, in turn, causes repetitive arousal from sleep to restore airway patency, which may result in daytime hypersomnolence or other daytime manifestations of disrupted sleep such as aggressive or distractible behaviour in children. The airway obstruction may also cause episodic sleep-associated oxygen desaturation, episodic hypercarbia, and cardiovascular dysfunction in the form of obesity hypoventilation syndrome (OHS) (Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea, Anesthesiology 2014). OSA is prevalent before MS in up to 94% of patients, with a significant number often undiagnosed (38%) (Rasmussen JJ et al. SurgObes Relat Dis.).

Diagnosis of OSA based on physical examination and review of past medical history is difficult. Several screening tools for sleepiness have been developed, such as the Epworth Sleepiness Score, the Maintenance of Wakefulness Test, the Berlin Questionnaire and the STOP-BANG Questionnaire, all with variable sensitivities and specificities (Abrishami A et al. Can J Anaesth. 2010). The standard

method of diagnosing OSA is via polysomnography (PSG), which requires an overnight stay in a sleep laboratory. During each hour of sleep, the number of apneas, defined as complete cessation of airflow, and hypopneas, defined as a 50–90% decrease in airflow and at least a 4% drop in oxygen saturation for > 10 seconds, are recorded. An “apnea hypopnea index” (AHI), or “respiratory disturbance index” (RDI) is used to quantitate these hypopneas and classify the degree of sleep disturbance. In general, an AHI of less than 5 is normal, 5–15 mild sleep apnea, > 15 moderate sleep apnea, and > 30 severe sleep apnea (Norman D, et al. Clin Geriatr Med. 2008).

The history should include focused questions related to snoring, apnea episodes, frequent arousals during sleep (e.g., vocalization, shifting position, and extremity movements), morning headaches, and daytime somnolence. We make use of the STOP-BANG Questionnaire. The physical examination should include an evaluation of the airway, nasopharyngeal characteristics, neck circumference, tonsil size, and tongue volume. We make use of a single pre-operative non-invasive extremity saturation measurement. If any characteristics noted during the preoperative evaluation suggest that the patient has OSA, the anesthesiologist and surgeon should jointly decide whether to (1) manage the patient perioperatively based on clinical criteria alone or (2) obtain sleep studies, or (3) initiate indicated OSA treatment in advance of surgery. As we do not have access to sleep studies, patients with a STOP-BANG score of > 5 are treated as having OSA, lung functions are performed, and perioperative precautions are taken accordingly. If venous saturation is below 94%, the concern for associated OHS increases, and patients are seen pre-operatively by anesthesiology to assess the need for echocardiography. All patients that have access to a home CPAP machine are encouraged to use this in the run-up to theatre. There is, however, no data in the literature regarding the optimal or minimum amount of time a patient with newly diagnosed OSA should be on CPAP therapy prior to surgery to decrease the risk of perioperative complications. Perioperative opiate use is routinely minimised in all patients undergoing MS, but even more so in the patient with superobesity.

Obesity hypoventilation syndrome (OHS) and obesity associated cardiomyopathy

OHS exists when an obese individual has awake alveolar hypoventilation (arterial carbon dioxide tension [PaCO2] >45 mmHg), which cannot be attributed to other conditions such as pulmonary disease, skeletal restriction, neuromuscular weakness, hypothyroidism, or pleural pathology. The prevalence of OHS increases as BMI rises. OSA is particularly common among patients with OHS, occurring in 85% to 92% of patients who have OHS (Macavei VM et al. J Clin Sleep Med. 2013). Conversely, OHS is less common among patients with OSA, occurring in 4% to 20% of patients with OSA (Lecube A et al. Obes Surg. 2010). Risk factors in obese patients are poorly defined but may include significantly increased waist/hip ratio (ie, central obesity), reduced lung function due to obesity, reduced inspiratory muscle strength and severe obstructive sleep apnea (AHI >50 events per hour). Unlike OSA, male gender is not a risk factor for OHS. Clinical presentation can be that of hypoxemic hypercapnic respiratory failure, right heart failure from pulmonary hypertension (dyspnea on exertion, elevated jugular venous pressure, hepatomegaly, and pedal edema) and less commonly, facial plethora from polycythemia. Patients presenting with hypoxemic hypercapnic respiratory failure are often misdiagnosed as having chronic obstructive pulmonary disease (COPD) or asthma, despite an absence of obstruction on pulmonary function testing. Daytime hypoxemia and significant and sustained reductions in overnight oximetry (eg, peripheral saturation < 80%) are features that are uncommon in OSA or obesity alone (Bingol Z et al. Respir Care. 2015). Almost all patients with OHS have an elevated serum bicarbonate (venous and/or arterial), which is usually a clue that the patient is chronically hypercapnic. However, it is nonspecific since other conditions can raise the bicarbonate level (eg, dehydration, medications) and it is not 100% sensitive since other

conditions (eg, lactic acidosis, chronic hyperventilation) may lower the bicarbonate level. Consistent with the phenomenon of hypoventilation, all patients with OHS have hypercapnia on arterial blood gas analysis when awake and on room air, and hypoxemia is usually present. Polycythemia due to recurrent hypoventilation- or OSA-associated hypoxemia is uncommon but may be present as a late manifestation.

Obesity not only places the heart at risk due to increased prevalence of coronary artery atherosclerosis and possible OHS, but obesity per se can cause heart failure. Mechanism for this is complex but we now understand that obesity leads to an increase in systemic mass and blood volume. This leads to structural cardiac changes such as increased left ventricular mass and hypertrophy, and left atrial enlargement (Kindel and Strande, Surg Obes Ass Dis 2018). Insulin resistance furthermore leads to myocardial mitochondrial dysfunction and can give rise to an obesity associated cardiomyopathy. An important consideration is that the usual clinical signs of heart failure (raised JVP and peripheral oedema) are almost impossible to ascertain (short neck), or universally present (peripheral oedema) in an obese individual, and tachycardia is often the only clinical sign present.

Our standard work-up includes chest radiography, a 12-lead echocardiogram, a fasting lipid profile and arterial blood gasses in all patients, with echocardiography performed only in selected cases. Serum lipid treatment is initiated according to the National Cholesterol Education Program Adult Treatment Panel III guidelines (see http://www.nhlbi.nih.gov/guidelines/cholesterol/ and https://www.aace.com/files/lipid-guidelines.pdf). We initiate evaluation for OHS in obese individuals with or without OSA who have the following clinical features: (1) unexplained awake room air peripheral saturation (SpO_2) ≤ 94% or an overnight nadir saturation < 80%, (2) unexplained dyspnea on exertion, (3) symptoms and signs of pulmonary hypertension and/or right-sided heart failure (eg, elevated jugular venous pressure, hepatomegaly, and pedal edema), (4) facial plethora, which may indicate polycythemia, and (5) a raised bicarbonate on venous blood sampling.

The difficult airway

Although increased BMI does not predict difficulty with laryngoscopy or tracheal intubation, larger neck circumference (>40 cm) and higher Mallampati score (>3) are predictors of a difficult intubation (Ramchandani L et al. Anesthesia considerations in the obese 2007). The probability of difficult intubation with a neck circumference of 40 cm is 5%, which increased to 35% with a 60-cm neck circumference (Kaw R et al. Obes Surg 2008). Besides for the calculation of a STOP-BANG score for each patient (that includes neck circumference, we also calculate the Mallampati score as a standard measure. There are certain precautions that we take in all patients undergoing MS, regardless of estimated risk for a difficult airway, including ramping, adjunctive measures being readily available should difficulty be encountered, preoxygenation, and awake extubation. A common intubation position for obese patients is the reverse Trendelenburg or head-up position of 25° to 40° with the use of shoulder towels (ramping). This position aids in improving oxygenation to prolong the time until desaturation, preventing aspiration, and offloading abdominal contents on the diaphragm, which increases FRC and reduces the formation of atelectasis (Leykin Y et al. Obes Surg 2006). Although most patients can successfully undergo tracheal intubation in a supine position, other adjuncts, such as awake intubation with a flexible fibreoptic scope, video-assisted laryngoscopy, and laryngeal mask airway (LMA), should always be readily available, especially if BMI > 60 (Pelosi P et al. Best Pract Res Clin Anaesthesiol 2010). The use of preoxygenation using 100% fraction of inspired oxygen (FiO_2) is recommended in all patients undergoing MS (Murphy C et al. Can J Anaesth 2013). The use of continuous positive airway pressure (CPAP) at 10 cm H_2O is also suggested in the pre-intubation phase to reduce the formation of atelectasis. Extubation should be performed once

return of protective airway reflexes and muscle strength recovery has been assessed, the patient is fully awake and able to follow commands, and in the reverse Trendelenburg position.

Suggested preoperative assessment

According to the ASMBS guidelines, cardiopulmonary testing should include at least an electrocardiogram and polysomnography preoperatively with further testing (echocardiography, spirometry, and arterial blood gases) guided by additional risk factors specific tests. Because we do not have easy access to polysomnography, OSA risk is estimated by the STOP-BANG score, supplemented by room air saturation and bicarbonate levels. Non-invasive cardiac testing beyond an electrocardiogram (ECG) is determined on the basis of the individual risk factors and findings on history and physical examination and after anaesthetic consultation. Pre- and intraoperatively, blood pressure cuffs should be long enough to encircle at least 75% of the arm and the wide enough to encircle 40% of the arm (Kuruba R et al. Med Clin North Am 2007). Given the increased size of extremities in some obese patients, ankle and wrist pressures are acceptable, if it is not possible to obtain routine arm non-invasive blood pressures, invasive arterial (or pulmonary) catheter monitoring may be needed in the superobese, patients with severe cardiopulmonary disease, those with access difficulties, and patients with unreliable non-invasive cuff readings. It is also important to take note of the fact that diabetics can have silent cardiac ischaemia. Postoperatively, we do ECG and cardiac enzymes in any patient not ready for discharge on morning of day 3, regardless of reason (nausea, tachycardia etc.).

Diabetes and Hypothyroidism

Hyperglycemia can delay wound healing, increase infection rate, and cause significant postoperative morbidity. For every elevation of HbA1C of 1% (above accepted 6%), there is a 1.4 rise in risk of severe complications (Guetta O et al. World J Diab 2019). Efforts should be made to reduce HbA1C levels preoperatively (ideally to below 9%) to reduce overall infection risk. The ASMBS guidelines endorse preoperative glycemic control targets of HbA1c of 6.5% to 7% or less. We refer patients with a HbA1C above 9% for endocrinological consultation and optimisation of glucose control before embarking on MS. Routine screening for primary hypothyroidism before bariatric surgery is not recommended, but currently we still perform a serum thyroid stimulating hormone level in all patients preoperatively.

Hepatobiliary Disease

Non-alcoholoc fatty liver disease (NAFLD) is subdivided into nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH). In NAFL, hepatic steatosis is present without evidence of significant inflammation, whereas in NASH, hepatic steatosis is associated with hepatic inflammation that may be histologically indistinguishable from alcoholic steatohepatitis (Ludwig J et al. Mayo Clin Proc. 1980). NAFLD is seen worldwide and is the most common liver disorder in Western industrialized countries, where the major risk factors for NAFLD, central obesity, type 2 diabetes mellitus, dyslipidemia, and metabolic syndrome are common. Most patients with NAFLD are asymptomatic, although some patients with NASH may complain of fatigue, malaise, and vague right upper abdominal discomfort [22]. Patients are more likely to come to attention because laboratory testing revealed elevated liver aminotransferases or hepatic steatosis was detected incidentally on abdominal imaging (Bacon BR et al. Gastroenterology. 1994). Patients with NAFLD may have mild or moderate elevations in the aspartate aminotransferase (AST) and alanine aminotransferase (ALT), although normal aminotransferase levels do not exclude NAFLD.

In patients with super obesity, histological testing confirms the incidence of NAFLD as follows: normal histology in 37%, steatosis in 62%, NASH in 30% and fibrosis in 30% (Udelsman BF et al. SOAD 2019). Preoperative triglyceride levels were positively correlated with NASH and high-density lipoprotein (HDL) levels were negatively correlated with NAFLD, supporting the utility of lipoprotein profiling preoperatively. Advanced NASH/NAFLD with compromised liver function greatly increases mortality. MS should probably not be performed if the MELD (Model for End-stage Liver Disase) score is > 8 and/or portal pressure is > 10 mmHg. Varices are a contraindication for both SG and RYGB due to the fact that staple lines are close to varices at the angle of HIS and there is evidence for an increased incidence of portal vein thrombosis. The ideal patient thus has NASH but not cirrhosis.

Fasting leads to gallbladder stasis and predisposes to the development of gallstones (Gustafsson U et al.). Formation of gallstones, as well as risk for symptomatic gallstones is increased after MS. Concomitant cholecystectomy (at the time of MS) is only recommended for symptomatic gallstones (Quesada BM et al. World J Gastroenterol 2010). The expected percentage of patients that will need postoperative cholecystectomy is estimated to be 10%. The treatment of choledocholithiasis is challenging after RYGB but can be approach with innovative techniques such as laparoscopic assisted transgastricendoscopic retrograde cholangiopancreatography (ERCP) at which time a concomitant cholecystectomy can be performed.

Metabolic surgery cases do not require extensive work-up for cholelithiasis or NAFLD. The ASMBS guidelines recommend work-up (abdominal ultrasonography) in symptomatic patients when preparing for weight loss surgery (Mechanick JI et al. Surg Obes Relat Dis 2013). We perform screening serum liver function testing in all patients undergoing MS. Abdominal ultrasound is not recommended as a routine screen for liver disease or gallstones. We perform ultrasonography in patients with a history of symptomatic gallstones, or if history and/or examination points to underlying liver disease.

Renal Disease

The comorbidities (cardiovascular disease, hypertension, diabetes) associated with obesity lead to an increase in chronic kidney disease. Obesity-related glomerulopathy is the process resulting in proteinuria and renal dysfunction associated with structural changes, such as glomerulomegaly and focal segmental glomerular sclerosis (Suneja M et al. J Crit Care 2014). The ideal candidate for MS is when the patient has microalbuminuria but no overt kidney failure yet.

A baseline renal panel is performed in the clinic as part of pre-operative blood testing. MS has been proven safe and effective if GFR is > 60. There is little evidence available on safety if GFR falls < 60. Fluid management in obese surgical patients can be difficult, because body fluid compartments are different compared with nonobese patients (Ingrande J et al. Int Anesthesiol Clin 2013). Patients are placed on a pre-operative 2 week low caloric liquid diet, and are encouraged to ensure intake of 1.5L - 2L of water per day, in order to avoid pre-operative worsening of renal function. Patients are encouraged to take clear liquids up to 4hrs before surgery. Sips of water and ice blocks are encouraged as soon as the patients is awake postoperatively, and liquids taken on the first postoperative night.

Deep Vein Thrombosis

Secondary to decreased mobility, increased pressure on the venous system, and increased venous stasis, obesity is a risk factor for deep venous thrombosis (DVT) and pulmonary embolism (PE) (Cullen A et al. Can J Anaesth 2012). Oral contraceptive use and smoking further increases risk. Other

risk factors include obesity hypoventilation syndrome, pulmonary hypertension, immobility, long operative times or an open approach, and male gender (ASMBS updated position statement on prophylactic measures to reduce the risk of venous thromboembolism in bariatric surgery patients. Surg Obes Relat Dis 2013). Even with perioperative prophylaxis, the estimated incidences of DVT and PE in obese patients range from 0.2% to 2.4%, therefore a combined protocol of pneumatic-compression lower extremity devices and anticoagulant chemoprophylaxis is needed to reduce the risk of DVT and PE (Ramchandani L et al. Surgical management of obesity. 1st edition. 2007).

A detailed history regarding previous DVT or PE should be performed, in which case adjunctive special investigations and/or measures (such as bridging warfarin, therapeutic doses of unfractionated heparin, and pressure bandages) might be employed. As a rule we make use of aggressive pre- and post-operative mobilisation (2hrs post-op patient mobilisation), intra-operative (continued for 24hrs) calf pumps, and postoperative prophylactic unfractionated heparin injections (continued for 2 weeks postop).

The Michigan Bariatric Collaborative study, which found that prophylactic IVC filter placement did not decrease VTE-related events or death, as well as the BOLD database, which reported that the risk of VTE was greater with IVC filters, has resulted in its use not recommend in guidelines (Mechanick et al. Surg Obes Relat Dis 2013).

Gastrointestinal Disease

We perform upper gastro-intestinal endoscopy on all patients before MS to check for the presence (and treat) H Pylori infection, or peptic ulcer disease, as our region has a high prevalence of H Pylori infection.H Pylori is eradicated in all patients preoperatively. Gastroscopy is also helpful to diagnose oesophagitis, Barrret's changes, and large hiatal hernias that might be a contra-indication to the performance of a sleeve gastrectomy. In patients with a history of reflux symptoms despite PPI therapy, oesophagitis or Barrett's on endoscopy, or a hiatal hernia > 3cm, SG should be avoided and RYGB considered a better option. Clinically significant gastrointestinal symptoms should be evaluated selectively before bariatric surgery with imaging studies or endoscopy as indicated. Despite the increased incidence of GERD in patients suffering from obesity (correlated to weight), we allow for clear liquids up to 2 hours before surgery as part of enhanced recovery after surgery (ERAS) to minimise the surgical stress response.

In patients with a history of previous surgery, MS is contraindicated only if severe adhesions are present, although sleeve gastrectomy can be considered if adequate pneumoperitoneum can be established. MS can lead to short gut syndrome in patients with Crohns disease. SG might be considered rather than RYGB after extensive consultation between the patient, surgeon and gastroenterologist in both these instances.

Psychiatric disease

Active, undiagnosed/untreated or uncontrolled drug addiction or psychiatric disease is a contra-indication to the performance of a MS procedure. Any patient considered for bariatric surgery with a known or suspected psychiatric illness, or substance abuse, or dependence, are referred for a formal mental health evaluation before performance of the surgical procedure. Surgery is only proceeded with after optimisation and stabilisation of the disease.

Pregnancy

Up to 80% of patients seeking metabolic surgery are female. Candidates for MS should avoid pregnancy preoperatively and for 12 to 18 months postoperatively. Pregnancy should be avoided in

the first year following a procedure due to nutritional deficiencies that might become apparent in the first postoperative year. The risk for internal herniation after RYGB increases from 15/year to up to 15% during pregnancy (Devangi MD et al Surg Obes Rel Dis 2019). This is thought to happen due to the growing uterus displacing small bowel into the upper abodinal cavity and thus closer to the mesenteric defects. The risk of internal herniation is decreased, but not eliminated, when mesenteric defects are closed at the time of primary surgery. We thus perform a pregnancy test and consultation in all female patients that enter the MS program.

Other considerations

Understanding of the procedure performed and lifelong implication, and commitment to lifelong adjustments in lifestyle, diet and micronutrient monitoring are important in all patients undergoing MS. All patients should undergo evaluation of their ability to incorporate nutritional and behavioural changes before and after MS. We perform this assessment at two small group dietitian sessions. Patients should be followed by their primary care physician and we supply an information booklet to all patients to provide to any other health care personnel that might take part in their care, both pre- and postoperatively.

Operating on patients with type I diabetes should be avoided.

Active or untreated non- skin cancer is a contra-indication to the performance of MS. We perform age and risk appropriate cancer screening before surgery in all patients.

All patients undergo an appropriate nutritional evaluation, including serum micronutrient measurements, before any MS procedure. In comparison with purely restrictive procedures, more extensive perioperative nutritional evaluations are required for malabsorptive procedures (RYGB).

Patients before MS are placed on a 2 week preoperative low caloric liquid diet (LCLD), not only to get used to the dramatically decreased intake that will be present in the first months postoperatively, but also to reduce liver volume. LCDL has been proven to facilitate surgical exposure and ease, but does not influence perioperative morbidity and mortality (Holderbaum M et al. SOAD 2018). Increased exercise and fitness have been proven to contribute to comorbidity improvement (Marcon ER et al. Obes Surg 2016).

Suggested References and Reading:

1. Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient–2013 update: cosponsored by American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery. Surg Obes Relat Dis 2013;9:159–91.

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Surgical risk in the severely morbidly obese patients PROF VAN DER WALT

Management of hypercalcaemia in the elderly DR BULABULA

MANAGEMENT OF GRAVES'DISEASE DURING PREGNANCY

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Controversies in Surgery 2019 (UP)

MANAGEMENT OF GRAVE'S DISEASE IN PREGNANCY

1.0. INTRODUCTION

Graves' disease (GD) is the most common cause of hyperthyroidism in women of child-bearing age; resulting from autoimmune disorder, with auto-antibodies directed to-, and stimulating TSH receptors – thyrotropin receptor antibodies (TRAb) - which are elevated in more than 90% of cases [1,2,3] It is the most common cause of hyperthyroidism with 20 to 30 cases per 100 000 per year, with life-time risk of developing the disease of 3% and 0.5% for women and men, respectively; with the peak incidence in the 30 to 60 years age groups; and affects 1 to 2 per 1000 pregnancies [3]

During pregnancy, overt GD is associated with both maternal, foetal, and neonatal complications as a result of the disease itself –maternal preeclampsia, cardiac failure, premature delivery, and foetal low birth-weight and foetal death - and treatment related embyopathy [1,3,6] On the other hand alteration in the thyroid physiology during pregnancy complicates the diagnosis of GD-hyperthyroidism (1)

To be covered in this discussion is the overview of diagnosis and diagnostic challenges, plus therapy and therapeutic challenges of GD-thyrotoxicosis during pregnancy.

2. VARIATION IN THE INCIDENCE OF GD AROUND AND DURING PREGNANCY (Danish and Japanese study)

There is wide variation in the incidence of GD-hyperthyroidism during and around pregnancy characterised by: periods of high incidence correspond with worsening of the current GD during pregnancy, and low incidence when the disease enters remission during the second half of pregnancy. Aggravation of GD hyperthyroidism is seen during early pregnancy due to elevated levels of hCG, remission during the second half of gestation is attributed to the immune suppressant effect of pregnancy, while the aggravation of the disease postpartum corresponds with postpartum immune recovery [1,8]

Figure 1: Incidence variation of GD around pregnancy (Danish study) /100 000 women.years

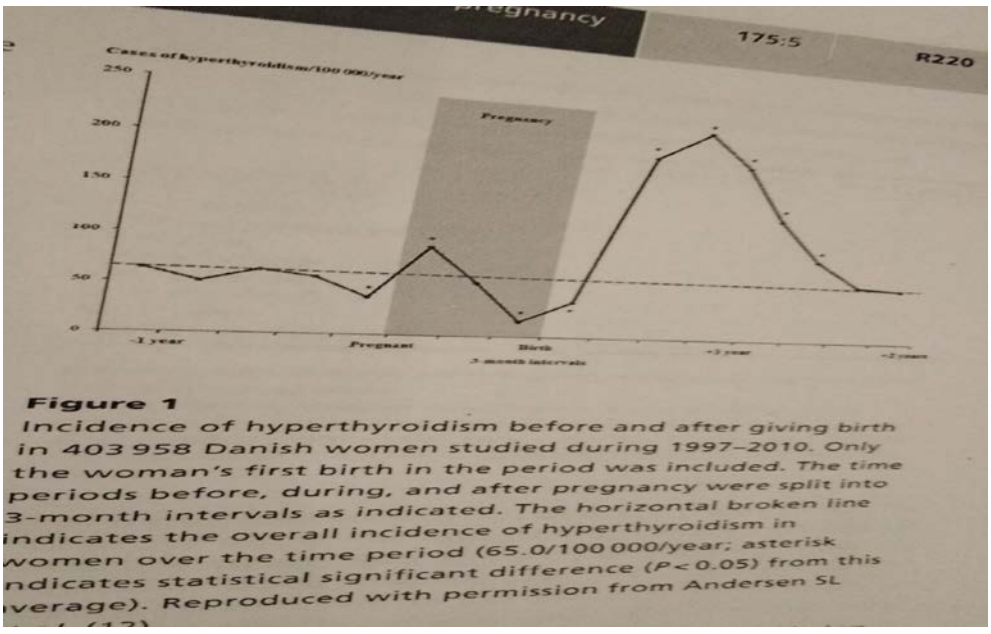


Figure 1
Incidence of hyperthyroidism before and after giving birth in 403 958 Danish women studied during 1997–2010. Only the woman's first birth in the period was included. The time periods before, during, and after pregnancy were split into 3-month intervals as indicated. The horizontal broken line indicates the overall incidence of hyperthyroidism in women over the time period (65.0/100 000/year; asterisk ndicates statistical significant difference ($P < 0.05$) from this verage). Reproduced with permission from Andersen SL

European

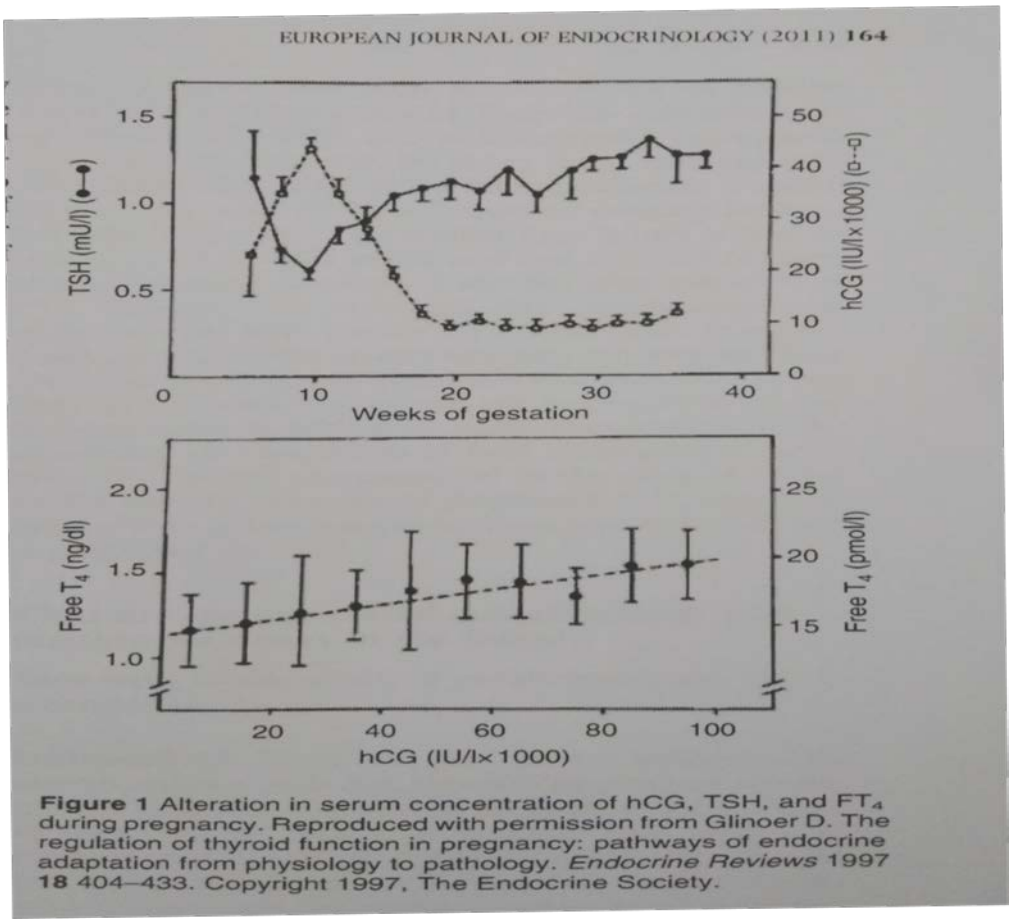
3. THYROID PHYSIOLOGY ADAPTATION IN PREGNANCY

During pregnancy, the thyroid gland undergoes compensatory enlargement due to relative iodine deficiency resulting from increased demand of up to 50% of daily requirement caused by the developing foetus and increased renal losses. Up to 50% of thyroid hormone production is seen during pregnancy. As a result of this increased iodine demand, in iodine replete countries the thyroid gland may increase by 10% of its size, while in iodine deficient areas it may increase by 20 to 40%. In healthy pregnant women these changes occur seamlessly, however thyroid dysfunction occurs as a result of pathological processes, such as in GD. These physiological adaptations pose a diagnostic challenges during disease conditions [8]

4. DIAGNOSIS OF GRAVE'S DISEASE AND DIAGNOSTIC CHALLENGES IN PREGNANCY

Diagnosis of hyperthyroidism is challenging during pregnancy due to pregnancy associated dynamic changes in diagnostic assay reference limits and pregnancy related variation of TSH, T4 and T3 levels as a result of hCG that stimulates TSH receptors (6). Pregnancy induced physiological goitre can further complicates diagnosis of GD in the setting of hCG induces gestational thyrotoxicosis.

Figure 2: Alteration in serum TSH, hCG, T4 during pregnancy



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4.1. Subclinical hyperthyroidism

Is diagnosed when serum TSH levels are below laboratory reference range with T4 and T3 levels within the reference range [1]

4.2. Overt hyperthyroidism

Is characterised by TSH level below reference range and both T4 and T3 levels above laboratory reference range [1].

4.3. GD hyperthyroidism

In addition to clinical signs of Graves's disease, 25% will have eye signs, Goitre is, however, not universally seen in patients with newly diagnosed GD as it is seen in 50% of cases. However TRAb are positive in more than 90% of patients with GD [1].

4.4. Differential diagnosis in pregnancy

4.4.1. Pregnancy related

4.4.1.1. Gestational thyrotoxicosis. This is a common differential diagnosis in pregnancy [1]. This is seen in about 20% of pregnancies during the first trimester due to hCG binding and stimulating TSH receptors resulting in increased levels of T4 with reciprocal decrease in the levels of TSH. The condition usually resolves after the first trimester and rarely requires treatment [3].

4.4.1.2. Struma ovaria

4.4.1.3. Chorio carcinoma

4.4.2. Non pregnancy Related

4.4.2.1. Recurrence of pre-existing GD

4.4.2.2. Toxic MNG

4.4.2.3. Toxic Nodule

4.4.2.4. Subacute (De Quaven's) thyroiditis

5. MANAGEMENT AND MANAGEMENT CHALLENGES IN PREGNANCY

Subclinical hyperthyroidism requires no treatment as it has not been shown to be associated with both maternal and foetal adverse outcome [4], therefore, the risk of ATD therapy out-weighs the benefit.

The objective of therapy is to achieve maternal euthyroid state while at the same-time preventing foetal and neonatal congenital defects, thyrotoxicosis and hypothyroidism.

The stage of pregnancy- as a determinant of the period of organogenesis, teratogenicity of ATD and their side effect to the mother- determines the choice of ATD therapy.

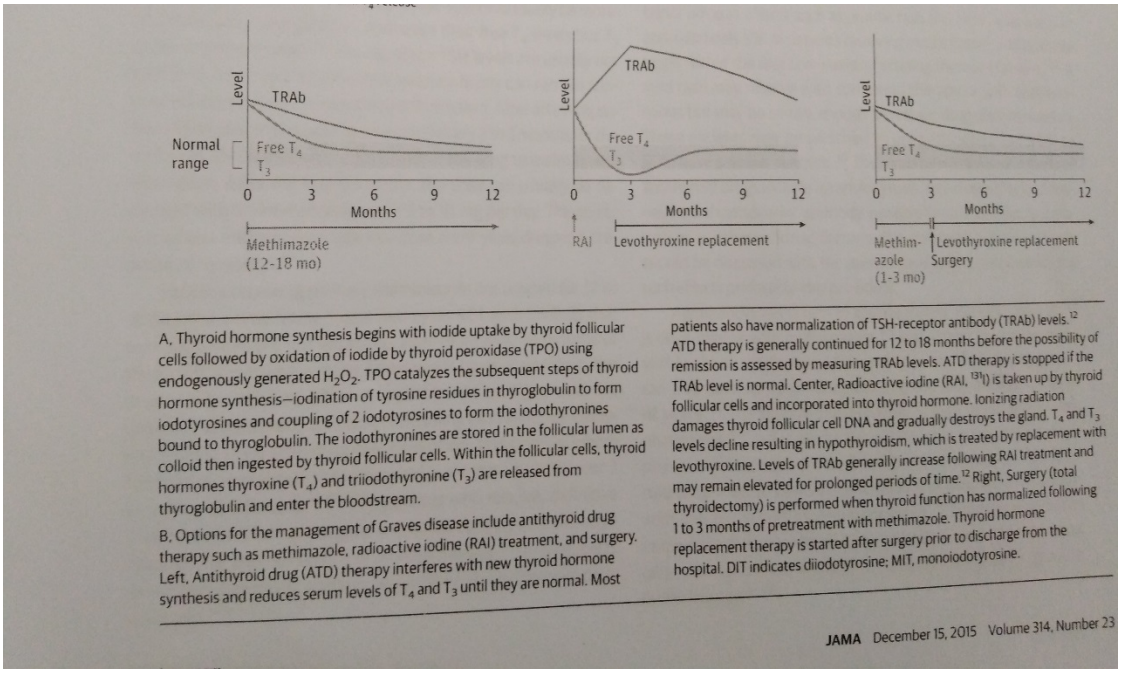
5.1. Medical Treatment

The mainstay of treatment for Graves' disease during pregnancy is medical. Surgery is reserved for failure or contra-indication of medical management. Radioactive iodine therapy is contraindicated during pregnancy for its teratogenicity.

5.1.1. Pre-existing GD (Pre-pregnancy)

TRAb may remain high in patients who received ablative therapy before pregnancy (RAI). They cross the placenta and cause foetal hyperthyroidism. Therefore patients who had undergone pre-pregnancy ablative therapy should have serum levels of TRAb measured in early pregnancy. If elevated "Block –and Replace" therapy is instituted whereby high doses of ATD (methimazole/carbimazole) are given, based on the immune-suppressant effect of these ATD and are transplacetally transferred to the foetus while the mother receives Levothyroxine to remain eathyroid [1, 5].

Figure 3: Effects of treatment modalities on serum T4 and TRAb levels



A, Thyroid hormone synthesis begins with iodide uptake by thyroid follicular cells followed by oxidation of iodide by thyroid peroxidase (TPO) using endogenously generated H_2O_2. TPO catalyzes the subsequent steps of thyroid hormone synthesis—iodination of tyrosine residues in thyroglobulin to form iodotyrosines and coupling of 2 iodotyrosines to form the iodothyronines bound to thyroglobulin. The iodothyronines are stored in the follicular lumen as colloid then ingested by thyroid follicular cells. Within the follicular cells, thyroid hormones thyroxine (T_4) and triiodothyronine (T_3) are released from thyroglobulin and enter the bloodstream.

B, Options for the management of Graves disease include antithyroid drug therapy such as methimazole, radioactive iodine (RAI) treatment, and surgery. Left, Antithyroid drug (ATD) therapy interferes with new thyroid hormone synthesis and reduces serum levels of T_4 and T_3 until they are normal. Most patients also have normalization of TSH-receptor antibody (TRAb) levels.[12] ATD therapy is generally continued for 12 to 18 months before the possibility of remission is assessed by measuring TRAb levels. ATD therapy is stopped if the TRAb level is normal. Center, Radioactive iodine (RAI, ^{131}I) is taken up by thyroid follicular cells and incorporated into thyroid hormone. Ionizing radiation damages thyroid follicular cell DNA and gradually destroys the gland. T_4 and T_3 levels decline resulting in hypothyroidism, which is treated by replacement with levothyroxine. Levels of TRAb generally increase following RAI treatment and may remain elevated for prolonged periods of time.[12] Right, Surgery (total thyroidectomy) is performed when thyroid function has normalized following 1 to 3 months of pretreatment with methimazole. Thyroid hormone replacement therapy is started after surgery prior to discharge from the hospital. DIT indicates diiodotyrosine; MIT, monoiodotyrosine.

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5.1.2. ATD therapy during pregnancy

5.1.2.1.First trimester: Period of organogenesis (particularly week 6 to 10).

Propylthiouracil (PTU) is the drug of choice as it is not associated with foetal defects seen with methimazole/carbimazole, which according the large Japanese and Denish study are seen in 1/30 pregnancies [1]

5.1.2.2. Second trimester until delivery: However, because of its associated complications: liver failure and agranulocytosis from second trimester until delivery treatment should be switched to methimazole/carbimazole [1,2,3,6].

5.1.3. Treatment-related foetal complications

Methimazole and its precursor- carbimazole, are associated with embryopathy/birth defects - when administered during week 6 to 10 of pregnancy – which is the period of organogenesis. ATD related birth defects may affect 1 in 30 pregnancies exposed to the drug during 6-10 weeks of gestation.

5.1.3.1.Foetal/Neonatal hyperthyroidism

High levels of maternal TRAb cross the placenta and cause neonatal GD. Therefore it is advocated that TRAb should be measured early in the third trimester when levels are expected to be at their lowest. Also in hypothyroid pregnant women treated with RAI pre-pregnancy- as the TRAb may persist in the maternal blood, cross the placenta and cause neonatal thyrotoxicosis [3]. ATD used to treat maternal disease cross the placenta, and therefore treatment of the mother and that of the foetus takes place simultaneously [1].

5.1.3.2.Foetal/Neonatal hypothyroidism

All ATD cross the placenta and tend to over-treat the foetus when the mother becomes euthyroid cause neonatal hypothyroidism [1].

To avoid neonatal hypothyroidism it is advocated that the ATD dose should be adjusted down to keep T4 levels at the upper limit of the reference range and the TSH below the reference range [1].

If the mother's TRAb become negative ATD therapy may be withdrawn; bearing in mind the high incidence of relapse post-partum.

Block + Replacement therapy (ATD + Levothyroxine) should not be used in pregnancy except in isolated foetal hyperthyroidism that may develop in women who previously received ablative therapy and whose TRAb remain high, cross the placenta and cause foetal hyperthyroidism [1]

5.2. Surgical treatment

There is agreement among most studies that surgery is rarely indicated for GD during pregnancy [1, 6, 4]. It has been reported to have an increased risk of spontaneous abortion and preterm labour [6]. It (surgery) is a last resort treatment strategy in patients who have severe adverse reactions to ATD therapy, persistently high doses of ATD are required to sustain control, non-compliance with therapy and therefore uncontrolled hyperthyroidism [6, 4], and a large goitre that requires high doses of ATD therapy [6].

5.2.1. Timing for Surgery

The optimum timing for surgery is during the second trimester when organogenesis is complete, and the risk of spontaneous abortion is low because the uterus is resistant to stimulating events [6, 4].

5.2.2. Ideal surgical option: Total thyroidectomy (TT) vs Subtotal thyroidectomy (TT)

Various systematic reviews - without supporting evidence -have recommended ST as the procedure of choice when surgery is indicated during pregnancy [4, 6]. This might have been based on the increased risk of RLN palsy and hypoparathyroidism previously associated with TT. However. Level I and II evidence in the general population has demonstrated no significant difference between TT and ST in terms of RLN palsy, transient and permanent hypo-parathyroidism. Hypothyroidism is inevitable with TT and there is 70% risk with ST. Therefore, performing ST with the aim of producing euthyroidism is unpredictable; and that follow-up on post TT and ST patients demonstrated no persistence or recurrence of the disease in the former group and 7.9% recurrence or persistence in the latter [7].

These may be transpolated to pregnant women. The surgical option may depend on patient and the surgeon's preference, given that risk of RLN injury is almost equal in both procedures and that the patient will accept life-long hypothyroidism (TT group) vs 30% chance of euthyroidism (ST group); and the risk of 7.9% recurrence/persistence with ST group.

5.3. Pre-thyroidectomy preparation: Achieving Euthyroid state

To avoid thyroid storm perioperatively, the patient should be rendered euthyroid before surgery. This should be achieve by ATD (PTU) 1-3 weeks pre-operatively. Potassium iodide (Lugol's solution) should be given 10 days before surgery. It reduces thyroid gland's vascularity and thereby reducing intra-operative blood loss. In addition, it has inhibitory effect on thyroid hormone synthesis [3, 4]. Patients with severe thyrotoxicosis, not responding to ATD or intolerant of ATD requiring urgent surgery can be prepared with Beta-Blockers, Potassium iodide, dexamethasone and cholestyramine has been recommended [3].

6. Monitoring of women treated for GD during pregnancy and postpartum [3].

- Monthly measurement of thyroid hormone levels throughout pregnancy.
- ATD to be adjusted down to achieve T4 levels at upper limit of reference range with mildly suppressed TSH levels to avoid neonatal hypothyroidism.
- In 30 to 50% of pregnant women amelioration of autoimmunity occurs during the second or third trimester or and therefore ATD therapy may be discontinued.
- Thyroid function testing should be monitored for every 2 to 3 months for 1 year post- partum as autoimmunity may recur and relapse of GD.

7. CONCLUSION

Graves' disease is the most common cause of hyperthyroidism during pregnancy. Its diagnosis can be complicated by relative thyromegally of pregnancy and hCG hormone levels that stimulate TSH receptors. High levels of TRAb are diagnostic of the disease. Untreated GD has adverse outcome for both the mother and the foetus. ATD therapy is the treatment of choice; with PTU being a drug of choice during the first trimester and methimazole/carbimazole during second and third trimester. During second and third trimester symptoms of the disease may ameliorate due to immune suppressant effect of pregnancy during which ATD therapy may be discontinued.

RAI therapy is contraindicated during pregnancy; while surgery may be done after the first trimester when indicated.

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Management of Phaeochromocytomas in Pregnancy

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Introduction

Phaeochromocystomas and functional paragangliomas (PGL's) are rare but dangerous catecholamine secreting tumours arising from chromaffin tissue. The majority (80 – 90%) of these tumours arise in the adrenal medulla (phaeochromocytomas) with the remaining tumours (PGL) located anywhere along the sympathetic chain.[1] While the presentation and management are similar, there are some differences. Phaeochromocytomas secrete both adrenaline and noreadrenaline whereas PGL's usually secrete only noreadrenaline and are more likely to be malignant and associated with inherited genetic disorders. [2]

For purposes of this discussion, phaeochromocytoma will be used as an overarching term for both types of tumours as their presentation and management in pregnancy are largely similar, though patients with paragangliomas may have better outcomes. [2]

Phaeochromocytoma is a rare disorder representing only 0.2% of all hypertensive patients. They usually present between the ages of 30 and 50 and younger age is more often associated with a familial syndrome. The commonest inherited genetic disorders associated with phaeochromocystomas are Von Hippel Lindau Syndrome, MEN 2a and b and Neurofibromatosis but there are a number of other germline mutations in the succinate dehydrogenase genes SDHA, SDHB, SDHC, SDHD and SDHAF2 that have also been identified.[3]

Presentation of phaeochromocytoma in pregnancy is rare but often dramatic with potentially fatal outcomes for both mother and foetus. Early recognition is not easy, as between 5 and 10% of pregnant women are hypertensive, either with pre-existing hypertension or pregnancy associated hypertension and phaeochromocytoma may be misdiagnosed as one of these conditions.[3] As phaeochromocytomas only occur in 0.002 and 0.007 pregnancies [4] (2-7/100 000 pregnancies), it is likely that most midwives and obstetricians will not manage a patient with this condition in their lifetime. However, an awareness and pre delivery diagnosis of a phaeochromocytoma has the potential to significantly reduce combined maternal and foetal mortality from approximately 50% to between 5 – 15%.[3]

Management guidelines for phaeochromocytomas are based on case reports, small series and expert opinion. Reviews on the subject are usually include between 2 and 6 case reports followed by a literature review of under 100 cases.

In the two South Africa studies published on phaeochromocytoma from WITS[5] and UKZN[6], the number of pregnant patients in their series were 9/54 and 3/35 respectively. This may indicate that, while phaeochromocytomas are rare, in a context where screening and early detection is not common, presentation in pregnancy represents a larger than usual proportion of all patients diagnosed with phaeochromocytomas.

Clinical Presentation in Pregnancy

As hypertension in pregnancy is relatively common and phaeochromocytomas rare, patients with this condition are often misdiagnosed with gestational hypertension or pre-eclampsia. The clinical presentation of phaeochromocytomas in pregnant patients mirrors that of non-pregnant patients

with episodic or sustained hypertension and the classic triad of headaches, diaphoresis (abnormal whole body sweating) and palpitations.[7] Unlike gestational hypertension, phaeochromoctyomas may present before 20 weeks, though the majority present in the second and third trimester. Between 75 and 80% of patients present at delivery either during labour or caesarean section. While pre-eclampsia is usually associated with oedema and proteinuria, these are usually absent in phaeochromocytomas.

Clinical clues that the hypertension is caused by a phaeochromocytoma include:

- The triad of headache, diaphoresis and palpitations
- Episodes of postural hypertension (up to 50% of pregnant patients will have episodes of hypertension hypotension)
- The paroxysmal, episodic nature of the hypertension
- Associated hyperglycaemia or new onset gestational diabetes
- Associated cardiomyopathy
- Increasing severity of the clinical picture with advancing gestational age due to increasing pressure of the growing uterus on the tumour, foetal movements and contractions. [7]

If not optimally controlled or undiagnosed, pregnant patients may present in hypertensive crisis with acute pulmonary oedema, malignant arrhythmias, myocardial ischemia or infarction, aortic dissection, cardiac failure and hemodynamic collapse – all well-recognized complications of pheochromocytomas.[8]

Diagnosis of Phaeochromocytoma in Pregnancy

Catecholamine release is not increased in pregnancy so measurement of 24 hour urine or, where available, plasma metanephrines and noremetanephrines remains reliable for diagnosis. As with non-pregnant patients, a level of 3 – 4 x normal is diagnostic of the condition. For location of the tumour, ultrasound and MRI are the diagnostic modalities of choice. A few case reports have utilised CT in the third trimester but this is generally not recommended due to the high radiation dose to the foetus. Nuclear medicine studies such as MIBG or Dota-scans are contraindicated in pregnancy to avoid radiation exposure to the growing foetus.[8]

As it is now known that up to 30% of patients with phaeochromocytoma will have an inherited genetic disorder and pregnant patients represent a younger cohort of patients, genetic testing is recommended for all patients. PTH and calcitonin levels should also be measured to exclude concomitant hyperparathyroidism and medullary carcinoma as occurs in MEN2.[8]

Management:

Management of phaeochromocytoma in pregnancy depends on the timing of diagnosis. There are three possible scenarios:

- Early antenatal diagnosis - before 24 weeks gestation (35-40%)
- Late antenatal diagnosis - after 24 weeks gestation (35-40%)
- Intrapartum diagnosis during labour or caesarean section (25%)

With this in mind, management of phaeochromocytoma in pregnancy includes:

a) Medical management
b) Timing of surgery for phaeochromocytoma excision
c) Timing and mode of delivery

a) Medical Management:

All patients require treatment with alpha blockers either as medical management in pregnancy if the diagnosis is after 24 weeks or as pre-treatment if surgery is planned during pregnancy. Phenoxybenzamine and doxazosin are the commonest drugs used for alpha blockade with doxazosin being more widely available in South Africa. Both drugs act as vasodilators.

It is important to note that while catecholamines cross the placental, the foetus is protected from these hormones through placental transporters which remove catecholamines from the foetal circulation. This is thought to protect the growing foetus from catecholamine surges during labour. However, the uteroplacental circulation has no intrinsic autoregulation and is therefore affected by surges in maternal blood pressure and the intense vasoconstriction that accompanies phaeochromocytoma episodes. This vasoconstriction places the foetus at risk of hypoperfusion, hypoxia and placental abruption. [7]

Alpha blockade is therefore critical to the management of this condition in pregnancy. Target blood pressure in non-pregnant patients are recommended to be BP <130/80 sitting with standing blood pressure of >90. There is no recommended level for pregnant patients though caution must be exercised as low blood pressures are associated with IUGR. For pregnant patients with hypertension, BP targets are adjusted upwards to >150/100 mmHg and, in the presence of end organ damage, to >140/90. A careful balance between adequate alpha blockade to prevent vasoconstriction of the uteroplacental vasculature and preventing hypotension and particularly profound postural hypotension is necessary.[3]

A consequence of long-term vasoconstriction is significant intravascular volume depletion. Alpha blockage must therefore be accompanied by intravascular volume replacement either with IVI fluids or increased oral intact. Patients are also placed on a high sodium diet to encourage full volume replacement. Adequate rehydration is particularly important during delivery and surgery and in the post-operative phase where resistant hypotension is easier to manage in a volume replete patient.

Both phenoxybenzamine and doxazosin cross the placental and are classified as Class C drugs in pregnancy (safety not established). Phenoxybenzamine is still the commonest drug used in case reports but has been associated with neonatal hypotension and respiratory depression as the effects can last up to seven days after dosage. Doxazosin transfer to the foetus is reported as less that phenoxybenzamine in at least one case report of measured cord blood and no incidents of foetal cardiovascular or respiratory depression have been reported. It is therefore being used more often with good neonatal outcomes thus far. Transfer into breast milk is minimal (1% for phenoxybenzamine and undetectable in doxazosin) so breastfeeding is not contraindicated though the neonate should be monitored carefully in the first 48 – 72 hours post-delivery. [9]

B Blockers are not routinely required in the medical pre-treatment of phaeochromocytomas and are usually only commenced in the presence of persistent tachycardia after adequate alpha blockade and rehydration. In pregnancy, B-blockers are associated with a significant risk of intra uterine growth restriction. Calcium channel blockers may be considered as an alternative.[9]

Caution should be exercised with use of other drugs commonly utilised in pregnancy as they may induce a hypertensive crisis. For example, corticosteroids, commonly used to enhance foetal lung maturation in preterm labour) have been associated with inducing a hypertensive crisis. Caution should also be used when prescribing opioids, such as morphine and pethidine, anti-emetics such as metoclopramide and anaesthetics agents such as thiopental, ketamine and ephedrine.[10]

b) Timing and method of Tumour Resection

Surgical excision of the tumour is the definitive treatment for this condition. In pregnancy, the timing of surgery is critical. If the phaeochromocytoma is diagnosed before 24 weeks of pregnancy, it is recommended that patients be prepared for 10-14 days with volume replacement and alpha blockade and then surgery performed in the second trimester. For tumours diagnosed after 24 weeks, medical management is recommended until the time of delivery. Patients diagnosed intrapartum (during labour or caesarian section) are at very high risk of hypertensive crisis and management is usually aimed at delivering the baby and stabilising the mother before attempting resection of the tumour.

Laparoscopy remains the recommended surgical approach for tumours 6 – 7 cm in size. This remains possible in the second trimester though in late second trimester, the size of the uterus may result in technical difficulties. The transperitoneal approach is preferred as it is not advisable to place a pregnant patient prone for a retroperitoneal approach. The position of patients in the near lateral position is recommended, though for a left sided tumour, after 20 weeks, compression of the IVC in the right lateral position may compromise foetal circulation. If diagnosed late in pregnancy, tumour resection may be planned simultaneously with caesarian section either via an open approach or with separate incisions for a laparoscopic resection. [11]

c) Timing and Mode of Delivery

If diagnosed early (before 24 weeks), once phaeochromocytoma resection has taken place, mode and timing of delivery and normal vaginal delivery vs Caesarian section are dependent primarily on obstetric concerns. Ongoing careful monitoring as for a high-risk pregnancy is still necessary as there is a possibility of synchronous or metastatic functional tumours not identified and resected at the tumour resection. At least two case reports document adverse outcomes for mother and foetus due to secondary functional tumours. [11]

For patients diagnosed after 24 weeks, medical management is used until foetal viability. Timing of delivery then depends on ongoing maternal and foetal wellbeing. Caesarian section has generally been recommended as the preferred mode of delivery as it can be accurately timed and represents a more controlled environment. It is, however, a more invasive procedure with the risks of haemorrhage, increased drug administration and the effects of spinal or general anaesthesia. There are therefore a few recent case reports of normal vaginal delivery in mulitiparous women. [12]

After delivery of the foetus, tumour resection may be done concurrently during the same anaesthetic if the patient is stable, after 3 days or within 2 – 6 weeks. The decision making regarding this timing is highly individualised and dependent on the unique situation of each patient as well as the context tumour resection and delayed (2 – 6 weeks) have documented safe and successful outcomes.[12]

The third scenario of diagnosis during labour or caesarian section (approximately 25% of patients), represents the most dangerous clinical scenario. In these patients, epidural and spinal anaesthesia, administered in an untreated phaeochromocytoma patient, may result in severe, refractory hypotension and highly labile blood pressure with up to 50% mortality for either mother or foetus or both. Survival depends on recognition of a potential phaeochromocytoma crisis, use of high doses of epinephrine and vasopressin to treat hypotension, expedited delivery of the foetus and then

stabilisation of the mother in ICU with maximum organ support. A case report of peripartum arrest and successful resuscitation with intracardiac balloon pump and continuous dialysis has be published in the literature. [13]

Outcomes

A recent review published in 2013 in the BJS reviewed reported outcomes from 77 case reports published between 2000 and 2011[12]. In this group, overall maternal and foetal morality were 8 and 17% respectively. Of the 56 diagnosed antenatally, 27 (36%) were diagnosed before 24 weeks, 29 (38%) later in pregnancy and 21 (27%) during labour or caesarean section. Of the early diagnosis group, 18 had tumour resection performed in the second trimester and 8 after delivery, half laparoscopic and half open (there was one first trimester miscarriage). In the later diagnosis group, 17 patients underwent phaeochromocytoma resection concurrent with delivery and 18 in the post-partum period. The majority of women who delivered with a phaeochromocytoma in situ had a caesarean section (15/18). For women diagnosed intrapartum, all underwent phaeochromoctyoma resection between 2 and 8 weeks post-partum. In this high risk group, only in 12/21 cases did both mother and baby survive.

Conclusion

Phaeochromocytoma in pregnancy is rare and may be missed due to confusion with other more common causes of gestational hypertension. Distinguishing features of hypertension associated with phaeochromocytoma in pregnancy is the classic triad of sweating, headache and palpations and the high rate of postural hypertension. Biochemical diagnosis is the same as in non-pregnant patients but imaging must avoid radiation exposure thus ultrasound and MRI are preferred. As these patients are younger, increased awareness of the risk of inherited genetic disorders and possibility of malignant or multiple tumours is important. Management depends on the timing of diagnosis and careful alpha blockade is the mainstay of medical treatment. Resection of the phaeochromocytoma is in the second trimester for the early diagnosis group or concurrent or post-partum in the late diagnosis group. Delivery is usually by caesarean section but in certain circumstances normal vaginal delivery can be attempted in multiparous women. Failure to diagnose phaeochromocytoma antenatally results in a high foetal and maternal mortality. Overall management of this diagnosis requires a multidisplinary team of specialists including surgeons, endocrinologists, anaesthetists and obstetricians.

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Challenges of Breast Cancer During Pregnancy

Sarah Nietz

Epidemiology

The term pregnancy-associated breast cancer (PABC) includes breast cancer during pregnancy (BCP) and those that occur in the first year postpartum or during lactation. It is important to distinguish these for both management and prognosis.

BCP is the most common invasive cancer during pregnancy with an estimated incidence of 6.5/100.000 live births. Although causes are multifactorial an increased maternal age of >35 years of age has been clearly identified as a contributing factor. Therefore, numbers are expected to further rise given the increasing number of women who opt to delay child bearing.

Presentation

Many women will present with lumps during pregnancy and the majority are benign. Health care professionals need to have a high index of suspicion as patients do not fit the typical breast cancer patient profile. We are also taught that pregnancies should be protective when in fact pregnancy has a bidirectional effect on breast cancer risk: women are at an increased risk following the first five years after pregnancy and the protective effect only sets in decades later.

Unfortunately, missed diagnoses and delays are common and pregnant women tend to present with larger tumours, more lymph node involvement and more distant metastases compared to women who are not pregnant.

Diagnosis

Early detection is critical and all women should have a thorough breast examination at their first antenatal visit and be encouraged to present immediately should they develop a lump. Women at high-risk (>35) should probably have a formal breast ultrasound and follow-up but there are no exact protocols available to date and resources are too limited in our setting. It is undisputed though that once a women presents with a lump which has

persisted for at least two weeks an urgent investigation is necessary. Following history and examination, the first step is an ultrasound and if findings are suspicious this has to be followed by a bilateral mammogram and core biopsy. Ultrasound has a similar sensitivity in non-pregnant women and mammogram is required to complement finding. A mammogram is completely safe with abdominal shielding and has an average fetal radiation exposure of 0.4 mrad. With regards to histopathological confirmation a core biopsy is preferred over fine needle aspiration as these can lead to overdiagnoses due to the proliferative state of the breast during pregnancy. Further description and immunohistochemistry does not differ from that in non-pregnant women. Tumours tend to be higher grade, commonly show lymphovascular invasion and may be hormone receptor-negative. Overall, tumour biology among pregnant women appears to be similar to age-matched non-pregnant women so it is critical to understand that age appears to determine biologic behaviour rather than the pregnancy itself.

Staging

Some modifications may be required to optimize fetal safety but staging procedures, including radiology, should always be performed if they are going to impact therapeutic decision and clinical practice. Deterministic radiation effects are only seen on fetal threshold doses of 0.1-0.2 Gy which is much higher than conventional imaging doses. Before commencing any staging procedures and treatment, I would strongly recommend a baseline obstetric evaluation. Chest X-ray (with abdominal shielding), liver ultrasound and baseline bloods are essential staging tests and can be performed safely. CT scans and bone scans should be avoided where possible and a skeletal MRI is the modality of choice to assess for bone metastases.

Management

The simple and golden rule is to follow the standards that are applied in non-pregnant women as closely possible. Data and level of evidence is limited by numbers and subject matter and international registries and cohort studies offer the best available guidance. Management of these patients is highly complex both from a clinical as well as a psychological perspective. They should only be treated by experienced subspecialists within

a multidisciplinary team and need to be expanded to include obstetricians and neonatologists. Most patients will benefit from genetic counseling and the need for psychological support is obvious.

All breast cancer patients should be treated with an individualized approach. I personally always consider three main factors which include tumour biology, patient preference and stage and add a fourth factor of gestational age in pregnant women. Therapeutic options are shown in figure 1.

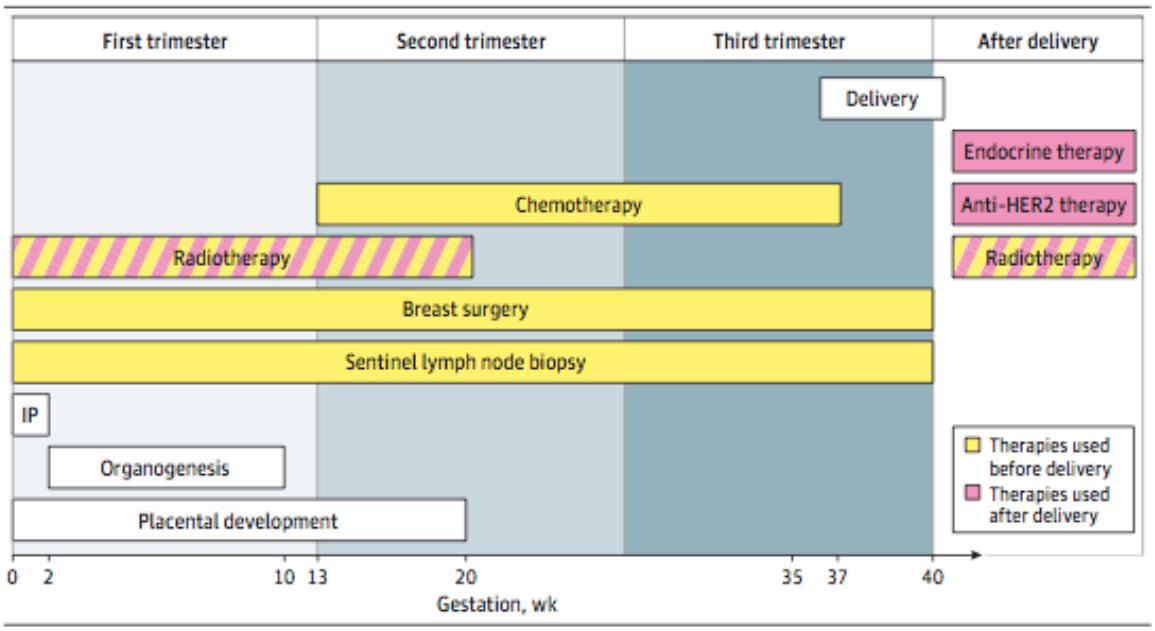

Figure 1: Therapeutic options (Loibl et al(1)*)*

Termination

Termination of pregnancy does not improve patient outcome and appropriate treatment is possible during pregnancy. It is a personal choice and women who opt for termination have a lower socio-economic standing, have less stable support structures and more advanced disease. The fear of the child growing up without a mother or any other caregiver seems to be the most influential factor.

Surgery

Surgery can be performed throughout pregnancy. Breast surgery does not have a higher rate of fetal loss in the first trimester compared to spontaneous miscarriage rates.

Breast conserving surgery is an option and has equal survival to mastectomy. Concerns over delays to radiotherapy are valid but can be overcome with appropriate treatment sequencing as the majority of these patients will require adjuvant chemotherapy. Reconstruction can be challenging and tissue expanders are preferred in patients undergoing an immediate reconstruction. Autologous reconstruction is best deferred to at least six months postpartum. For all surgeries, drains should be placed in all patients to address potentially increased postoperative drainage.

With regards to the axilla, sentinel node biopsy is safe and accurate. Radiocolloid is the preferred tracer with a very low fetal exposure rate whereas blue dye should be avoided due to its anaphylactic potential and unknown teratogenicity.

Chemotherapy

Chemotherapy is indicated in the majority of cases due to tumour biology and more advanced stage at presentation. Although there is an increased risk of miscarriage and malformations in the first trimester, fetal malformation rates drop to <4% after organogenesis in the second and third trimester. Eyes, CNS, genitals and haematopoietic system remain vulnerable to chemotherapy after organogenesis and most experts recommend to wait until 14 weeks of gestation before initiating cytotoxic treatment.

Regimens follow standard regimens in non-pregnant women and are most commonly based on anthracyclines and taxanes. There is limited data but platinum salts and dose-dense regimens appear to be safe.

Intrauterine growth retardation is a concern and regular antenatal scans are mandatory. Treatment should be completed or interrupted after 35 weeks or within three weeks of delivery and can be commenced immediately after an uncomplicated vaginal delivery and one week post uncomplicated caesarean section.

Tamoxifen

Treatment is deferred to postpartum as it may cause genital and craniofacial malformations.

Trastuzumab

HER-2 is expressed in the fetal renal epithelium and administration during pregnancy may cause oligohydramnios, renal failure and fetal death. It is therefore also deferred to the postpartum period.

Radiation Therapy

Generally deferred to the postpartum period. Some European centers do radiate in early pregnancy when the fetus is below the pelvic brim.

Sequencing of therapy

Options of treatment during pregnancy include surgery and chemotherapy with other modalities added postpartum in our setting. The choice of first modality depends on stage, biology and gestational age. It is critical not to delay therapy and to deliver all required treatments in a safe sequence.

Prognosis

Literature has shown poorer outcomes but these are most likely related to more advanced presentation and omission or delays of treatment over concerns of fetal outcome. Direct pregnancy-related effects such as elevated hormone levels, or vascularization and inflammatory cell recruitment have not been proven. However, postpartum breast cancer occurring during lactation or in the first year postpartum has a significantly poorer outcome and therefore should be seen as a separate subgroup.

Take home message

Treatment is possible and safe during pregnancy but requires modified staging and treatment sequencing and should take place in subspecialized multidisciplinary teams. Treatment omissions or delays must be avoided.

Recommended reading

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Breast cancer in the elderly

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Introduction

Breast cancer [BC] is the most common cancer in women world-wide, including countries like the US and South Africa [SA], though it rates second to basal cell carcinoma and cervical cancer [CA] in White and Black women respectively in SA.

The incidence of BC increases with age. The average age at diagnosis is 61years, it is younger for Black American women [59yrs] and is 63yrs in Whites. The majority of deaths occur after the age of 65yrs, for 2017, 70% of the estimated death was in patients older than 60yrs.The same age-group[s] constituted 58% of estimated newly diagnosed patients for 2017.

Definition of the elderly

Besides the lack of consensus on the cut-off age for defining the elderly patient [≥65yrs or ≥70yrs], the is also a controversy concerning the use of the term “elderly”, with some suggesting the use of “older” or “geriatric” patient as being more appropriate for this age-group.

Some suggest that the term “elderly” is ageist, thus promoting ageism, which is similar to racism or sexism and is defined as prejudice and discrimination against a particular age-group, in this case, promoting less than optimal treatment and care, with negative impact on survival.

Because of the heterogeneity of this group of patients in terms of co-morbidity, life expectancy, functional status, cognitive function and “frailty”, the is a move towards using this biological or physiological parameters to identify these patients rather than using chronological age, hence the endorsement of the comprehensive geriatric assessment [CGA] tools in the management of this group of patients.

Facts to consider

1 BC is a disease associated with ageing.

2 Almost 50% of new BC cases are diagnosed annually in women ≥65yrs in the USA.

3 Major improvements in public health and medical care have resulted in dramatic increases in longevity/life expectancy especially in developed countries. The segment of population ≥65yrs in the USA is increasing rapidly.

4 Life expectancy in the USA in in 2017 was 81.1yrs in females 76.1yrs in males [average 78.6yrs] In Africa in 2018 was 64yrs in females and in 61yrs Globally in 2018 74yrs in females and 70yrs in males.

5 Breast cancer in older women has more favorable biological characteristics [receptor positive, HER 2 negative] compared to young patients.

6 Outcomes of BC in younger patients have shown substantial improvements as a result of advances in treatment and screening, but not in the elderly.
BC specific mortality generally decreased by 2.5% per year in women $\leq$75yrs, including younger women vs 1.1% in those $\geq$75yrs between 1990 and 2007.
2000-2004 decreased by 13%, 17% [25-64yrs]vs 6%[>65yrs]

7 BC patients >70yrs are usually excluded from current screening strategies leading to late diagnosis and advanced disease.

8 Elderly patients are less likely to be treated according to guidelines vs younger patients. Why ?

9 Lack of evidence due to under-representation in randomized controlled trials [RCT], testing efficacy and safety of drugs [concerns about co-morbidity and drug toxicity vs tolerance], thus leading to under-treatment and poorer outcome.

Biological changes associated with ageing

1 **Changes in tumorigenesis and host defenses**

Increased risk of CA may be attributed to:

a. Slow accruing damage to DNA-carcinogenic chemicals
-radiation exposure
-viruses
-reactive 02 species

b. Progressive decline in host defenses against tumor growth
Carcinogenesis is a time-consuming process, hence the incidence of many types of cancer increasing with age

2 **Specific age related pharmacokinetics**

a. Volume of distribution shrinkage due to:
- Decrease in total body water
- Anaemia, mainly due to chronic disease, affects drugs that binds to erythrocytes eg anthracyclines.
- Hypoproteinemia due to inadequate synthesis, excessive renal loss of albumin and other carrier proteins, affect drugs that bind to albumin.

b. Decrease in glomerular filtration rate due to:
- Gradual loss of nephrons, affect drugs with clearance depending heavily on renal excretion
  Methotrexate, bleomycin, carboplatin

c. Decrease in hepatic excretion

3 **Changes in pharmacodynamics**

Changes resulting in increase in anti-tumour activity

- Express a multidrug resistance [MDR] gene
  Loss of apoptosis
- Low blood circulation leading to tumour anoxia
  Tumoricidal effects of both chemotherapy and radiotherapy are best in well oxygenated and rapidly proliferating cells.

4 **Changes in cancer activity**

- Ageing leading to decline in tumour aggressiveness associated with decline in chemo effectiveness
- Tumour indolence due to natural selection
- Thus tumour aggressiveness at younger age.

5 **Disease factors**

- Cancer diagnosed at more advanced stage due to reluctance in seeking treatment or due to bias against aggressive treatment by physician

6 **Patient factors**

- Clinical work-up and comprehensive geriatric assessment should document potential risk factors that could affect outcome
- Decline in physiological function: CVS, renal, hepatic, hematopoietic reserve.

Screening for BC in the elderly

Screening has a clear long-term beneficial effect with a 20% reduction in BC associated mortality. A meta-analysis of mammogram screening trials showed a BC mortality benefit for all age-groups, yet screening programs from many countries exclude women $\geq$70yrs.

Table 1. Recommendations for Breast Cancer Screening in Average-Risk Women ⇦

	American College of Obstetricians and Gynecologists	U.S. Preventive Services Task Force	American Cancer Society	National Comprehensive Cancer Network
Clinical breast examination	May be offered* every 1–3 years for women aged 25–39 years and annually for women 40 years and older.	Insufficient evidence to recommend for or against.†	Does not recommend‡	Recommend every 1–3 years for women aged 25–39 years. Recommend annually for women 40 years and older.
Mammography initiation age	Offer starting at age 40 years.§ Initiate at ages 40–49 years after counseling, if patient desires. Recommend by no later than age 50 years if patient has not already initiated.	Recommend at age 50 years.‖ Age 40–49 years: The decision to start screening mammography in women before age 50 years should be an individual one.¶	Offer at ages 40–45 years.¶ Recommend at age 45 years.#	Recommend at age 40 years.
Mammography screening interval	Annual or biennial§	Biennial‖	Annual for women aged 40–54 years‡ Biennial with the option to continue annual screening for women 55 years or older‡	Annual
Mammography stop age	Continue until age 75 years. Beyond age 75 years, the decision to discontinue should be based on a shared decision-making process that includes a discussion of the woman's health status and longevity.	The current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women 75 years and older.†	When life expectancy is less than 10 years‡	When severe comorbidities limit life expectancy to 10 years or less

In SA, because of lack of resources and infrastructure in the public health care, screening mammography is only for identified high risk patients.

- Women ≥40yrs, attending Primary Health Care Clinic-provider Initiated Screening Clinical Breast Examination [PI-SCBE] biannually + risk assessment.
- Referred for mammogram if symptomatic or if increased risk for BC [screening]

  Moderate to high risk

  Yearly mammogram ages 40-50

  Biennial mammogram ≥ 50

- If <40yrs with moderate to high risk:

  Annual PI-CBE from 10yrs younger than the age of onset of the youngest patient in the family.

  Annual MRI where available

  Guidelines according to National Department of Health June 2017

Clinical assessment and work-up

- Triple assessment.
- Comprehensive geriatric assessment [In preparation for surgery, chemotherapy and radiotherapy]

Key elements of comprehensive geriatric assessment

Medical assessment
Problem list
Comorbidities
Medications
Nutritional assessment
Functional assessment
Basic activities of daily living
Instrumental activities of daily living
Gait and balance assessment
Exercise/activity assessment
Psychological assessment
Cognitive status
Assessment of mood
Social assessment
Informal social support
Environmental assessment
Care resource eligibility/financial assessment
Home safety
Access to transport facilities

Realm	Screening
Mental status (performance-based test)	Ask patient to remember 3 objects (e.g., tree, cat, ball) and ask them to recall them in a few minutes
Emotional status	Ask patient, "Do you often feel depressed or sad?"
Functional status	
Activities of daily living	Ask patient, "Can you get out of bed yourself?" "Can you dress yourself?"
Instrumental activities of daily living	Ask patient, "Can you make your own meals?" "Can you do your own shopping?"
"Timed up and go" test (performance-based test)	Individual is asked to get up from an armchair without using their arms, walk 10 feet forward briskly, turn around, walk back to the chair, and then sit down again; ≤ 10 seconds to complete test is considered normal.
Social support	Ask patient, "Who would be able to help you in case of illness or an emergency?"
Comorbidity	Evaluate for the presence of following conditions from the review of systems: congestive heart failure; coronary artery disease; valvular heart disease; chronic lung disease; cardiovascular disease; peripheral neuropathy; chronic renal insufficiency; hypertension; diabetes; coexisting malignancies; collagen vascular diseases; incapacitating arthritis
Nutrition	Weigh patient, measure height, body mass index, inquire about weight loss (unintentional loss of ≥ 10% of body weight in prior year; body mass index < 22 kg/m^2)
Polypharmacy	Review number and type of medications

The role of surgery

The gold-standard of treatment for early BC in all age-groups is surgery, unless the patient refuses or have limited life- expectancy.

A Cochrane meta-analysis concluded that primary therapy with tamoxifen alone was inferior to surgery.

Concerns in the elderly

- Fitness for anaesthesia and surgery
- Role of BCT vs mastectomy
- Role of SNLB and axillary dissection
- Recurrence and mortality rates

Surgical mortality rate in older women with BC is negligible [1%], was 0.5% in octogenarians with BC in a study of 5 390 patients (including other cancers ie colorectal cancer, endometrial, stomach etc) by Damhuis et al.

Body image and cosmesis is important as in younger women, therefore elderly women with early BC should be offered BCT with sentinel lymph node biopsy [SLNB], and adjuvant radiation, according to guidelines. Welsh et al, identified patients who were low risk, and ideal for omission of SLNB. These patients had G1 cTmi-T1c [<2cm] or G2 cT1mi-T1b tumours.

The recommendations of the Society for Surgical Oncology, in their “choosing wisely” guidelines in 2016, was not to do routine SLNB in Clinically node-negative women ≥ 70yrs, with early BC, with hormone receptor [HR] positive/HER2 negative invasive BC. Omission of SLNB in this group of patients does not result in increased loco-regional recurrence and does not impact on BC survival.

Tamarisa et al, from a NCDB review analysis [2004-2014], of T1-3,N0 ca patients who had BCT with or without lymph node evaluation suggested a selective approach to axillary staging in patients ≥ 70yrs.

The role of reconstructive surgery

Very few studies have addressed this issue.

The percentage of patients receiving reconstructive surgery decreased dramatically with age, from 53% -≤ 50yrs to 8.3%-≥65yrs. Other factors being low income group and African Americans.

The National Comprehensive Cancer Network [NCCN] Task Force 2008, recommended that that women of all age-groups should be of offered consultation with a reconstructive surgeon.

Further investigations needed to determine if unique risks exist for elder women who undergo reconstruction. There is also a suggestion of less complicated alternatives like contralateral breast reduction with implant reconstruction vs full breast reconstruction.

Prophylactic mastectomy

Studies reporting on trends of contralateral prophylactic mastectomy [CPM] In the US, concentrated in young patients. Marmor et al, in a [SEER] Population based study, reported an increase in rate of CPM from 1% to 3% from 2004 to 2014 for all patients treated with surgery among 261 281 patients ≥65yrs.Patients choice and life expectancy plays an important role in decision making.

Role of radiotherapy

- Adjuvant radiotherapy [RT] is recommended for women of all age groups according to guidelines.
- Its role in reducing the rates of loco-regional recurrence has been demonstrated in landmark trials like the NSABP-B04 [19%] and B06 [39.2%] for lumpectomy only vs 14.3% for lumpectomy and radiotherapy after 25 and 20 yrs follow up respectively. There was no survival benefit.
- The Early Breast Cancer Trialist collaborative Group [EBCTCG] in a meta-analysis of 17 studies that randomized women post BCT, to RT or no RT, the 10yr risk of locoer-regional recurrence was reduced by 15.7% and risk of BC death by 3.8%.

- The impact of RT on mortality is difficult to assess in the elderly.
- Over- all survival[OS] benefit has not been shown in RCTs but by NCDB analysis, probably due to RCT not being powered due to small numbers.
- A SEER analysis of 11 594 women aged ≥70yrs [1992-1997], showed that post mastectomy radiotherapy [PMRT] was associated with
  Improved survival for high risk BC [T3/4 N2/3], with a 5yr survival of 50%
- Cao et al studied 111 patients [2007-2013], ≥65yrs, with 1-3 positive LNs. There was improved distant disease free survival, recurrence free survival [RFS] and marginal OS only in tumors>5cm in size.
  He recommended that PMRT should not be compromised in all elderly patients with tumours >5cm.

RT after BCT in older woman

- In a CALGB 9343 trial, 636 women ≥70YRS with stage 1 ER positive tumours, post BCT, were randomized to RT+ tamoxifen vs tamoxifen only. After 5yrs, the only significant difference was in loco-regional recurrence,1% [RT + tam] vs 4% [tam only]
- PRIME 2 trial by Kunkler et al, studied women ≥65yrs, tumors ≤ 3cm, G1/2, ER pos, LN negative, with clear margins, randomized to whole breast irradiation [WBI] or no irradiation.
  5yr relapse rate was 1.3% vs 4.1% and 10-year relapse rate 2% vs 10%.
  No difference in survival.

Alternatives to WBI, suitable for the elderly

A. **Hypo-fractionation**

- Shortens the overall course of treatment.
- Most common schedule utilized in the US is the “Canadian regimen”
- 16 fractions of 2.66 Gy for a total of 42.56 Gy, no boost
- Limitations: body habitus
- Recommended by ASTRO “CHOOSING WISELY’’ guidelines
- Shortens period of radiation from 5-7 weeks to 3 weeks

B. **Accelerated partial breast irradiation [APBI]**

- Delivered twice daily for 5 consecutive days 6 hours apart
- Age important factor-elderly considered most suitable
- ASTRO: age ≥60 yrs ,T1 Pn0, ER pos, no lymphovascular invasion[LVI] negative margins [>2mm], unifocal / unicentric, no extensive intra-ductal component.
  Concern: Higher rate of side effects than WBI

RAPID Study

C. **Intra-operative radiotherapy [IORT]**

TARGIT Trial

Elliot trial>1300 patients ≤75yrs, 2,5cm tumour, 21Gy IORT

Tumour recurrence rate 4.4% IORT vs 0.4 WBI

D. **Gamma Pod Sterotactic Breast Radiotherapy and other ablative therapies.**

Summary

RT should be offered to elderly patients, according to tumour biology and stage, after considering/weighing risks [co-morbidities, toxicity, frailty, functional status, life expectancy] and benefits and also patient's choice.

Chemotherapy in the elderly

The benefit of adjuvant chemotherapy on DFS and OS vs surgery alone was established in land-mark trials by the Milan group and the NSABP [eg NSABP B13]. Adjuvant chemotherapy of choice should be anthracycline and or taxane based poly or combination regimen, as they have demonstrated survival benefit in a number of studies.

Little data exist on the benefit of chemotherapy in patients ≥70yrs due to underrepresentation in clinical trials.

A [CALGB]49907 Trial, randomized 633 women ≥65yrs to CMF, TC [docetaxel and cyclophosphamide] and capecitabine, concluded Adjuvant chemotherapy improves survival among elderly patients, though with greater toxicity.

Summary

- There is no upper age limit for utilization of chemotherapy.
- No chemotherapy drug is contra indicated in the elderly including cardiotoxic drugs [anthracyclines, taxanes, herceptin], provided cardiac function is optimal.
- Chemotherapy should not be with-held on the basis of chronological age, patients should be individualized according to functional status, co-morbidities, life expectancy etc.
- Prevention and management of chemotherapy induced toxicity: ECHO/MUGA Scan, FBC+ differential count, U&E + C, LFT.
  NB: Role of tools like www.adjuvant online.com, crash score for chemotherapy toxicity.

Role of genomic essays

- TAILORx Trial; Oncotype Dx [21 gene essay]
- MINDACT Trial; MamaPrint [70 gene essay]

Role of endocrine therapy

- Clear benefits in ER positive EBC.
- Most widely used form of adjuvant treatment for BC in the elderly.
- Majority of cases ER positive.
- Favourable toxicity profile [compared to chemotherapy] and effectiveness in improving disease free survival [adjuvant]
- Endometrial ca and thromboembolic phenomena [tamoxifen]
- Masculoskeletal pain, accelerated bone loss [osteoporosis, osteopenia, osteonecrosis, risk of fractures (aromatase inhibitors).
- Bone density studies to be done before.
- Role of bisphosphonates [antiresorptive therapy]

Clinical trials of neoadjuvant endocrine therapy in elderly patients with breast cancer.

Study	Design	Number of patients	Treatment	Primary end point	Results	
PROACT [5]	Phase 3, randomized, double-blind	451	Anastrozole 1 mg versus tamoxifen 20 mg	OR	39.5 versus 35.4%; odds ratio 1.24	0.29
IMPACT [6]	Phase 3, randomized, double-blinded	330	Anastrozole 1 mg versus tamoxifen 20 mg versus anastrozole 1 mg + tamoxifen 20 mg	OR	37 versus 36 versus 39%	
Z1031 [7]	Phase 2, randomized	374	Exemestane 25 mg versus letrozole 2.5 mg versus	OR	62.9 versus 74.8 versus 69.1%	

			anastrozole 1 mg			
Eiermann et al. [8]	Phase 3, randomized, double-blinded	337	Letrozole 2.5 mg versus tamoxifen 20 mg	OR	55% versus 36%	<0.001
Semiglazov et al. [9]	Phase 2, randomized	239	Anastrozole 1 mg or exemestane 25 mg versus doxorubicin + paclitaxel	OR	64.5 versus 63.6%	>0.5
GEICAM/2006-03 [10]	Phase 2, randomized	95	Exemestane 25 mg versus EC-T	OR	48 versus 66%	0.075

No, number; OR, objective response; EC-T, epirubicin and cyclophosphamide followed by docetaxel.

Clinical trials of adjuvant endocrine therapy in elderly patients with breast cancer.

Study	Design	Number of patients	Treatment	Primary end point	Results	
ATAC [11]	Phase 3, randomized	9366	Anastrozole 1 mg versus tamoxifen 20 mg versus anastrozole 1 mg + tamoxifen 20 mg	DFS	A versus T; HR 0.91, 95% CI 0.83–0.99	0.04
BIG 1-98 [12]	Phase 3, randomized, double-blind	8010	T-L versus letrozole L-T versus letrozole	DFS	HR 1.05, 99% CI 0.84–1.32 HR 0.96,	

					99% CI 0.76–1.21	
MA. 17 [13]	Phase 3, randomized, double-blind	5187	Tamoxifen-letrozole versus tamoxifen-placebo	DFS	HR 0.58, 95% CI 0.45–0.76	<0.001

No, number; DFS, disease-free survival; A, anastrozole; T, tamoxifen; HR, hazard ratio; CI, confidence interval; L, letrozole.

Clinical trials of palliative endocrine therapy in elderly patients with breast cancer.

Study	Design	Number of patients	Treatment	Primary end point	Results	
First line						
TARGET [14]	Phase 3, randomized, double-blind	668	Anastrozole 1 mg versus tamoxifen 20 mg	TTP OR	8.2 versus 8.3 mths, HR 0.99 32.9 versus 32.6%	0.941 0.787
Nabholtz et al. [15]	Phase 3, randomized, double-blind	353	Anastrozole 1 mg versus tamoxifen 20 mg	TTP OR	11.1 versus 5.6 moths HR, 1.44 21 versus 17%	0.005

Paridaens et al. [16]	Phase 3, randomized, open-label	371	Exemestane 25 mg versus tamoxifen 20 mg	PFS	HR 0.84, 95% CI 0.67–1.05	0.121
Mouridsen et al. [17]	Phase 3, randomized, double-blind	916	Letrozole 2.5 mg versus tamoxifen 20 mg	TTP	9.4 versus 6.0 moths, HR 0.72	<0.0001
PALOMA-1/TRIO-18 [18]	Phase 2, open-label, randomized	165	Letrozole 2.5 mg versus letrozole 2.5 mg + palbociclib 125 mg	PFS	10.2 versus 20.2 mths, HR 0.488	≤0.001
FIRST [19]	Phase 2, open-label, randomized	205	Fulvestrant 500 mg versus anastrozole 1 mg	CBR	72.5 versus 67%	0.386
Second line						
BOLERO-2 [20]	Phase 3, randomized, double-blind	724	Everolimus 10 mg + exemestane 25 mg versus exemestane 25 mg	PFS	6.9 versus 2.8 mths, HR 0.43	<0.001
PALOMA3 [21]	Phase 3, randomized, double-blinded	521	Palbociclib 125 mg + fulvestrant 500 mg versus. fulvestrant 500 mg	PFS	9.2 versus 3.8 mths, HR 0.42	<0.001

No, number; TTP, time to progression; OR, objective response; mths, month; HR, hazard ratio; PFS, progression-free survival; CBR, clinical benefit rate (proportion of patients with objective response or stable disease for ≥24 weeks).

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MAJOR GIT SURGERY FOR GASTROINTESTINAL CANCER

Worldwide populations are getting older (1). The incidence of cancer increases with increasing age (2, 3). Currently 60% of malignant disease occurs in people over 65yrs. More than half are over 70yrs and 25% over 80 years. (2)

Elderly patients are likely to present in an emergency situation and this increase risk. Increasing age is also associated with increase in mortality (4, 5).

DEFINITION OF ELDERLY

The world health organisation defined old age as 60yrs and older, in low income countries, age of 50-55 years can be used. {WHO definition of an older or elderly person} (6). In the UK, old age is classified into 3 stages (See table 1). This shows importance of physiological state and disease state effect on individuals.

TABLE 1

Group	Age	Goals
Entering old age		
Completed their career in paid employment and/or child rearing Are active and independent and many remain so into late old age	Includes people as young as 50 years old, or from the official retirement ages of 60 for women and 65 for men	Promote and extend healthy active life Compress morbidity (the period of life before death spent in frailty and dependency)
Transitional phase		
In transition between healthy, active life and frailty	This transition often occurs in the seventh or eighth decades of life but can occur at any stage of older age	Identify emerging problems ahead of crisis Ensure effective responses that will prevent crisis and reduce long-term dependency
Frail older people		
These people are vulnerable as a result of health problems such as stroke or dementia, social care needs, or a combination of both	Frailty is often experienced only in late old age, so services for older people should be designed with their needs in mind	Anticipate and respond to problems, recognizing the complex interaction of physical, mental, and social care factors, which can compromise independence and quality of life

Frailty

Geriatricians define frailty as a geriatric syndrome that is distinct and independent from medical comorbidities. Markers of frailty include sarcopenia, low physical activity and endurance.

It has been found to be predictive of increased mortality (7). Frailty index can safely predict which elderly would do bad and therefore not to be considered for major surgery. Selection is therefore key.

Elderly patients face different issues, e.g. Equality and quality

Elderly patients are often denied appropriate surgical intervention (Access denied). The quality of care is often poor as it is not geared to geriatric practice. The question arising is should age by itself be a bar to surgery? It is very difficult to prove that age in the absence of significant disease is a prognostic factor in GIT surgery (8).

The referral pattern demonstrates few referral of elderly for surgery as an assumption of comorbities is always assumed (9).

The atypical presentation in elderly patients is another reason for none referral or late referrals to surgical units which impacts on outcome (10).

ETHICAL ISSUES

Surgery in elderly brings diverse and difficult ethical debates, even when extensive GIT surgery for cancer would benefit the elderly but there is shortage of high care beds, the arguments is that a younger person should take priority. The 1992 BMA conference concluded that "No patient should be denied an operation just because of advanced age" {BMA Ethics, Science & information division (11)}.

The other principle of" Do not harm" raises serious dilemma. Elderly patients may be denied elective surgery that it would harm them only to present later as an emergency. Initial assessment should be thorough and rather consideration for elective surgery should be done where care may be possible.

Principles of autonomy comes in as in an elderly patients there is no upper legal age limit for consent, A mentally incompetent elderly who cannot consent, it is the doctors decision based on " duty of care" who decides and not the family.

MAJOR SURGERY FOR OESOPHAGEAL CANCER

Majority of patients with oesophageal cancer are old {Average age of 68-70 years} and 30% are over 75 years at time of diagnosis (2, 12). In China majority are over 60 years and the highest incidence is between 75 years and 85 years (13).

Elderly patients are less likely to be referred and less likely to receive treatment irrespective of stage or comorbidies (14). Combination therapy is felt to be toxic for most elderly patients. Many studies have shown that surgery in elderly patients with oesophageal cancer do not have poor prognosis compared to younger patients.

Age alone as a factor had no difference in outcome. In the met analysis of 8 studies on surgical treatment, only 3 studies showed differences in outcomes. One study showed a median survival of 151-306 days vs 350-944 days (14).

The study by MA JY(15) showed increase in Cardiac and pulmonary complications in elderly compared to younger patients ,43, 3% v/s 28% (Pulmonary) and 28, 3% v/s 19,8 % (Cardiac).

The other studies showed no significant difference in mortality, morbidity or long term survival in younger and older patients (15).

LIU H et al showed minimal invasive surgery is beneficial only for early lesions. There was a tendency in some studies to do less invasive surgery in elderly patients when more radical surgery could have benefited those patients. Elderly patients who survive immediate postoperative cardiac and pulmonary complications have similar outcomes as younger patients.

Post-operative care is the main determinant of long term outcome. Early post-operative mobilization, chest physiotherapy, appropriate analgesic and deep breathing exercises can improve pulmonary complications following major oesophageal cancer surgery in the elderly. Once they

survive immediate post-operative complications, the long term survival is similar to younger patients.

Preoperative cardiology and anaesthetics consult is critical in optimizing this risk. Nutritional support is important as poor nutrition is associated with poor outcome especially in elderly. The centre where surgery takes place should be a high volume centre (at least 13 Oesophagectomy per year).

Oesophagectomy can be performed in the elderly with acceptable morbidity and mortality. Patients' selection is important, multidisciplinary approach combined with best clinical care is prudent. Example of the Nottingham University group bears testimony; they achieved a 5 years survival of 20% or more in all ages with combination of thoracotomy and extensive mediastinal dissection regardless of age (16). In elderly patients attention to perioperative care is the main determinant of outcome and not age alone. Pre-operative nutritional support to increase albumin level, cardio-pulmonary care in a specialised oesophageal unit which is also geared to geriatric care will achieve good outcomes.

Patients with early stage cancer, stage 1 and 2, less radical surgery is advised which results in good survival outcomes. The stage 3 cancer in a patient with no comorbidities , the same radical surgery as would be done for younger patients is advocated with thoracotomy and extensive lymph node dissection if curative intent is to be achieved. The role of laparoscopic surgery in elderly with oesophageal cancer has not been conclusively determined. The benefits of lower rates of pulmonary complications have been reported but whether it provides long term survival still requires further research (17).

MAJOR SURGERY FOR GASTRIC CANCER

Increasing life expectancy resulted in gastric cancer among elderly patients. Japanese study showed that surgical treatment is associated with better prognosis than supportive care in gastric cancer patients over 80 years of age (18).

The rate of mortality is often higher due to other comorbidities and surgery is often avoided in older patients. (19, 20).

The study by Min Sung Kim, Outcome of Gastric Cancer Surgery in Elderly patients demonstrated that there is no difference in surgical outcome between elderly and young patients undergoing surgery for gastric cancer with curative intent (21).

Table 2

Surgical outcomes in patients who underwent curative resection

Variable	Young group (n=404)	Elderly group (n=31)	P-value
Length of stay (d)	14.5±11.0	13.7±7.3	0.675
Duration of surgery (min)	212.0±61.0	200.0±52.0	0.283
Type of surgery			1.000
Subtotal gastrectomy	328 (81.2)	25 (80.6)	
Total gastrectomy	76 (18.8)	6 (19.4)	
Mortality rate	7 (1.7)	2 (6.5)	0.129
Complications			0.905
None	294 (72.8)	23 (74.2)	
Local	101 (25.0)	7 (22.6)	
Systemic	9 (2.2)	1 (3.2)	

Values are presented as mean±standard deviation or number (%).

TABLE 3

Post operative complications in patients undergoing curative resection

Variable	Young group (n=404)	Elderly group (n=31)	P-value
Total complication	110 (27.2)	8 (25.8)	1.000
Wound problems	65 (16.1)	4 (12.9)	
Leakage	20 (5.0)	1 (3.2)	
Respiratory problems	4 (1.0)	1 (3.2)	
PRC transfusion	11 (2.7)	1 (3.2)	
Ileus	4 (1.0)	1 (3.2)	
Intra-abdominal fluid collection	3 (0.7)	0	
Cardiovascular problems	3 (0.7)	0	
Severe complications (grade 3/4/5)*	48 (11.9)	5 (16.1)	0.565
Wound problems	19/0/0	2/1/0	
Leakage	15/0/4	0/0/1	
Respiratory problems	3/1/0	1/0/0	
Intra-abdominal fluid collection	2/0/1	0/0/0	
Cardiovascular problems	0/0/3	0/0/0	

TABLE 4

Variable	Complications		Severe complications	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Sex (male)	2.0 (1.2~3.3)	0.005	2.7 (1.3~5.5)	0.009
Age (≥80 yr)		0.454		0.623
ASA score		0.034		0.097
1	1		1	
2	1.4 (0.8~2.3)	0.240		
3	2.9 (1.3~6.4)	0.009		
STG/TG		0.128		0.118
Preoperative serum albumin level		0.350		0.193

Postoperative complications were similar, except were higher in male patients and patients with high ASA score.

Multivariate analysis for risk factors of complications did not show effect of age on complications.

FIGURE 1

Fig. 1 shows the DFS of patients who underwent curative resection for gastric cancer. The mean DFS was 93.6±1.5 months (95% confidence interval [CI], 90.6~96.9 months): patients in the young group had a mean DFS of 93.5±1.6 months (95% CI, 90.4~96.9 months), while patients in the elderly group had a mean DFS of 61.6±3.3 months (95% CI, 55.2~68.0 months). There was no significant difference in the 5-year DFS rates between the two groups (young group, 88.7% vs. elderly group, 92.9%; P=0.680). The recurrence rates were 8.2% (33/404) and 3.2% (1/31) in the young and elderly groups, respectively, with no statistical difference (P=0.496).

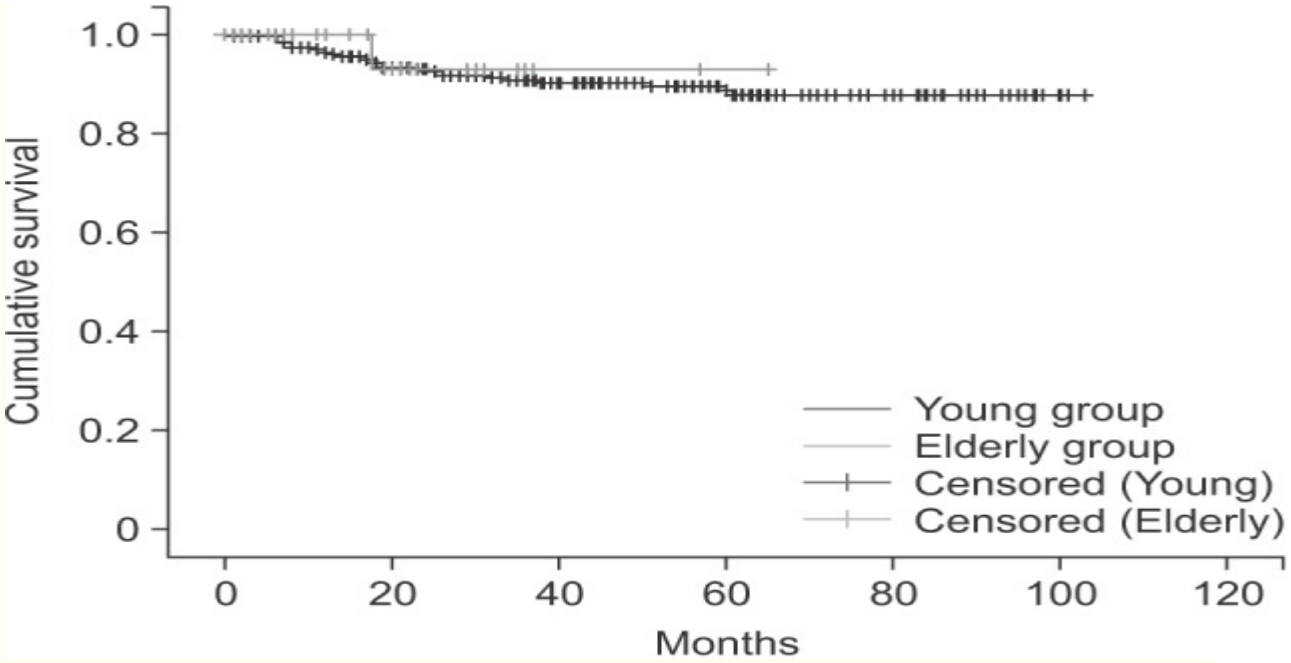

Fig. 1
Disease free survival of curative resected patients. Young group, <80 years old; Elderly group, ≥80 years old.

Recurrence rate was also similar for both groups

The other study by also confirmed similar results(22).

Conclusion: Age is not a risk factor but patients with high ASA score may have to be selected for lesser procedure or alternative therapy, but if curative resection is possible, then surgery should be a first consideration.

The Japanese study found no difference between young and old age for cancer stage 1 even with limited surgery, but stage 2 cancers benefited from radical lymphadenectomy. The survival for stage 3 was lower in elderly patients compared to younger patients although the younger group had adjuvant treatment whereas older group did not receive adjuvant therapy (23).

Rimantas et al comparing outcomes of patients with T1-T2 gastric cancer in elderly concluded that in early cancer, limited surgery offers similar outcomes and therefore patients with high ASA score should still be considered for surgery albeit limited. Stage 2 patients require extended lymphadenectomy for bettering outcomes. Stage 3 maybe offered limited surgery with adjuvant therapy but data is not available to argue for this approach.

Poor prognostic outcomes in elderly were found to be total gastrectomy and severe post-operative complications. Preventing complications by limited surgery and use of chemotherapy may be acceptable practice (24).

Laparoscopic gastrectomy in elderly is feasible but incidence of 30-day post-operative pulmonary infections is higher than in young patients. Major complications were similar though between the 2

groups. Tumour recurrence in terms of disease free survival and 5-year overall survival also was similar between the open and laparoscopic group (25).

COLORECTAL CANCER

Incidence of colorectal cancer increases with age (1, 2), 60% of cancers occur in people over 65 year, more than half being over 70 years and 25% over 80 years(2) . Elderly with colorectal cancer are more likely to come as emergencies which increases risk of poor outcome (3), About 40% of patients over 70 years with colorectal cancer require emergency treatment (26).

Intrinsic reduction in tolerance to stressors, presence of more medical disorders, polypharmacy and delayed diagnosis increase the risk of poor outcome, therefore multidisciplinary team is important to better select patients with better prognosis and exclude high risk or those with poor prognosis (27).

PREOPERATIVE ASSESSMENT

Nutritional assessment: May be poor due to poor intake, illness or pre-existing comorbid condition. Poor nutrition can lead to nosocomial infections, poor wound healing and organ dysfunction. 40% of elderly hospitalised for cancer are at risk of malnutrition leading to prolonged hospital stays, high morbidity and mortality in patients undergoing elective GIT surgery. (28, 29)

Malnutrition was found to be an independent predictor of poor outcome in elderly with CRC (30). Patients with CRC often have cardiovascular and respiratory problems which often affect decisions on their suitability for surgery. A study on patient over 67 years with primary diagnosis of stage i-iii CRC showed that comorbidities had substantial influence on survival, with a 5 year survival of stage I being 50% v/s 78% in those without comorbidities(31).

A higher Charlson comorbidity index was associated with a higher postoperative complication (32). Psychosocial issues like disorientation, anxiety and depression is associated with increase mortality and poor surgical outcome, and these are major issues in elderly patients (33). Poor support system including lack of home care also contributes to poor outcomes in elderly patients (34).

Frailty as a syndrome is another risk factor; this is associated with poor physiological reserve making patients less resistance to stressors (35). These patients are prone to falls, disability, prolonged hospitalisation, inability to perform daily activities. Tools to identify this patient have been developed like timed up and go (TUG) test, this tests a person's gait speed and mobility.

Stoma v/s no stoma for rectal cancer have shown no difference in quality of life among elderly patients.

Colon cancer treatment should not be different. It is under treatment that leads to poorer outcomes. (Study by chang et al) found increased use of local excision, decrease use of radical surgery and decrease use of multimodal treatment in elderly patients (36).

Decreased in survival in elderly was due to early mortality, those surviving first year of surgery had similar long term outcome as young once, therefore focus should be on perioperative care and first postoperative year(37).

SURGICAL CONSIDERATION IN ELDERLY WITH CRC

Advanced cancer: Role of surgery is limited. It should be only for palliation, to relieve obstruction or for bleeding.

Resectable liver metastasis: Adam et al found similar survival between younger group and elderly (57 v/s 60%) after liver resection for CRC metastasis. Liver resection for metastatic CRC in elderly can achieve reasonable survival rate (38).

Obstruction: 20% will present as emergency with bowel obstruction. Right sided tumours will invariably always require surgery whilst left sided is a subject of debate between stenting and Resectional surgery. SEMS may be a better option in elderly as a bridge to surgery (39, 40).

Two randomised control trials failed to define a decisive clinical advantage between Colonic stenting and emergency surgery. (41, 42).

Stoma use : Two studies showed a few leakage rate in elderly compared to young age group following an anterior resection for low rectal cancer but among those with a leak more than 50% demised in 6 months' time which was significant compared to younger age group (22,9% v/s 7%) (43, 44). The elderly do not seem to tolerate this complication and thus a stoma is advisable, moreover the quality of life does not seem affected between those with or without a stoma. The use of adjuvant therapy also confers survival advantage and should not be withheld fearing toxicity (45).

MAJOR PANCREATIC CANCER RESECTIN IN ELDERLY

Pancreatic cancer and periampullary cancer is rising among elderly population due to rapidly increasing population of aged. Several studies conclude that major surgery is feasible and safe in elderly patients but the risk of postoperative complication and troubled outcome objectively exist.

This may explain reluctance to perform such complex surgery in elderly. Careful selection is important. It is reasonable to consider elderly with 2 or 3 ASA slove, with a low comorbidity and good performance study as good candidates.

There is a need for centralization for such resection. Survival seems similar in old and young patients but data on th quality of life is missing.

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Fertility issues in young colorectal cancer patients.

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Introduction

Worldwide, colorectal cancer (CRC) is the third most common cancer and the fourth leading cause of cancer related death (Ferlay, Soerjomataram et al. 2015). In America, the relative 5 yr. survival for CRC patients is 65% and drops to 58% at 10 years (Siegel, Miller et al. 2017). CRC can be broadly divided into sporadic (65%) and hereditary (35%) CRC. While sporadic CRC often occurs in older patients, hereditary CRC is often diagnosed in younger patients (<50 years).

CRC is potentially curable not only when diagnosed early but even when it presents as a locally advanced or metastatic cancer. This is due to the advances in surgical technique resulting in more complete oncological tumour resections (Ro resections), advances in immunology and pharmacology that have resulted in the availability of good effective biologic and chemotherapeutic agents against it and also advances in radiation oncology that allow for administration of higher and more focused doses of radiotherapy. Due to these factors, CRC has a good prognosis when compared to many other malignancies such as pancreatic, breast or skin cancers.

The incidence of CRC in patients under 40 is 3–6% (Spanos, Mamopoulos et al. 2008). Lynch syndrome is associated with a decreased Age- specific fertility in female CRC survivors (Stupart, Win et al. 2015). With the increasing diagnosis of CRC in younger patients, 40 years or less (the childbearing years) and the improved survival, quality of life (QOL) after cancer survival is becoming an important factor. Fertility after CRC treatment is a question these younger patients are now beginning to ask physicians.

Effects of CRC treatment on fertility

Surgery: Pelvic surgery for rectal cancer (lower anterior resection [LAR] and abdominal perineal resection [APR]) i.e. resection below the peritoneal reflection may result in lower fertility and fecundity rates. A similar effect has been noted in pelvic surgery for ulcerative colitis (UC) and familial adenomatous polyposis (FAP).

Chemotherapy: While 5-FU may not have significant effects, oxaliplatin based chemotherapy may be more harmful. The risk of premature ovarian insufficiency (POI) is moderate if only chemotherapy is given but high for chemo-radiotherapy. In rectal cancer, there is >90% POI if a dose of 45–50 Gy is given (Schüring, Fehm et al. 2018).

Radiotherapy: Premature ovarian failure may occur as a result of adjuvant and neo-adjuvant radiation therapy.

Disease process: Progression of the CRC to locally advanced stage e.g. with uterine infiltration requiring en bloc resection or pelvic exenteration or to metastatic disease e.g. ovarian metastasis, also affects fertility.

The increased incidence of CRC in young patients coupled with the current population trend of delayed child-bearing may not be a concern in the state sector currently but in the private sector, it is a rising trend, meaning that physicians should familiarize themselves with the challenges associated with treatment of a pregnant patient with CRC(Rogers, Dasari et al. 2016).

Options for fertility preservation

Established methods for fertility preservation include standard practice procedures such as ovarian stimulation for trans-vaginal oocyte retrieval and cryopreservation, sperm cryopreservation and embryo cryopreservation. Other investigational techniques of FP available include: ovarian transposition surgery if pelvic radiotherapy is anticipated for rectal cancers, ovarian or testicular tissue cryopreservation, ovarian suppression, the use of apoptotic inhibitors and *in vitro* follicle maturation (Redig, Brannigan et al. 2011).

In countries where it is legal, gestational surrogacy is another option following cryopreservation of oocytes or ovarian tissue (von Wolff, Germeyer et al. 2018).

Summary

For informed consent before cancer therapy, the American Society of Clinical Oncology Clinical Practice Guidelines indicate that health care providers should have a documented discussion addressing the possibility of infertility with patients treated during their reproductive years (or with parents or guardians of children) to education them on available FP options or refer them to appropriate reproductive specialists. This discussion should be done as early as possible in the treatment process so as to allow for the widest array of options for fertility preservation. (Loren, Mangu et al. 2013)

In countries such as Canada, oncologists often act as gate keepers and are instrumental in initiating FP consultations (Yee 2016). Locally, surgeons are often the initial contact physicians that diagnose, stage the malignancy and present the patient at the multi-disciplinary team (MDT) meeting. Delays to oncology treatment appointments in the state sector, mean that surgeons need to play a more pivotal role in the provision of fertility services by being knowledge brokers, referral initiators and supporting these patients as they make important FP decisions in conjunction with the consultation provided by a fertility specialist.

A Canadian study of breast surgeons in 28 centers found that only 18% had a referral protocol for FP in place (Warner, Yee et al. 2016). Locally, most academic centers e.g. Steve Biko Academic Hospital (SBAH), have referral protocols that surgeons need to familiarize themselves with.

It is mandatory that young CRC patients (<40yrs of age) be informed of the effects of treatment on fertility and an MDT approach including consultation with a fertility specialist be under taken to educate them on the available options for fertility preservation.

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Elective surgery in cirrhotic patients, when to operate, when to manage conservatively.

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Scope of the problem

Patients with liver cirrhosis that undergo emergency or elective general surgical procedures have higher mortality and morbidity rates that those without cirrhosis. A recent series of patients undergoing non-hepatic general surgery compared 135 cirrhotic to 86 non-cirrhotic patients; there was a 16.3% 1-month mortality rate in the cirrhotic patients compared to 3.5% in the non-cirrhotic. (del Omo et al.) Another series reported outcomes of cirrhotic patients undergoing any emergency or elective general surgical procedure, overall 30-day mortality was 17.5% and the 3-month mortality was 30%. (Farnsworth et al.) There was a significant difference in the 1-month and 3-month mortality between the emergent and elective groups, for emergency surgery there was a 19% 1 month and 44% 3 month mortality rate as opposed to 17% 1 month and 21% 3 month mortality rate after elective surgery.

Whenever contemplating surgery for a cirrhotic patient, the stakes are high for each patient as a result of the observed significantly high morbidity and mortality rates secondary to the increased risks for general anesthesia, the stress of surgery itself, and the ability to recover from post-operative complications. A decision to proceed with surgery for cirrhotic patients must be weighed carefully because these patients often have poor hepatic
reserve with increased risk for bleeding, the development of postoperative hepatic coma, and death. Hence consideration must be given to the need for the surgical intervention, consequences of not having the surgery and urgency of the intervention.

Approach

The following questions should be considered in cirrhotic patients requiring non-hepatic surgical interventions:

1. What is the degree of liver cirrhosis?
2. What is the extent of the proposed general surgical procedure?
3. What are the risks of not operating on the patient?

Assessing the degree of liver cirrhosis: Child Pugh versus MELD score

Drawbacks of the Child Pugh score relate to the unavoidable variability in assessing the sometimes subjective variables of ascites and encephalopathy. The MELD score only uses objective laboratory determined variables. A recent study (Peng et al.) compered Child Pugh score to MELD score in predicting 1and 3 month mortality rates in emergency and elective surgical interventions in known cirrhotic patients. There was good overall correlation between the CTP and MELD scores ($r = 0.76$); the correlation between the CTP and MELD scores was greater in the emergency surgery group than in the elective surgery group ($r = 0.81$ and $r = 0.65$ respectively). (Farnsworth et al.)
There are few other studies that compare these tools in this setting. In conclusion the MELD score is objective but requires a calculator, the Child Pugh score has two relatively subjective parameters; use whichever one is easier for you to use, but use

one and document it in your operative notes!

Extent of the surgical procedure
When considering the Child Pugh score to predict mortality risk for elective and emergency surgical procedures consider once a general anesthetic is applied Child Pugh A has a 10% and 22% mortality rate, Child Pugh B a 30% and 38% mortality rate and Child Pugh C a 76% and 100% mortality rate respectively. (Frye et al.)

The two most common general surgical procedures in this population include:
Laparoscopic cholecystectomy
A meta-analysis (Laurence et al.) reported an increase overall morbidity rate of 21% versus 6% in patients with and without cirrhosis respectively. There was also an increase rate of intra-operative hemorrhage, 26% versus 3%, and an increased need for conversion to an open cholecystectomy of 7% versus 4% in cirrhotic versus non-cirrhotic respectively. There was no difference in all-cause mortality.
An important tip is not to place the umbilical port first due to the risk of a recanalised umbilical vein and para-umbilical venous collaterals but rather a subxiphoid port off the mid line and then place the remaining ports under direct vision. Patients with recurrent acute cholecystitis and Child-Pugh C cirrhosis should not have a cholecystectomy but rather an endoscopically placed cystic duct drain.

2. Umbilical herniorapphy
The most common hernia in cirrhotic patients is an umbilical hernia due to an increased intra-abdominal pressure secondary to ascites and an umbilical fascial weakening. A study assessed conservative management of these hernias and demonstrated that 77% of these patients eventually required an emergency repair of these patients there was a 15% mortality rate. (Coelho et al.) Whether or not to use a mesh with the repair has bee studied. There was an increased incidence of surgical site infection in the mesh group compared to the primary tissue repair group, 16% versus 9%, all were managed conservatively. At 6 month follow-up there was an increased recurrence rate in the primary repair group versus mesh group of 14% versus 3%. A meta-analysis addressed whether or not a pre-hernia repair shunt should be placed to control ascites and the outcome was an odds ratio for hernia recurrence 8.5 if the shunt was not placed. (KASL)
In conclusion, umbilical hernias in cirrhotic patients should be repaired electively using mesh following placement of a shunt if there is significant ascites.

Assess the risks of not operating on the patient
As stated in the previous section Child Pugh status guides mortality prediction, but one must balance this mortality prediction with the risk of complications and mortality from the condition requiring a surgical intervention. There are no hard and fast rules dictating this, common sense and experience should be followed. Also keep in mind that conservative measures that may sometimes be used in non-cirrhotic are not always an option, as failure of the measure would still require surgery. Cirrhotic do not have much physiological reserve to withstand failed conservative management. Appropriate counseling of the patient and their family members is imperative.

Peri-operative optimization
Patients, especially in the Child Pugh B group may be optimized pre-operatively to improve their operability. (Abbas et al.) Specific factors include (Pandey et al):

- Protein-energy malnutrition may be corrected in an attempt to decrease infections, wound dehiscence, ascites and mortality
- Coagulopathy
- Electrolyte correction, especially sodium imbalance and renal dysfunction
- Gut decontamination with lactulose and oral metronidazole

Conclusion
Elective surgery is well tolerated in Child Pugh A patients, Child Pugh B patients are unlikely to tolerate major surgical interventions but attempts should be made to optimize them and reassess their operability, Child Pugh C's do not survive surgery.

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Approach and challenges to surgery in HIV infected patients

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The World Health Organization (WHO) recorded 36.9 million people living with human immunodeficiency virus (HIV) infection worldwide in 2017.[1] HIV impairs or destroys CD4 T lymphocytes.[2] Surgery is complicated by HIV either directly or indirectly. The treatment with antiretroviral medication (ARV) has improved the immune status of the HIV+ patient but has side effects which can alter surgical outcomes.

HIV stimulates the inflammatory system, the result of which can cause conditions related to premature aging and therefore higher risk of age related co-morbidities.[3] The inflammatory effects can be seen with morphological changes in red blood cells and platelets.[4] Inflammation, as evident with raised interleukin 6 and tumour necrosis factor alpha, is also closely linked with activation of the coagulation system resulting in a hypercoagulable state.[5] Patients are therefore at higher risk for venous thromboembolism. Prophylactic measures to prevent venous thromboembolism, including anticoagulation prophylaxis, should be in place.

Due to the immunocompromised state, risk of opportunistic infections are increased. Certain viruses can increase the incidence of certain cancers, such as Kaposi sarcoma, aggressive B-cell non-Hodgkin lymphoma and cervical cancer.[6] These cancers are AIDS-defining according to the WHO clinical staging.[1] Opportunistic infections can also mimic surgical pathology, which can mislead the surgeon operating on a patient that requires non-operative management.

Postoperative sepsis causes increased morbidity and has approximately 41% incidence in HIV+ patients.[7] Risk factors for postoperative sepsis include a low CD4 count (less than 200 cell/µl), hypoalbuminemia (less than 35g/L), presence of infection during the operation and major surgery.[8,9,10] The indication for surgery is also associated with increased postoperative sepsis. Surgery due to trauma has a higher rate of postoperative sepsis.[9] Surgical HIV+ patients also tend to have higher risk of complications, longer hospital stay and increased mortality. [11,12]

Antiretroviral medication have multiple complications. For certain operations, the effects of ARVs is a potential concern such as transplantation with HIV+ donors to HIV+ recipients. HIV+ transplantation appears to have a good outcome provided patients are selected appropriately.[13, 14] The ARVs, in donors and recipients, may have nephrotoxic side effects, esp. in kidney transplantation. The ARVs may also affect the immunosuppressant medication. [15]

The effects of the type of surgery may also affect the ARV plasma concentrations. Bariatric surgery in HIV+ patients appears to have a good outcome, although only a few case series have been reported. The effect of bariatric surgery may decrease ARV absorption, resulting in decreased plasma concentrations.[16,17] There are too few cases reported on bariatric surgery in HIV+ patients to make a conclusion though.

Lastly, although the risk of HIV infection is low (percutaneous 0.3% and mucocutaneous 0.09%[18]) the occupational risk to the medical personal caring for HIV+ patients should not be overlooked and safety precautions should always be practiced.

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Preparation And Management of Patients On Anti-Coagulation or Anti-Platelet Therapy for Elective or Emergency Surgery..

N Pearce

INTRODUCTION:

Many of the patients we treat are taking some form of anticoagulant agent due to co morbid diseases such as atrial fibrillation, mechanical heart valve, venous thromboembolism and prothrombotic blood abnormalities such as protein C & S deficiencies.

The peri-operative management of patients taking such agents is often a challenge to the treating surgeon.

This paper intends to highlight the guidelines recommended for the management of patients on anticoagulants undergoing surgical procedures (elective and emergency).

ANTI-THROMBOTICS:

- **ANTICOAGULANTS**:
  -Warfarin
  -Unfractionated Heparin
  -Low molecular weight heparin
  -Direct thrombin inhibitors(Dabigatran,Lepirudin)
  -Direct factor Xa inhibitors (Fondaparinux,Rivaroxaban)

- **ANTI-PLATELET AGENTS**:
  -Aspirin
  -NSAIDs
  -Thienopyridines (clopidogrel,ticlopidine)
  -Platelet glycoprotein (II*b*/III*a*) inhibitors

- **FIBRINOLYTIC DRUGS**:
  -Streptokinase
  -Alteplase
  -Reteplase
  -Tenecteplase

Elective surgery:

The management of anticoagulation in patients undergoing elective surgical procedures is challenging because interrupting anticoagulation for a procedure transiently increases the risk of thromboembolism (TE).

At the same time, surgery and invasive procedures have associated bleeding risks that are increased by the anticoagulants administered for thromboembolism prevention.

Therefore a balance between reducing the risk of thromboembolism and preventing excessive bleeding must be reached for each patient.

A) GENERAL PRINCIPLES:

FACTORS TO TAKE INTO ACCOUNT WHEN MAKING A DECISION:

- *Estimate bleeding risk*
- *Estimate thromboembolic risk*
- *Timing of anticoagulation interruption*
- *Determine whether to use bridging anticoagulation*

1) ESTIMATE BLEEDING RISK:

The risk of bleeding is determined by the type of surgery or invasive procedure. The procedures can be classified into the following 5 groups:

Very high risk:

- Neurosurgery (intracranial or spinal surgery)
- Cardiac surgery (coronary artery bypass or heart valve replacement)

High risk:

- Major vascular surgery (AAA repair, aorto-femoral bypass)
- Major urologic surgery (prostatectomy, bladder tumour resection)
- Major orthopaedic surgery (hip/knee joint replacement surgery)
- Intestinal anastomosis surgery
- Permanent pacemaker insertion or internal defibrillator placement

- Selected invasive procedures (kidney biopsy, prostate biopsy, cervical cone biopsy, colonic polypectomy)
- Any procedure lasting >45 minutes

Intermediate risk:

- Other intraabdominal surgery
- Other intrathoracic surgery
- Other orthopaedic surgery
- Other vascular surgery

Low risk:

- Laparoscopic cholecystectomy
- Laparoscopic inguinal hernia repair
- Dental procedures
- Dermatologic procedures
- Ophthalmologic procedures
- Coronary angiography
- Gastroscopy or colonoscopy
- Selected invasive procedures (bone marrow biopsy, lymph node biopsy, paracentesis)

Very low risk:

- Single tooth extraction or teeth cleaning
- Selected skin biopsy, skin cancer removal, cataract removal

2) ESTIMATE THROMBOEMBOLIC RISK:

A higher thromboembolic risk increases the importance of minimizing the interval without anticoagulation.

If thromboembolic risk is transiently increased for e.g. recent stroke or recent pulmonary embolism it is recommended to delay surgery until the risk returns to baseline if possible.

The major factors that increase thromboembolic risk are atrial fibrillation, prosthetic heart valves, and recent venous or arterial thromboembolism (e.g. within the preceding 3 months).

The risk for thromboembolism can be classified into the following:

High risk:

- Any mechanical prosthetic mitral valve
- Older generation (cage-ball, tilting disc) mechanical prosthetic aortic valve
- Atrial fibrillation (CHADS2 score=5-6)
- Recent (within 3 months) arterial thromboembolism (stroke, systemic embolism, TIA)
- Recent (within 3 months) venous thromboembolism (DVT, PE)
- Prior arterial or VTE during interruption of warfarin
- Selected prothrombotic blood abnormalities (deficiency of protein C, protein S or antithrombin, antiphospholipid antibodies)

Moderate risk:

- Newer generation (bileaflet) mechanical prosthetic aortic valve
- Bioprosthetic aortic valve
- Chronic atrial fibrillation (valvular or nonvalvular) ***and*** at least 1 major stroke risk factor: prior stroke/TIA, left ventricular dysfunction, hypertension, diabetes, or age >75 years
- Prior venous thromboembolism within last 3 to 12 months

Low risk:

- Chronic atrial fibrillation (valvular or nonvalvular) ***and*** no major stroke risk factors
- Prior venous thromboembolism over 12 months ago

The American College of Chest Physicians (ACCP) recommends patients with a *high or intermediate risk* for thromboembolism to receive bridging anticoagulation, whereas low risk patients it is not recommended.

3) TIMING OF ANTICOAGULATION INTERRUPTION:

GENERAL POINTS:

- If the patient is having a **major** surgical or other major invasive procedure, interruption of anticoagulant therapy is typically needed to minimize the risk for perioperative bleeding.
- If the patient is undergoing a **minor** surgical or invasive procedure (e.g. dental, skin or cataract) interruption might not be required.
- Once the thromboembolic and bleeding risks have been estimated, a decision can be made about whether the anticoagulant should be interrupted or continued.

- Data comparing the relative benefits of continuing anticoagulation vs interrupting an anticoagulant are limited, and decisions that balance thromboembolic and bleeding risks must be made on a case-by-case basis. *NO SCORING SYSTEM CAN SUBSTITUTE FOR CLINICAL JUDGMENT IN THIS DECISION MAKING.*
- In general, the anticoagulant must be discontinued if the surgical bleeding risk is high.
- Those at high or moderate thromboembolic risk should limit the period without anticoagulation to the shortest possible interval; this typically involves the use of a bridging agent (e.g. a low molecular weight heparin) if the patient's usual anticoagulant is a vitamin K antagonist. Often, bridging is not required for those with high or moderate thromboembolic risk who are receiving a direct thrombin inhibitor or factor Xa inhibitor, because of the shorter half-lives of these agents.
- Patients undergoing selected low bleeding risk surgery often can continue their anticoagulant.

RECOMMENDATIONS:

BLEEDING RISK	TE RISK	RECOMMENDATION
High/Intermediate	High (transient)	Delay surgery if possible until TE risk has returned to baseline
High/Intermediate	High (chronic)	Bridging anticoagulation to minimize the period without it
High/Intermediate	Moderate	Bridging anticoagulation
High/Intermediate	Low	Interruption without bridging
Low	Low	Continue anticoagulation (If on warfarin-confirm INR not exceed therapeutic range)

4) DETERMINE WHETHER TO USE BRIDGING ANTICOAGULATION:

Bridging anticoagulation involves the administration of a short-acting anticoagulant, typically a low molecular weight heparin, during the interruption of a longer-acting agent like warfarin.

There is no data on using the newer target-specific oral anticoagulants (e.g. direct thrombin inhibitors, direct factor Xa inhibitors) as bridging agents, furthermore these agents lack a specific reversal strategy should bleeding occur. Therefore, low molecular weight heparin or unfractionated heparin is used when bridging is required.

The intent of bridging is to minimize the time the patient is not anticoagulated, thereby minimizing the risk for perioperative thromboembolism. However, this needs to be balanced with the importance of mitigating the risk of postoperative bleeding.

The need for bridging is driven by the patient’s risk for TE:

- **High-risk patient**: The need to prevent TE will dominate management irrespective of bleeding risk; the potential consequences of TE justifies bridging.
- **Moderate-risk patient**: A single perioperative strategy is not dominant and management will depend on individual patient risk assessment.
- **Low-risk patient**: The need to prevent TE will be less dominant and bridging may be avoided.
- **All patients**: judicious use of postoperative bridging is needed to minimize bleeding that would have the undesired effect of delaying resumption of anticoagulant therapy after surgery.

BRIDGING ANTICOAGULATION REGIMENS:

- "High dose" (therapeutic dose) regimen involves giving a dose similar to that used to treat acute VTE or ACS (e.g. enoxaparin 1mg/kg bd or 1.5mg/kg od, dalteparin 100IU/kg bd or 200IU/kg od, tinzaparin 175IU/kg od, IV UFH to attain aPTT 1.5 to 2 times the control aPTT)
- "Intermediate dose" regimen e.g. enoxaparin 40mg bd
- "Low dose" (prophylactic dose) regimen involves giving a dose used typically to prevent postoperative VTE (e.g. enoxaparin 30mg bd or 40mg od, dalteparin 5000IU od, UFH 5000-7500 IU bd)

WHEN TO USE WHICH DOSES:

- **Therapeutic dose**: Individuals with a potential arterial thromboembolic source (eg, atrial fibrillation, mechanical heart valve) or VTE within the preceding month.
- **Intermediate dose:** Individuals with atrial fibrillation or VTE within the preceding month when bridging is needed but concerns about bleeding are greater.
- **Prophylactic dose:** Generally not used for bridging in patients with atrial fibrillation, because there is no evidence that prophylactic dose heparin prevents stroke in this setting. This dose level may be reasonable in patients who have had a VTE event between within the preceding two to three months.

WHEN TO BRIDGE: PREOPERATIVE, POSTOPERATIVE, OR BOTH

- **Preoperative bridging** – For individuals with nonvalvular atrial fibrillation receiving warfarin for thromboprophylaxis who are undergoing a procedure associated with a very high bleeding risk (eg, intracranial, spinal, cardiac), bridging preoperatively should be done, but not postoperatively, because postoperative bridging increases, rather than decreases, serious morbidity. Restarting warfarin on the second postoperative day is preferable to minimize the risk of bleeding, as long as adequate hemostasis has been achieved.

- **Preoperative and postoperative bridging** – For individuals considered to be at highest risk for TE, including patients with atrial fibrillation and a high $CHADS_2$ score, patients with a mechanical mitral valve replacement, or those within the first month after an acute episode of VTE, bridging both preoperatively and postoperatively should be done. This practice is based on the high incidence of recurrence without anticoagulation, of approximately 1% per day. While postoperative intravenous heparin doubles the rate of bleeding, there is a net reduction in serious morbidity in such patients since the risk of postoperative recurrent VTE is high.

- **Postoperative bridging** – For individuals greater than one month after an acute episode of VTE, postoperative bridging, typically with a low dose LMW heparin regimen (e.g. enoxaparin 40 mg daily) is recommended, but not preoperative bridging. This practice is based on the significantly reduced risk of VTE recurrence after the first month, to the point that preoperative bridging is probably not justified unless there are other risk factors for TE (e.g. prolonged hospitalization and immobility. Therapeutic-dose heparin is used postoperatively because the postoperative state further adds to VTE risk.

B) <u>RECOMMENDATIONS FOR SPECIFIC AGENTS</u>:

1) RECOMMENDATIONS FOR PATIENTS ON WARFARIN:

- **Minor procedures (low bleeding risk):**
  -Dental: Continue warfarin with co-administration of an oral prohemostatic agent or stopping warfarin 2-3 days before the procedure.
  -Skin procedures: Continue warfarin around the time of the procedure and optimize local hemostasis.
  -Cataract surgery: Can continue warfarin around the time of the surgery.

- **Major surgery with low risk for TE: No bridging needed here**
  Day -5: stop warfarin (last dose on Day -6)

  Day -1: INR testing (if INR>1.5, administer vitamin k 1 – 2 mg orally)

  Day 0: Resume warfarin on evening after surgery if patient drinking fluids

  Day +1 to +3: Resume warfarin when patient drinking fluids

- **Major surgery with high risk for TE: Bridging needed here**
  Day -5: stop warfarin (last dose on Day -6)

  Day -3: start IV UFH or SC LMWH

Day -1: INR testing (if INR>1.5, administer vitamin K 1 – 2 mg orally).
Last preoperative dose of LMWH 24 hr before surgery.

Day 0: Stop UFH 4 hrs before surgery, assess postoperative surgical site haemostasis, resume warfarin on evening after surgery if patient drinking fluids.

Day +1 to +3: Resume UFH or LMWH when hemostasis secured, but not earlier than 12 hrs after surgery. Resume warfarin when patient drinking fluids

Day +5 to +6: Stop UFH or LMWH when INR within therapeutic range.

- ✓ **When is it safe to resume bridging anticoagulation after surgery/procedure?**

Deciding on when to resume bridging anticoagulation is important to minimize the risk for bleeding, which occurs at the surgical site in >90% of cases. Minimizing bleeding is important because of morbidity associated with bleeding (i.e. emergency re-operation, blood transfusion). Furthermore, a bleed will delay the resumption of warfarin for 1-4 weeks, thereby exposing patients to an increased risk for thromboembolism4-8.

The resumption of bridging anticoagulation after a procedure is dependent on the bleeding risk of the procedure and is predicated on adequate postoperative hemostasis.

Assessing postoperative hemostasis is subjective and includes inspecting wound bandages and drainage tubes to detect bleeding. Adjunctive measures to minimize the risk for perioperative bleeding include good suturing technique, wound-site pressure (e.g., pressure dressings), use of ice packs and, when indicated, use of anti-fibrinolytic agents (e.g., tranexamic acid mouthwash for dental procedures).

Postoperative resumption of bridging anticoagulation: treatment options
Very high risk bleeding procedure • Low dose LMWH, starting 12-24hrs after surgery • Alternate management: resume warfarin alone with no postoperative heparin **High risk bleeding procedure** • Therapeutic dose LMWH/UFH starting 48-72 hrs after surgery • Alternate management: low dose LMWH, starting 12-24hrs after surgery **Moderate risk bleeding procedure** • Therapeutic dose LMWH/UFH starting 24-48 hrs after surgery **Low risk bleeding procedure** • Therapeutic dose LMWH/UFH starting 12-24hrs after surgery

2) RECOMMENDATIONS FOR PATIENTS ON HEPARIN:

- **LMWH** should be discontinued 24 hrs before the planned surgery or procedure.
  If a twice-daily LMWH regimen is given, the evening dose the night before surgery is omitted, whereas if a once-daily regimen is given (e.g. dalteparin), one-half of the total daily dose is given on the morning of the day before surgery. This ensures that no significant residual anticoagulant will be present at the time of surgery.
- **UFH**– For therapeutic dose of UFH, intravenous infusion is continued until 4 to 5 hrs before the procedure, based on the biologic half-life of intravenous UFH of approximately 45 minutes.
  If subcutaneous UFH is used, typically with a dose of approximately 250 international units/kg twice daily, the last dose can be given the evening before the procedure.

- **Restarting** - For those undergoing **major surgery** or those with a high bleeding risk procedure, therapeutic-dose UFH or LMWH should be delayed for 48 to 72 hours after haemostasis has been secured.
  For most **minor procedures** associated with a low bleeding risk in which bridging is used (e.g. laparoscopic hernia repair), therapeutic-dose UFH or LMWH can usually be resumed 24 hours after the procedure.

3) RECOMMENDATIONS FOR PATIENTS ON ASPIRIN OR CLOPIDOGREL:

Patient management is similar to that of warfarin-treated patients in that the need for aspirin/clopidogrel interruption should be initially addressed. Antiplatelet drugs probably can be continued for patients undergoing very low or low bleeding risk procedures.

In patients undergoing intermediate or high bleeding risk procedures, antiplatelet therapy should be interrupted. Because aspirin and clopidogrel irreversibly inhibit platelet function, 7-10 days (platelet lifespan) is required after treatment interruption to eliminate a residual antiplatelet effect prior to surgery. Interrupting aspirin/clopidogrel 3-4 days before surgery will result in ~50% of platelets have normal function and this may be sufficient for some procedures. There is no known short-acting antiplatelet drug that can be used, like UFH or LMWH, as bridging antiplatelet therapy.

SPECIAL CIRCUMSTANCES - RECOMMENDATIONS:

- **Patient with coronary stents requiring surgery**:
  - In patients with a coronary stent who are receiving dual anti-platelet therapy and require surgery, surgery should be deferred for at least 6 weeks after placement of a bare-metal stent and for at least 6 months after placement of a drug-eluting stent *instead of* undertaking surgery within these time periods.
  - If the patient requires surgery within 6 weeks of placement of a bare-metal stent or within 6 months of placement of a drug-eluting stent, dual anti-platelet therapy should be continued around the time of surgery *instead of* stopping dual anti-platelet therapy 7-10 days before surgery.

4) RECOMMENDATIONS FOR PATIENTS ON DIRECT THROMBIN INHIBITORS(DABIGATRAN):

- **Discontinuation** – Dabigatran can be discontinued 2 – 3 days before a surgical procedure in patients with normal or mildly impaired renal function (i.e. CrCl >50 ml/minute), with the longer interval used for higher bleeding risk procedures and the shorter interval for surgeries with less bleeding risk.
  Therefore, for high bleeding risk procedures, the patient will skip four doses of dabigatran, and not receive any doses on surgical days minus 2, minus 1, or the day of surgery. These intervals are based on an elimination half-life of 12 to 14 hours in patients with normal renal function.
  For those with renal insufficiency (CrCl 30-50ml/min) Dabigatran should be discontinued 2 - 4 days before the procedure.
  Unlike the PT/INR for warfarin, routine coagulation tests have not been validated for ensuring that Dabigatran effect has resolved.
  A normal or near-normal PTT may be used in selected patients to evaluate whether Dabigatran has been adequately cleared from the circulation prior to surgery (e.g. patients at high risk of surgical bleeding).

- **Use of bridging** – In general, the rapid offset and onset of dabigatran activity obviates the need for bridging anticoagulation.
  Bridging anticoagulation may be indicated for selected individuals who are at high risk for postoperative TE and require extended interruption of Dabigatran. E.g. include postoperative bridging in patients who are unable to take oral medications postoperatively due to intestinal ileus from gastrointestinal surgery.

- **Restarting** - Dabigatran should be resumed postoperatively when hemostasis has been achieved, at the same dose the patient was receiving preoperatively.

Since Dabigatran has a rapid onset of action, with peak effects occurring two to three hours after intake, caution should be used in patients who have had major surgery or other procedures associated with a high bleeding risk.

It is recommended to delay resumption of Dabigatran for 2 - 3 days after high bleeding risk procedures and, if needed, administer a lower Dabigatran dose for the initial two to three postoperative days (e.g. 110 mg once daily) or use prophylactic dose LMWH for this period.

For low bleeding risk surgery (if it was interrupted) one can restart Dabigatran one day after the surgery.

5) RECOMMENDATIONS FOR PATIENTS ON DIRECT FACTOR Xa INHIBITORS (RIVAROXABAN):

- **Discontinuation** – Rivaroxaban can be discontinued approximately 2 - 3 days before a procedure, with the longer interval for higher bleeding risk procedures and the shorter interval for lower bleeding risk procedures. Therefore, for high bleeding risk procedures, the patient will skip two doses of Rivaroxaban, and not receive any doses on surgical days minus 2, minus 1, or the day of surgery.

  These intervals are based on the elimination half-life of 7 to 11 hours and apply to individuals with normal renal function or mild renal insufficiency (e.g. CrCl >50 mL/minute), who are likely to be receiving the 20 mg once daily dose; and to those with moderate renal insufficiency (e.g. CrCl 30 - 50 mL/minute), who are likely to be receiving the 15 mg once daily dose.

  Rivaroxaban interacts with dual inhibitors of CYP-3A4 and P-glycoprotein (e.g. systemic ketoconazole, ritonavir); dose adjustment or substitution of heparin may be appropriate if these dual CYP-3A4 and P-glycoprotein inhibitors are used perioperatively.

  Unlike the PT/INR for warfarin, routine coagulation tests have not been validated for ensuring that the Rivaroxaban anticoagulant effect has resolved.

- **Use of bridging** – In general, the rapid offset and onset of rivaroxaban obviates the need for bridging anticoagulation.

- **Restarting** – Rivaroxaban can be resumed postoperatively when hemostasis has been achieved, at the same dose the patient was receiving preoperatively. Since rivaroxaban has a rapid onset of action, caution should be used in patients who have had major surgery or other procedures associated with a high bleeding risk.

C) <u>RECOMMENDATIONS FOR ENDOSCOPIC PROCEDURES:</u>

- **GENERAL APPROACH TO PATIENTS ON ANTITHROMBOTICS WHO NEED ENDOSCOPY:**
  - Delay elective endoscopy until patient at lower risk for TE if possible.
  - Consult physician/hematologist if any doubt

- Realize that only limited data exist
- Need to weigh the risks and benefits for each individual patient

UPPER GI ENDOSCOPY

Procedure	Bleeding Risk	Stop Aspirin?	Stop Clopidogrel?
Scope ± biopsy	Low	No	No
Scope + stricture dilatation	Low	No	No
Scope + stent placement	Low	No	Yes
Scope + variceal band ligation	High	No	Yes
Scope + PEG placement	High	No	Yes

COLONOSCOPY PROCEDURES

Procedure	Bleeding Risk	Stop Aspirin?	Stop Clopidogrel?
Scope ± biopsy	Low	No	No
Scope + polypectomy <1cm	Low	No	No
Scope + polypectomy >1cm	High	No	Yes

ERCP PROCEDURES

Procedure	Bleeding Risk	Stop Aspirin?	Stop Clopidogrel?
ERCP Diagnostic	Low	No	No
ERCP + stent placement	Low	No	No
ERCP + sphincterotomy	High	No	Yes
ERCP + sphincterotomy and large balloon papillary dilation	High	Yes	Yes

EUS PROCEDURES

Procedure	Bleeding Risk	Stop Aspirin?	Stop Clopidogrel?
EUS Diagnostic	Low	No	No
EUS + FNA solid mass	Low	No	Yes
EUS FNA cysts	High	Yes	Yes

- **WARFARIN MANAGEMENT PRIOR TO ENDOSCOPY:**
  - Avoid using Vitamin K to reverse anticoagulation before elective procedures because this delays therapeutic re-anticoagulation after procedure.
  - Warfarin can usually be stopped for 4-7 days and then be restarted the following day.
  - 1% risk of thromboembolic events after temporary warfarin cessation (Garcia, Arch Intern Med 2008)
  - High risk patients for thromboembolic events should consider bridging therapy with low molecular weight heparin.

GUIDELINES FOR CARDIAC PATIENTS ON WARFARIN:

TABLE 5. Periprocedural management of warfarin for patients with atrial fibrillation or valvular heart disease undergoing elective endoscopy

Condition	Associated diagnosis	Management
Atrial fibrillation	None	Hold warfarin 3-5 days before procedure. Restart warfarin within 24 h.*
	Mechanical valve(s) and/or history of cerebrovascular accident, transient ischemic attack, or systemic embolism	Hold warfarin and start UFH when INR $\leq$2.0. Stop UFH 4-6 h before procedure and restart after procedure. Resume warfarin on the evening of the procedure and continue both agents until INR is therapeutic.* Therapeutic doses of SQ UFH or LMWH may be considered in lieu of IV UFH.
Valvular heart disease	Mechanical bileaflet, aortic valve	Hold warfarin 48-72 h before procedure for a target INR $<$1.5. Restart warfarin within 24 h.*
	Mechanical mitral valve or mechanical aortic valve plus any of the following: atrial fibrillation, previous thromboembolic event, left ventricular dysfunction, hypercoagulable condition, mechanical tricuspid valve or $>$1 mechanical valve	Hold warfarin and start UFH when INR $\leq$2.0. Stop UFH 4-6 h before procedure and restart after procedure. Resume warfarin on the evening of the procedure and continue both agents until INR is therapeutic.* Therapeutic doses of SQ UFH or LMWH may be considered in lieu of IV UFH.

UFH, Unfractionated heparin; *INR*, international normalized ratio; *SQ*, subcutaneous; *LMWH*, low molecular weight heparin.
*Continuation or reinitiation of anticoagulation should be adjusted according to the stability of the patient and estimated risks surrounding the specific intervention/procedure performed. This table was adapted from the following guidelines: 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines[50] and American College of Cardiology/American Heart Association 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.[52]

SUMMARY:

- Most endoscopic procedures are safe to perform even if patient taking aspirin and/or NSAIDs.
- Continuing antithrombotic therapy may improve overall outcomes (i.e. survival after ACS) even if higher rate of re-bleeding.
- Need to individualize for each patient given limited data available for guidelines.

EMERGENCY SURGERY/PROCEDURES:

- **GENERAL POINTS**:
  -Reversal of the patient's usual anticoagulant may be required for more urgent or emergent surgery or procedures, or to treat perioperative bleeding.
  -Agents with a potential prothrombotic effect (e.g. prothrombin complex concentrates [PCCs], plasma products) should be reserved for the treatment of severe bleeding or anticipated severe bleeding (e.g. intracranial hemorrhage, emergent major surgery with elevated prothrombin time/internationalnormalized ratio [PT/INR]).

AGENT-SPECIFIC STRATEGIES INCLUDE THE FOLLOWING:

1) **WARFARIN:**
   -If reversal of warfarin or other vitamin K antagonists is required, the appropriate reversal strategy is determined by the degree of anticoagulation (e.g. PT/INR, clinical bleeding), urgency of the procedure, and degree of bleeding risk.

   -If ***semi-urgent*** reversal of warfarin is required (e.g. within one to two days), warfarin should be withheld and ***vitamin K*** administered (e.g. 2.5 to 5.0 mg of oral or intravenous vitamin K). Usually no need for FFPs.
   -If ***immediate reversal*** is required (e.g. for emergent surgery or active bleeding), this can be achieved via the use of ***prothrombin complex concentrates (PCCs)*** or ***plasma products (e.g. Fresh Frozen Plasma***) along with ***vitamin K***. Four-factor PCCs contain adequate amounts of all vitamin K-dependent clotting factors, whereas three-factor PCCs may require supplementation with FFP for adequate factor VII.
   -However, there is a thrombotic risk associated with these products, and they should be used only if there is life-threatening bleeding and prolongation of the INR by a vitamin K antagonist.

2) **DIRECT THROMBIN INHIBITORS (e.g. DABIGATRAN) AND DIRECT FACTOR Xa inhibitors (e.g. RIVAROXABAN):**

-Unfortunately there is no specific reversal agents for these class of anticoagulants.

-Generally one needs to wait until the anticoagulation effect has fully resolved if the urgency of the procedure/surgery permits it.

- Usually it requires about 5 half-lives to have elapsed since the last dose for the anticoagualation effect to have resolved.

●Dabigatran – (Half life=12 to 17 hours); five half-lives will have elapsed by day 2.5 to 3.5 after the last dose.

●Rivaroxaban – (Half life=7 to 17 hours); five half-lives will have elapsed by day 1.5 to 3.5 after the last dose.

3) ANTI-PlATELET AGENTS:

- In patients who require urgent surgery that necessitates eliminating the antiplatelet effects of aspirin/clopidogrel (i.e. moderate to high bleeding risk surgery), administering 5-10 units of platelets can be done.

CONCLUSION:

- Perioperative anticoagulant management involves a team of health care providers which include the surgeon, anesthetist, internist/hematologist, nurse and the patient. Effective communication of planned management among health care providers and with the patient is essential to optimize patient care.

- The anesthetist should communicate about the planned anesthesia since the type used (i.e. general vs. spinal/epidural) will have implications on ensuring no residual antithrombotic effect at the time of surgery and the type of postoperative anticoagulation.

- The surgeon and haematologist should confer on the adequacy of postoperative haemostasis and safe time to resume postoperative bridging anticoagulation.

- The patient should be provided with clear instruction regarding the perioperative stopping/starting of warfarin and LMWH.

- **Management of antithrombotic agents in the <u>ELECTIVE</u> endoscopic setting**

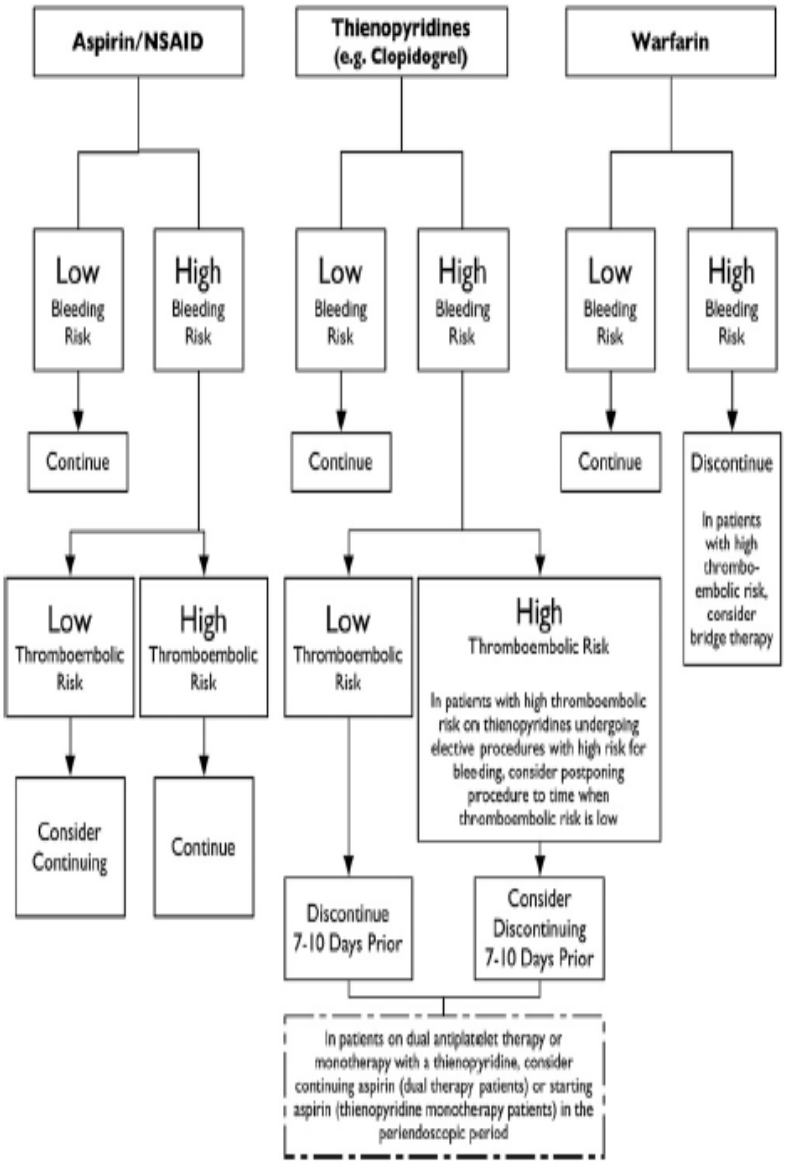

Figure 1. Management of antithrombotic agents in the elective endoscopic setting.

- **Management of antithrombotic agents in the <u>URGENT</u> endoscopic setting**

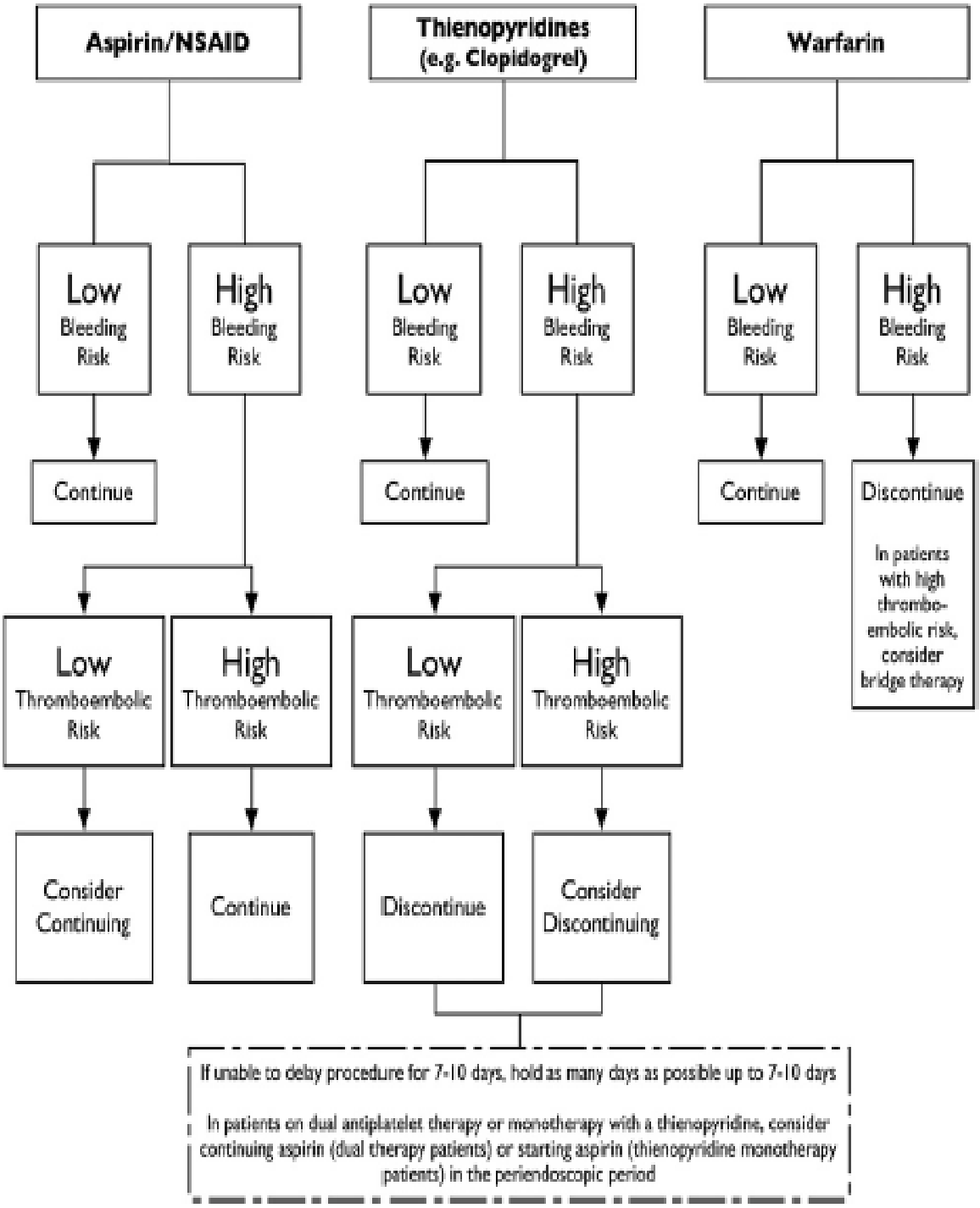

Figure 2. Management of antithrombotic agents in the urgent endoscopic setting.

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CHALLENGES OF LAPAROSCOPIC SURGERY IN THE ELDERLY

CHRONOLOGIC AGE ALONE IS A POOR PREDICTOR OF OUTCOME

The elderly are increasingly fit and healthy. Chronologic age is a marker of declining physiologic reserve and the likelihood of comorbidities. This does not necessarily translate to poorer operative outcomes(1). A more accurate predictor of outcome in the elderly patient is an assessment of frailty, disability and comorbidity. These factors are more likely to render a patient less resistant to physiological stressors such as major surgery. A simple suggestion to measure these variables is depicted in the table below(2).

Frailty	Disability	Comorbidity
Cognition (Mini-Cog test ≤3) Falls ≥ 1 in last six months Albumin ≤33 g/l Haematocrit ≤35%	Dependence on ≥ 1 activity of daily living	Charlson index ≥3

Surgery in the elderly is generally delayed and becomes complicated for two main reasons. A missed or delayed diagnosis secondary to atypical presentation of disease and the postponement of elective surgery because of the misconception that that an elderly patient will suffer a poorer outcome because of advanced age alone(3).

LAPAROSCOPIC SURGERY IN THE ELDERLY

Laparoscopy has become the gold standard for many surgical procedures. The benefits of laparoscopy are well documented, however there is concern in the elderly frail patient whether they reap the same benefits that are seen in younger patients. The risk associated with the physiological demand of laparoscopy may outweigh the benefits(4).

The Physiology of Ageing and Laparoscopy

Laparoscopic surgery presents unique hemodynamic and ventilatory effects that may increase the risk of cardiovascular and pulmonary complications, particularly in the elderly patient with several comorbidities(3). As the body ages, there is a decline in the normal function of most organ systems. These changes have the potential to become significant with the stress of surgery (5).

AGE-RELATED CHANGES IN PHYSIOLOGY THAT AFFECT OPERATIVE RISK(5)	
Pulmonary	**Neurologic**
Decreased alveolar elasticity Increased residual volume Decreased chest wall compliance	Blunted autonomic reflexes Increased risk of delirium
Cardiac	**Metabolic**
Increased incidence of arrhythmia Decreased cardiac output Increased prevalence of coronary artery disease	Decreased lean body mass
Vascular	**Immune system**
Decreased vessel compliance Increased prevalence of atherosclerosis	Decreased T-cell and antibody responses
Renal	**Skin**
Decreased GFR Altered electrolyte regulation	Atrophy Loss of collagen

The physiologic changes during laparoscopic surgery occur mainly due to two reasons; creation of the pneumoperitoneum and patient position during surgery(6). Other challenges in the elderly are abdominal access and duration of laparoscopic compared to open surgery.

Pneumoperitoneum

The gas most commonly used for creation of pneumoperitoneum is carbon dioxide (CO_2). The CO_2-induced pneumoperitoneum exerts its physiological effects via two different mechanisms:

1. Mechanical effects due to increased intraperitoneal pressure
2. Chemical effect of CO_2 used for insufflation

Mechanical effects

- Pulmonary - pneumoperitoneum leads to an increase in intra-abdominal pressure and consequent elevation of the diaphragm. This results in collapse of basal lung tissue ultimately causing decreased functional residual capacity, ventilation perfusion ratio mismatch and increase intrapulmonary shunting of blood, which all lead to hypoxaemia(6,7). Ageing diminishes respiratory reserve. Elderly patients have decreased sensitivity to hypoxia and hypercapnia, which results in a diminished ventilatory response to heart failure, infection, or exacerbation of underlying lung disease all of which may contribute to postoperative morbidity(4).

- Cardiovascular - pneumoperitoneum causes compression of the inferior vena cava, which leads to a reduction in venous return resulting in decreased cardiac output and increased central venous pressure. There is a rise in mean arterial pressure and systemic vascular resistance which further decrease cardiac output. Rapid stretch of the peritoneum can cause a vagovagal reflex with bradycardia and hypotension(1). The age-related changes described above together with the effects of pneumoperitoneum place the patient at risk for myocardial infarction and heart failure(4,8).

- Renal - pneumoperitoneum has important effects on renal physiology. Direct compression of the renal vasculature, ureters and kidneys can lead to a reduction in renal blood flow, glomerular filtration rate, and oliguria. The physiological effects of ageing on the kidney in combination with pneumoperitoneum may provoke renal failure(8).

Chemical affects

CO2 pneumoperitoneum may result in a significant rise in serum CO2, which converts to carbonic acid and translates to a decreased serum pH. Patients with severe cardiac or pulmonary disease are at risk from the resulting acidosis(7). The hypercarbia, acidosis, sympathetic stimulation from decreased venous return and vagal stimulation by stretching of peritoneum disturb cardiac rhythm. Another problem with CO2 is retained pockets of gas, most commonly under the diaphragm, which causes abdominal pain referred to the shoulder(9). Although this generally resolves within 24 to 48 hours it may compromise respiration and increase postoperative analgesia requirements.

Patient position

Laparoscopic procedures are performed in either the Trendelenburg or reverse Trendelenburg positions. This impacts cardiopulmonary function(7).

- Trendelenburg: there is an increase in preload due to an increased venous return from the lower extremities. There is also cephalic shifting of viscera, which accentuates the pressure on the diaphragm(6).
- Reverse Trendelenburg: produces favourable ventilatory changes yet unfavourable cardiovascular effects. There is caudal shifting of the viscera, which relieves pressure on the diaphragm and improves tidal volume. There is also decrease in the preload and venous return

which result in hypotension. Pooling of blood in the lower extremities predisposes to deep vein thrombosis(6,11).

Abdominal access

Elderly patients have reduced muscle mass, thinner fascial layers, reduced subcutaneous fat and thinner skin. In addition, these patients are more likely to have undergone previous abdominal surgery, simply by being alive for longer, which adds the issue of adhesions. This makes laparoscopic entry more challenging and potential exists for visceral and vascular injury.

Longer operating times

Laparoscopic procedures can take significantly longer than their open counterparts. This is especially true for surgeons less experienced with a procedure. There is an association between operating time and complications such as venous thromboembolism, surgical site infection, bleeding, haematoma formation and pneumonia (12). This can be particularly detrimental to elderly patients who are prone to complications.

STEPS TO ENSURE SAFE LAPAROSCOPY IN THE ELDERLY

General measures

- Reduced insufflation pressure: literature suggests keeping pressures between 8mmHg and 12mmHg(10).
- Ventilatory strategies: increased respiratory rate and FiO2 with a PEEP of around 5cm H_2O (6).
- Adequate preoperative hydration to minimise cardiovascular and renal compromise.
- Minimise operating time by enlisting the help of an experienced laparoscopic surgeon.
- Avoid extreme positioning of the patient.
- Sequential compression stockings to prevent deep vein thrombosis.
- Preoperative consultation with a geriatric physician and anaesthetist for all patients with cardiopulmonary compromise.

Alternatives to CO2 pneumoperitoneum

- Gasless pneumoperitoneum using abdominal wall retraction devices
- Alternate gasses for pneumoperitoneum: Identifying an ideal insufflation gas to replace carbon dioxide has attracted much research. Gases such as helium, argon, nitrous oxide, and room air have been studied as alternatives to carbon dioxide. Each has shortcomings and has not found place for routine use.

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MANAGEMENT OF MAJOR ABDOMINAL TRAUMA IN PREGNANCY

Mr Thabo Mothabeng

INTRODUCTION

Over the years, trauma has remained a leading cause of non-obstetric maternal mortality, with a significant number of deaths directly related to injuries (kuhlman 1994, Aggarwal, 2018).

In South Africa the leading causes of trauma in pregnant patients are motor vehicle accidents and intimate partner violence; other common causes are falls and parasuicide.

The challenges of managing a pregnant injured patients are exacerbated by physiologic and anatomical changes, effects of radiologic exposure on the foetus and need for a multidisciplinary team and advanced care facilities to manage the these patients.

SCOPE OF PRESENTATION

This presentation briefly discusses an approach to the patient while considering the following points.

a. Physiologic and anatomic changes in a pregnant patient.
b. Evidence based approach to the management of maternal trauma
c. Perimortem caesarean section
d. General principles for the primary care giver

SUMMARY

Management of pregnancy trauma patient focuses on initial assessment and resuscitation of the mother according to priorities. The approach should focus on optimal management of the mother in order to ensure foetal wellbeing (Nel, 2018)

This should take into account physiologic and anatomic changes that require modifications of technique. Foetal monitoring throughout resuscitation is crucial.

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Challenges of severe trauma in children PROF SHAIK

Transitional care in the child with pediatric surgical disease

According to Wikipedia transitional care refers to the coordination and continuity of health care during movement from one healthcare setting to another as care needs change during the course of chronic or acute illness.

Families with children with chronic illness often have a network of providers from the time of birth. Relationships form between families and providers and often providers and families are reluctant to transition of care to a new group as children grow up. However, adolescents develop very different relationships with parents as well as physicians. Establishing independence and taking on more responsibility for their own care is a vital part of young adulthood. Transfer of care from a pediatric to an adult provider or team is a part of this important process as well. Suggestions for timing of transition include life milestones such as completion of high school, 18 years of age, marriage, pregnancy, or disease-free interval that make transition easier for the patient and the provider.

Disease-specific knowledge

It is important that an adolescent who is about to change over to the care of an adult practitioner has an understanding of his disease. A lack of understanding of concerning symptoms, or complications may delay seeking treatment and may impede care delivery when the parents are not always available anymore to assist their child.

Becoming an independent decision maker with regard to follow-up and continuing care can be a particular challenge in adolescents and young adults with chronic disease, as they may experience psychosocial developmental delay.

Differences in child-centered and adult-oriented care

Adult practitioners rely on subspecialty referral and coordination by primary care providers, whereas pediatric practitioners may have a more multidisciplinary, family-focused approach. Appointments for adult patients may be shorter than pediatric patients, and providers are likely to expect from the young grown ups to provide a relevant history and to be knowledgeable about their disease. Adult providers may have different goals for visits compared with their pediatric counterparts, for example, valuing independence and the ability to undergo procedures without sedation, while patients and families might still be anxious and unable to let go from each other. Being aware of the problems the patient encounters when becoming an adult helps with smooth transition from pediatric to adult care.

Transitional care model

Arranging a single combined visit with pediatric and adult practitioners in the adult care office is beneficial to decrease family anxiety about transition and increase adherence to the plan of care. A collaborative approach in which the pediatric surgeon remains available and involved with the adult gastroenterologist and adult surgeon offers the highest likelihood of patient and family satisfaction and the best outcome for the patient.

Patients, families, and providers will feel more comfortable transitioning to an adult provider who is familiar with complex gastrointestinal disease and who has been provided relevant medical records. Fur-

thermore, it is important to help patients and families identify reliable sources of information beyond the physician, including patient associations or disease-specific support groups, as follow-up visits may be less frequent in adult care centers.

Considerations in the transitional care for specific pediatric gastrointestinal surgical conditions

Short bowel syndrome

Short bowel syndrome (SBS) is most often a result of an initial insult that requires massive bowel resection. A central principle of the standard treatment of infants and children with SBS is the provision of safe parenteral nutrition (PN) via a tunneled, long-term central line. PN is lifesaving and provides caloric, fluid, and electrolyte needs for adequate homeostasis and growth. Despite this, long-term PN carries the known risks of catheter-associated blood stream infections, PN-associated liver disease (PNALD), and venous thrombosis, especially when used over a long period of time. When possible, enteral nutrition is optimal, as direct mucosal stimulation by food promotes intestinal adaptation that can partially or fully compensate for functional loss of the resected bowel. Dysmotility and intestinal dilatation can predispose to luminal bacterial overgrowth and sometimes sepsis. While many children with SBS are able to eventually achieve enteral autonomy, some remain PN-dependent over the long-term and some, although not needing PN anymore, may still require fluids, electrolytes, and other supplements.

Hirschsprung Disease

Hirschsprung Disease (HD) is one of the most common defects in colorectal function, affecting roughly 1 in 5000 live births. Characterized by aganglionosis of the rectum extending proximally for a variable distance into the colon, HD is most often limited to the rectosigmoid, but total colonic aganglionosis and even more rarely panintestinal aganglionosis have been reported. Treatment involves a pull-through procedure that is most commonly performed in neonates or infants. Historically favorable functional outcomes have been reported in the pediatric literature; however, defecation disorders, dysmotility, enterocolitis, and stricture remain important long-term complications. Follow-up studies extending into adulthood report impaired bowel function of variable degrees. In addition, studies on quality of life show lower scores for HD patients in physical health and psychosocial wellbeing compared with healthy controls. For the above reasons, although a significant portion oft he treatment of HD occurs during infancy and childhood, problems can persist and require care into young adulthood and beyond. In patients who have ongoing concerns into adolescence, transition should occur to adult practitioners who have a working knowledge of the care of patients with HD. A complete summary of the history is important (length of Hirschprung segment and type of resection including perioperative complications), and an appreciation for complications such as stooling dysfunction and Hirschsprung-associated enterocolitis is critical. A combined effort for long-term follow-up involving general surgeons and gastroenterologists can provide the needed expertise for patients with HD, and input from the pediatric surgeon should be available as needed.

Anorectal malformation

Anorectal malformation(ARM) is a broad term that encompasses diseases involving the anus and the rectum, as well as the urinary and/or genital tracts, and is one of the most common anatomic colorectal defects affecting 1 in between 3000 and 5000 live births. The severity of the abnormality can range from a mild or “low” defect to a severe or “high” defect, and long-term outcomes in these patients depend

heavily upon the extent of disease and structures impacted by surgical repair. Surgical treatment of ARMs has undergone significant change over the last 50 years. The current approach involves a midline posterior sagittal incision with identification of the rectum, division of any connections between the rectum and the urinary or reproductive tracts, and creation of an anoplasty at the location of the sphincter musculature. During the evaluation and treatment of patients with ARMs, preservation of bowel function, bladder control, and sexual function is considered important, since these appear to most directly impact eventual quality of life. ARMs can be associated with other congenital abnormalities such as cardiac, tracheo-esophagel, genitourinary, and spinal anomalies. The presence or absence of associated abnormalities should be evaluated and documented for future reference. Surgical repair of an ARM most commonly occurs in patients at birth or before 1 year of age. On occasion, an older patient with a subtle anomaly may present for surgical consultation regarding a previously unrecognized ARM. While it is difficult to predict all the needs for adult patients with ARM, a team including a general or colorectal surgeon, a gastroenterologist, and a gynecologist for female patients, should be capable of providing the necessary care as ARM patients reach adulthood.

Childhood cancer survivors

Nephrectomy is a common pediatric cancer surgery used for Wilms tumor. Nephrectomy may affect future renal function, although this relationship is confounded by the impact of neph-rotoxic chemotherapy. Survivors with a single kidney should have their blood pressure, renal function and electrolytes checked annually. Nephrotoxic drugs (eg aminoglycoside antibiotics) should be avoided and NSAIDs used cautiously.

Splenectomy as part of staging laparotomy is no longer a standard practice in children with Hodgkin's lymphoma.

Spinal surgery (laminectomy) or radiotherapy that involves the spinal column can lead to scoliosis and kyphosis. Both intraspinal tumors and tumors that develop adjacent to the spine (eg neuroblastoma) can be indications for spinal surgery. These patients should undergo yearly spinal exam to assess for scoliosis and kyphosis until growth is completed.

Secondary malignant neoplasm (SMN) occurs in about 10 - 30% of long term childhood cancer survivors and is associated with chest radiotherapy (RT) for Hodgkin's lymphoma. These patients should get early surveillance with MRI and mammography. Previous RT might impede healing after biopsy and surgery and may prevent lumpectomy as an option as further radiation exposure may not be possible. Patients who received more than 35-Gy radiation exposure to the abdomen have a high risk to develop secondary colon cancer and therefore should receive early surveillance with colonoscopy starting at 35 years of age.

Survivors who have been treated with anthracycline chemotherapy (doxorubicin and daunorubicin) are at increased risk for cardiomyopathy because of cardiac myocyte damage. Anthracyclines are used by about 50% of children with cancer. Cardiac dysfunction in most cases manifests only after years or decades after treatment. If surgery is needed in a previous childhood cancer survivor one should watch out for any clinical or subclinical manifestation of cardiac disease.

Pulmonary late effects: Knowledge of previous therapy with certain chemotherapy agents (bleomycin, busulfan, nitrosoureas) or radiation of a field that involved the lungs is important for making decisions

about the safety of surgery and anaesthesia. Interstitial lung disease is the most frequent manifestation of cancer therapy, but airways disease and pulmonary vascular disease can also occur.

Challenges in surgery for preterm babies PROF LOVELAND

(CHALLENGES IN) Management of burns in children PROF SHAIK

Ethical Considerations in Bariatric Surgery in a Developing Country

PROF THERESA ROSSOUW

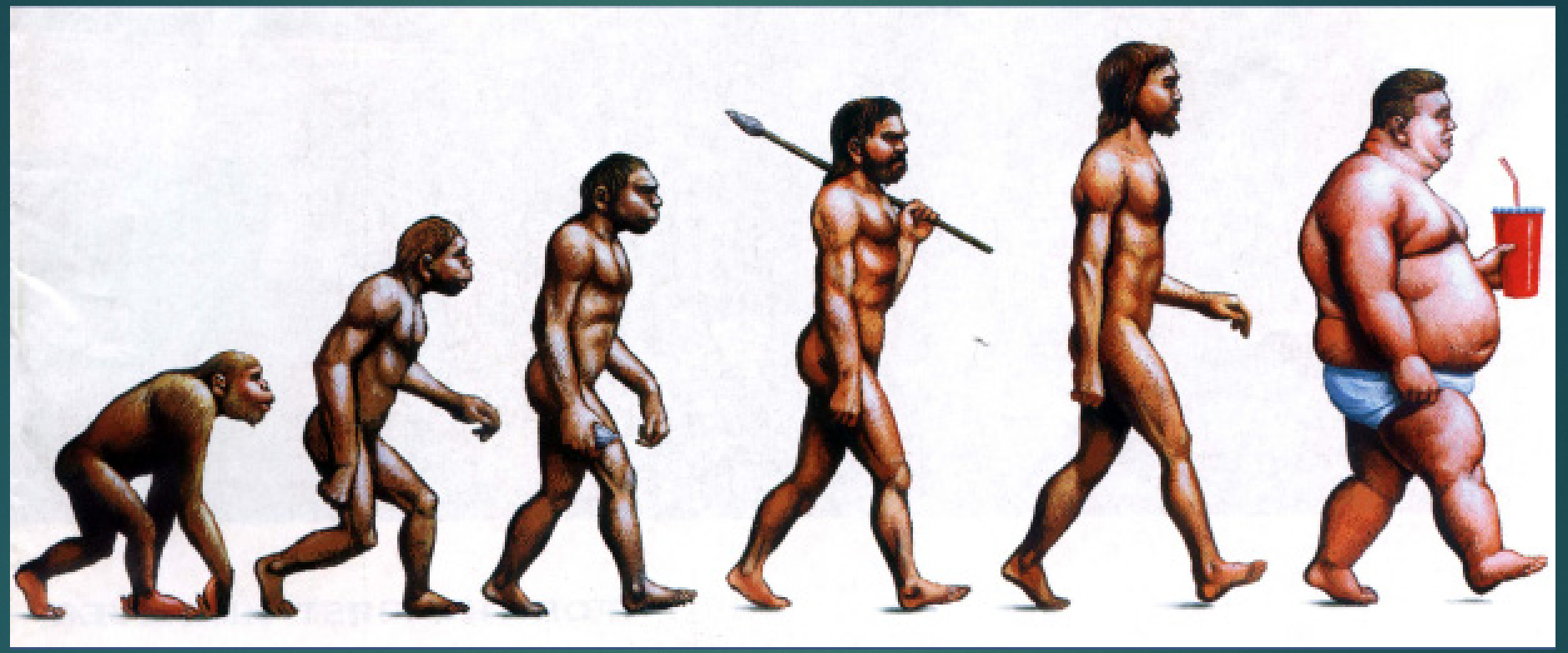
UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

23rd Annual Controversies and Problems in Surgery Symposium

Outline of Presentation

- Setting the scene
  - Morbid obesity
  - Bariatric surgery
- Ethical considerations
  - Responsibility
  - Genetic determinism
  - Medicalization on obesity
  - Autonomy
  - Distributive justice

Obesity is the fastest growing health problem worldwide



What is Obesity?

- An energy surplus over time, stored in the body as fat
- Calculated with Body Mass Index (BMI)
  - BMI= 25+ → Overweight
  - BMI= 30+ → Obese
  - BMI= 40+ → Morbidly Obese

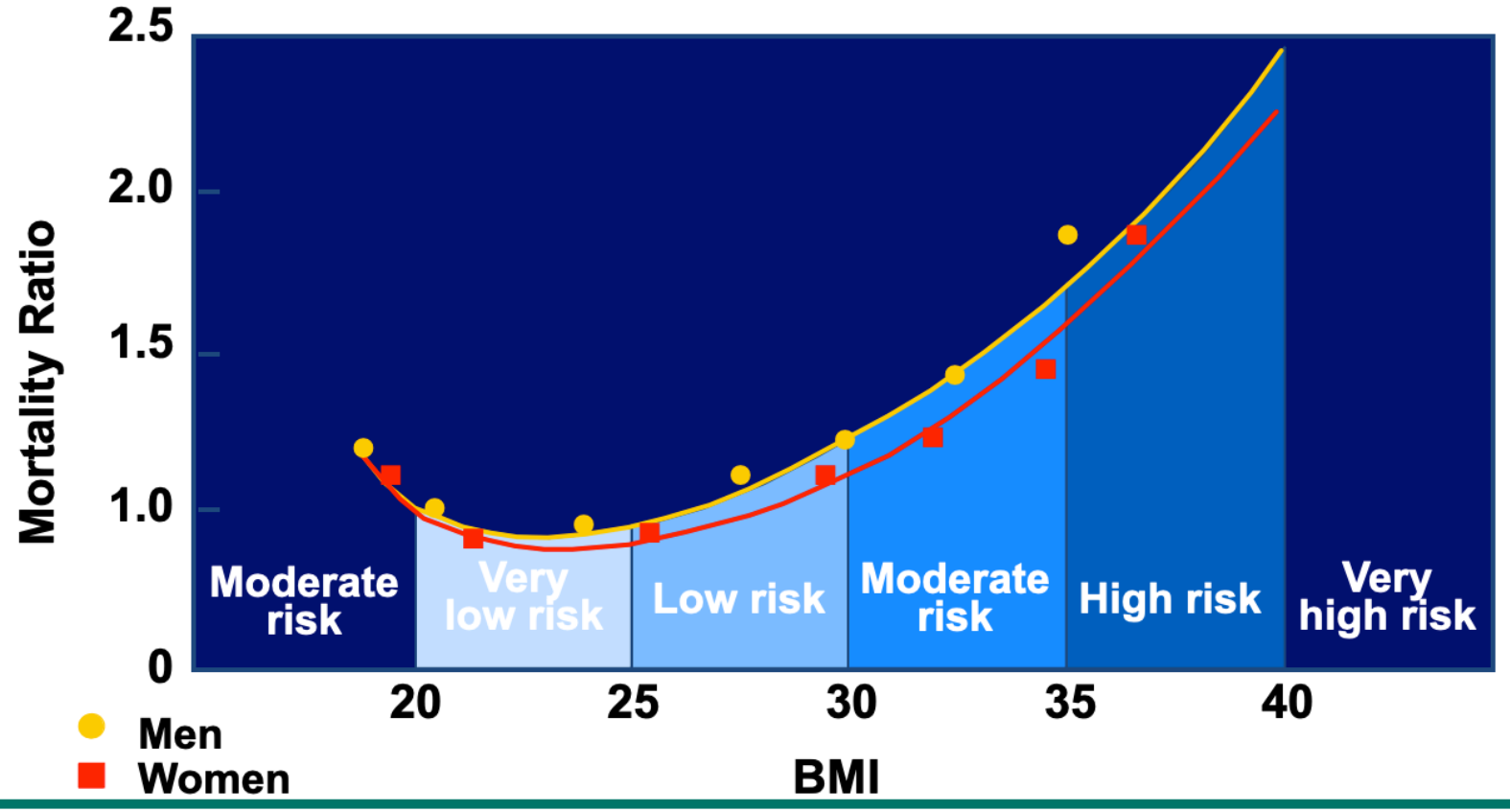
WEIGHT	lbs	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250	260	270	280	290
	kgs	41	45	50	54	59	64	68	73	77	82	86	91	95	100	104	109	113	118	122	127	132
HEIGHT			Underweight					Healthy				Overweight				Obese				Extremely Obese		
ft/in	cm																					
4'8"	142.2	20	22	25	27	29	31	34	36	38	40	43	45	47	49	52	54	56	58	61	63	65
4'9"	144.7	19	22	24	26	28	30	32	35	37	39	41	43	45	48	50	52	54	56	58	61	63
4'10"	147.3	19	21	23	25	27	29	31	33	36	38	40	42	44	46	48	50	52	54	56	59	61
4'11"	149.8	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	51	53	55	57	59
4'12"	152.4	18	20	21	23	25	27	29	31	33	35	37	39	41	43	45	47	49	51	53	55	57
5'1"	154.9	17	19	21	23	25	26	28	30	32	34	36	38	40	42	43	45	47	49	51	53	55
5'2"	157.4	16	18	20	22	24	26	27	29	31	33	35	37	38	40	42	44	46	48	49	51	53
5'3"	160.0	16	18	19	21	23	25	27	28	30	32	34	35	37	39	41	43	44	46	48	50	51
5'4"	162.5	15	17	19	21	22	24	26	27	29	31	33	34	36	38	39	41	43	45	46	48	50
5'5"	165.1	15	17	18	20	22	23	25	27	28	30	32	33	35	37	38	40	42	43	45	47	48
5'6"	167.6	15	16	18	19	21	23	24	26	27	29	31	32	34	36	37	39	40	42	44	45	47
5'7"	170.1	14	16	17	19	20	22	24	25	27	28	30	31	33	34	36	38	39	41	42	44	45
5'8"	172.7	14	15	17	18	20	21	23	24	26	27	29	30	32	33	35	37	38	40	41	43	44
5'9"	175.2	13	15	16	18	19	21	22	24	25	27	28	30	31	33	34	35	37	38	40	41	43
5'10"	177.8	13	14	16	17	19	20	22	23	24	26	27	29	30	32	33	34	36	37	39	40	42
5'11"	180.3	13	14	15	17	18	20	21	22	24	25	27	28	29	31	32	33	35	36	38	39	40
5'12"	182.8	12	14	15	16	18	19	20	22	23	24	26	27	28	30	31	33	34	35	37	38	39
6'1"	185.4	12	13	15	16	17	18	20	21	22	24	25	26	28	29	30	32	33	34	36	37	38
6'2"	187.9	12	13	14	15	17	18	19	21	22	23	24	26	27	28	30	31	32	33	35	36	37
6'3"	190.5	11	13	14	15	16	18	19	20	21	23	24	25	26	28	29	30	31	33	34	35	36
6'4"	193.0	11	12	13	15	16	17	18	19	21	22	23	24	26	27	28	29	30	32	33	34	35
6'5"	195.5	11	12	13	14	15	17	18	19	20	21	23	24	25	26	27	28	30	31	32	33	34
6'6"	198.1	10	12	13	14	15	16	17	18	20	21	22	23	24	25	27	28	29	30	31	32	34
6'7"	200.6	10	11	12	14	15	16	17	18	19	20	21	23	24	25	26	27	28	29	30	32	33
6'8"	203.2	10	11	12	13	14	15	16	18	19	20	21	22	23	24	25	26	27	29	30	31	32
6'9"	205.7	10	11	12	13	14	15	16	17	18	19	20	21	23	24	25	26	27	28	29	30	31
6'10"	208.2	9	10	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
6'11"	210.8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	25	26	27	28	29	30

Image: www.bmicalculator.mes.fm/bmi-chart

Common Co-morbidities

Obesity Increases Mortality

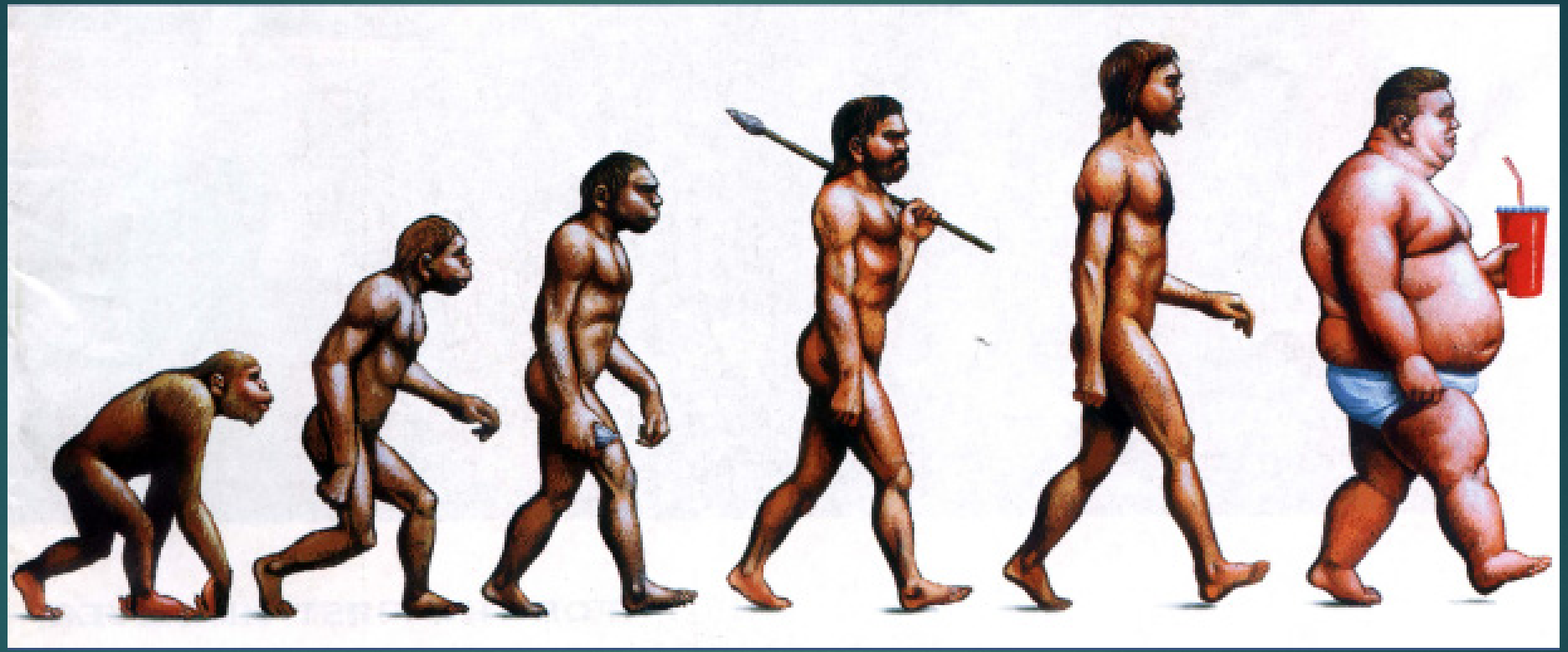
*Reprinted from Medical Clinics of North America, Vol 73, Gray DS, Diagnosis and prevalence of obesity, pp1-13, Copyright 1989, with permission from Elsevier.



Annals of Internal Medicine

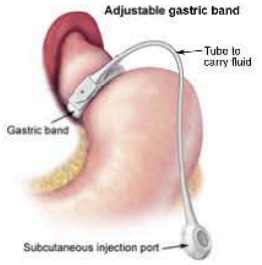
Beth Israel Deaconess Medical Center

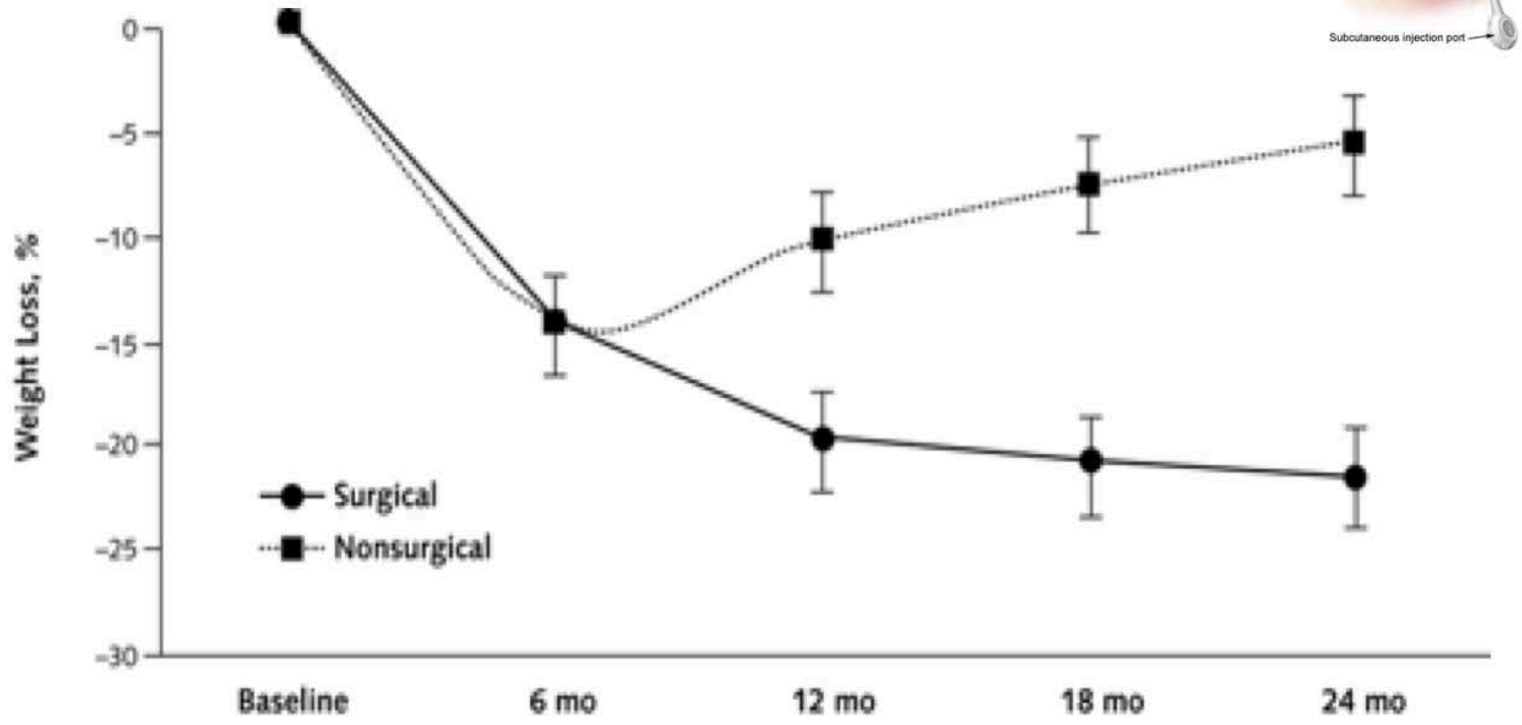
Obesity is the fastest growing health problem worldwide



Desire for early visible results with apparently no effort and low risk

LAGB vs. Diet/Exercise





*O'Brien PE, Dixon JB, Laurie C, Skinner S, Proietto J, McNeil J, et al. Treatment of mild to moderate obesity with laparoscopic adjustable gastric banding or an intensive medical program: a randomized trial. Ann Intern Med. 2006;144:625-633.

*Adapted from Atlas of Metabolic and Weight Loss Surgery published by Cine-Med Publishing, Inc., 2010, www.cine-med.com.

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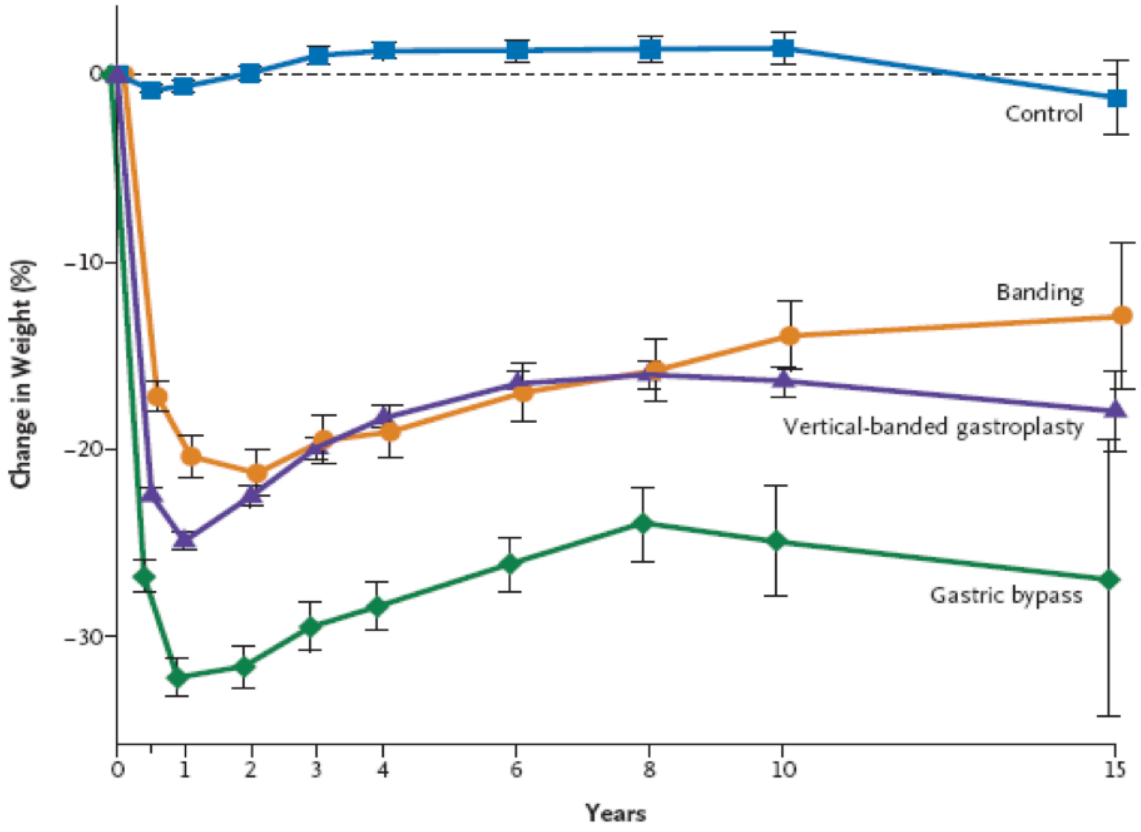
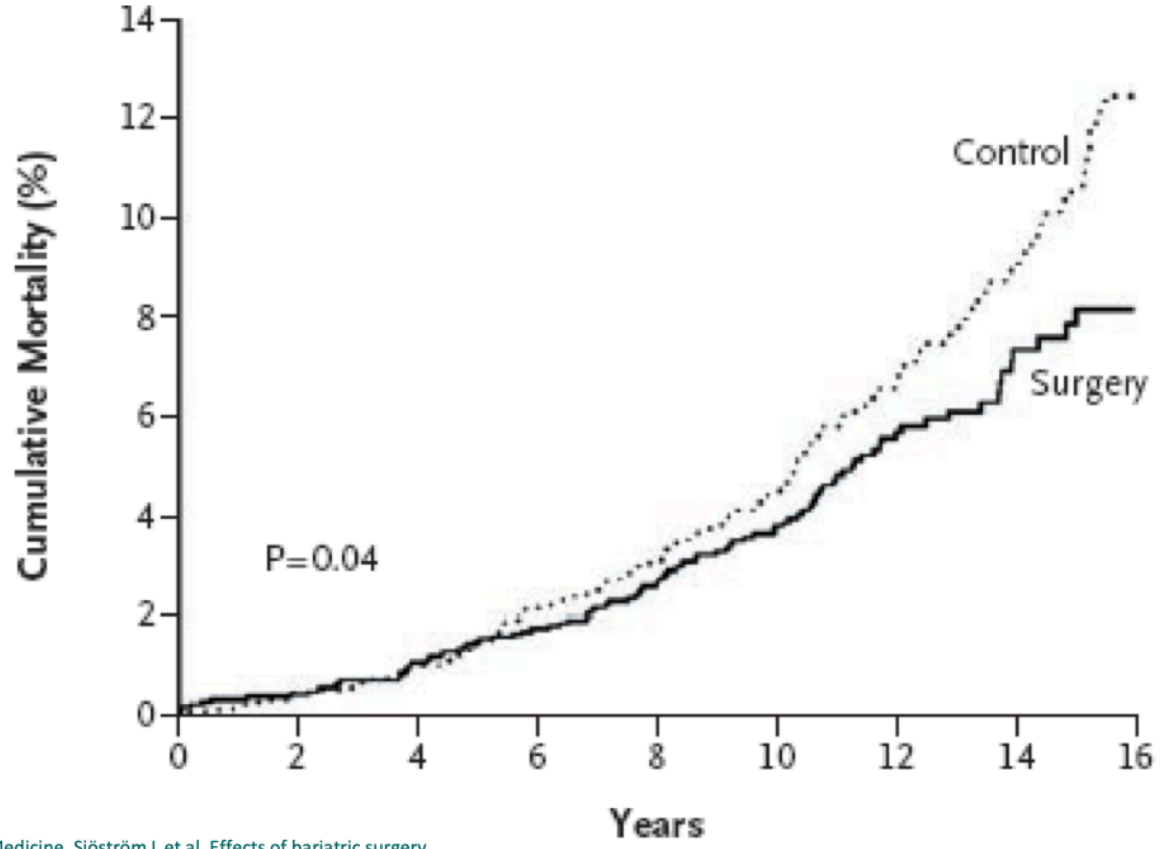
Diets don't work



*From New England Journal of Medicine, Sjöström L et al, Effects of bariatric surgery on mortality in Swedish obese subjects, Vol 357, pp741-752. Copyright © 2007. Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

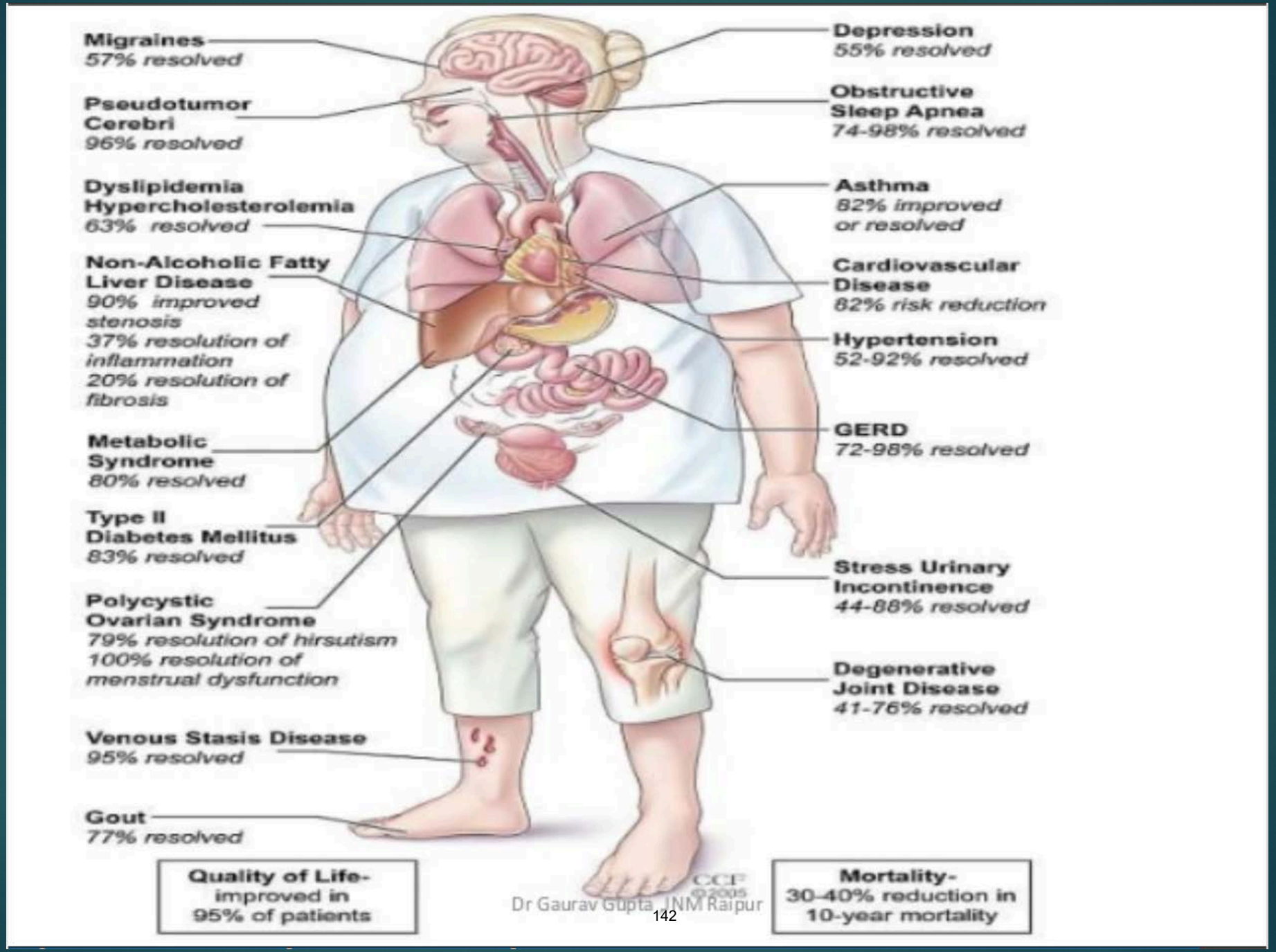
Die earlier if don't get surgical treatment



*From New England Journal of Medicine, Sjöström L et al, Effects of bariatric surgery on mortality in Swedish obese subjects, Vol 357, pp741-752. Copyright © 2007. Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Is Bariatric Surgery a Safe and Effective Method to Treat Obesity?

- Good data
  - Weight loss
    - 95% weight loss of at least 25% of excess body weight
      - Puia et al. Ethical considerations in bariatric surgery in a developing country. Clujul Medical Vol.90, No.3, 2017: 268-272
  - Normalisation of glycaemia
  - Normalisation of blood pressure etc


Migraines
57% resolved
Pseudotumor Cerebri
96% resolved
Dyslipidemia
Hypercholesterolemia
63% resolved
Non-Alcoholic Fatty Liver Disease
90% improved stenosis
37% resolution of inflammation
20% resolution of fibrosis
Metabolic Syndrome
80% resolved
Type II Diabetes Mellitus
83% resolved
Polycystic Ovarian Syndrome
79% resolution of hirsutism
100% resolution of menstrual dysfunction
Venous Stasis Disease
95% resolved
Gout
77% resolved
Depression
55% resolved
Obstructive Sleep Apnea
74-98% resolved
Asthma
82% improved or resolved
Cardiovascular Disease
82% risk reduction
Hypertension
52-92% resolved
GERD
72-98% resolved
Stress Urinary Incontinence
44-88% resolved
Degenerative Joint Disease
41-76% resolved
Quality of Life-
improved in
95% of patients
Mortality-
30-40% reduction in
10-year mortality
©2005

Limited Information

- Mortality benefit
- Other long-term data mostly from:
  - Observational cohorts with inadequate comparators (no active intervention control, limited matching)
  - Caucasian/ middle-aged, RYGB
  - Mortality benefit greater for BMI >45
- RCTs
  - Small, short-term
  - Limited to T2DM/ BMI 30-40
- Incomplete data
  - Changes in levels of microelements
  - Changes in bone minerals, density and fracture risk

*Admiraal WM, Celik F, Gerdes VE, Dallal RM, Hoekstra JB, Holleman F. Ethnic differences in weight loss and diabetes remission after bariatric surgery: a meta-analysis. Diabetes Care. 2012;35:1951-1958.
*Wood GC, Benotti PN, Lee CJ, Mirshahi T, Still CD, Gerhard GS, et al. Evaluation of the Association Between Preoperative Clinical Factors and Long-term Weight Loss After Roux-en-Y Gastric Bypass. JAMA Surg. 2016;151:1056-1062.

*Amouyal C, Andreelli F. What is the evidence for metabolic surgery for type 2 diabetes? A critical perspective. Diabetes Metab. 2017;43:9-17.
*Adams TD, Gress RE, Smith SC, Halverson RC, Simper SC, Rosamond WD, et al. Long-term mortality after gastric bypass surgery. N Engl J Med. 2007;357:753-761.

Risks of Bariatric Surgery

- Weight regain over time
  - 20% weight loss in 10 years
    - 75% of RYGB
    - 25% of gastric banding
  - Worst results: remove the adjustable gastric ring → 90% returning to at least the initial weight
- Relapse in co-morbidities (1/3 for DM)
- Unknown long-term consequences
  - ↑ alcohol/ substance abuse
  - 8% develop new high-risk drinking
  - ↑ risk of suicide/ accidents/ overdose

*Adams TD, Gress RE, Smith SC, Halverson RC, Simper SC, Rosamond WD, et al. Long-term mortality after gastric bypass surgery. N Engl J Med. 2007;357:753-761.
*King WC, Chen JY, Mitchell JE, Kalarchian MA, Steffen KJ, Engel SG, et al. Prevalence of alcohol use disorders before and after bariatric surgery. JAMA. 2012;307:2516-2525.
*Wee CC, Mukamal KJ, Huskey KW, Davis RB, Colten ME, Bolcic-Jankovic D, et al. High-risk alcohol use after weight loss surgery. Surg Obes Relat Dis. 2014;10:508-513.

Risks of Bariatric Surgery

- RYGB - ↑ PUD risk → NSAIDs contra-indicated
- Preferential loss of muscle/bone → ↑ risk of sarcopaenia, bone loss
  - RYGB: 35% weight loss; 10% bone loss
  - Lifestyle: 10% weight loss; 1-2% bone loss
  - 2-3 x higher ratio bone loss to weight loss

*Carrasco F, Ruz M, Rojas P, Csendes A, Rebolledo A, Codoceo J, et al. Changes in bone mineral density, body composition and adiponectin levels in morbidly obese patients after bariatric surgery. Obes Surg. 2009;19:41-46.
*Shapses SA, Sukumar D. Bone metabolism in obesity and weight loss. Annu Rev Nutr. 2012;32:287-309.

Lifestyle Interventions Better than Believed?

- Data based on large, long-term RCTs
  - 5-10% over long-term
  - Prevents T2DM by 50%, ↓ CV risk
  - Better safety
- 60% more effective in older patients
- High protein diet + resistance exercise minimizes preferential loss of muscle vs. fat

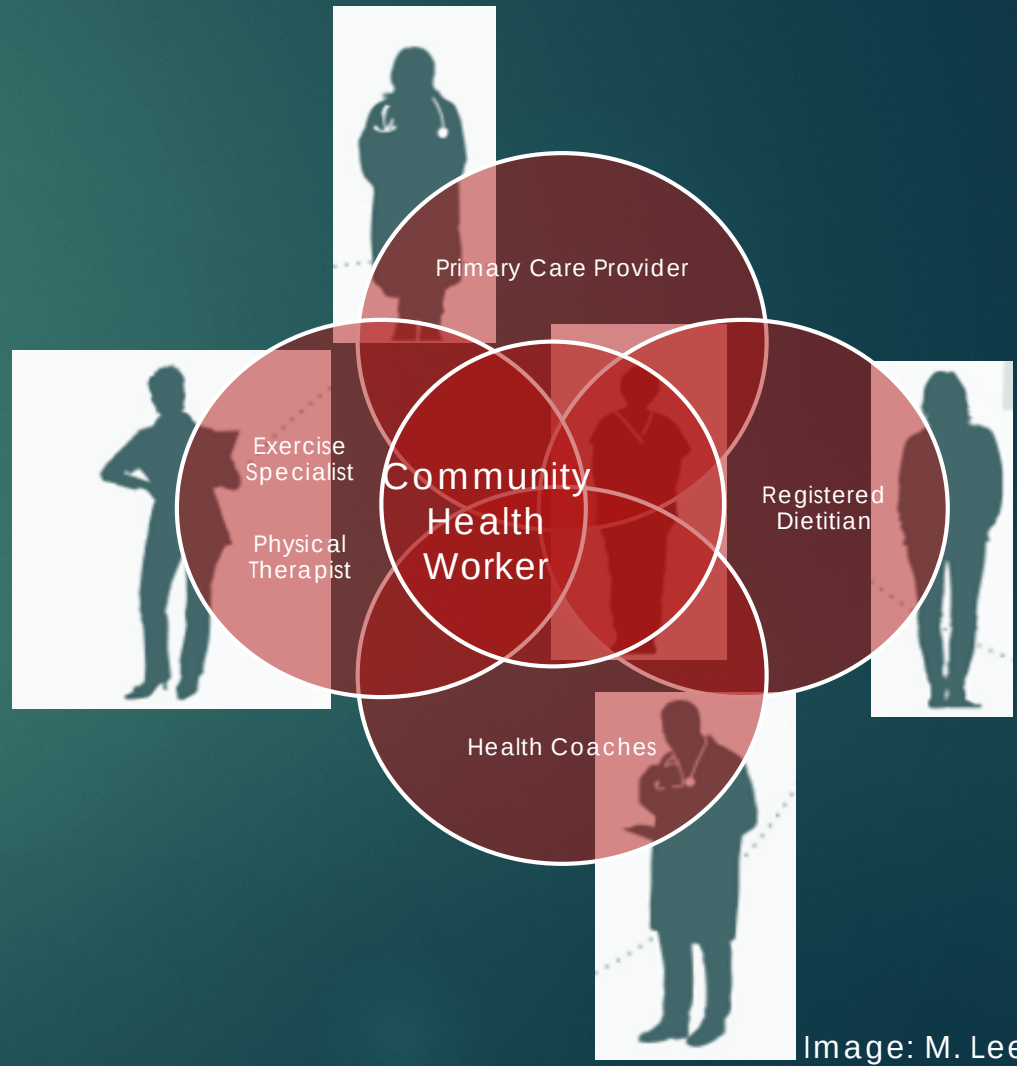
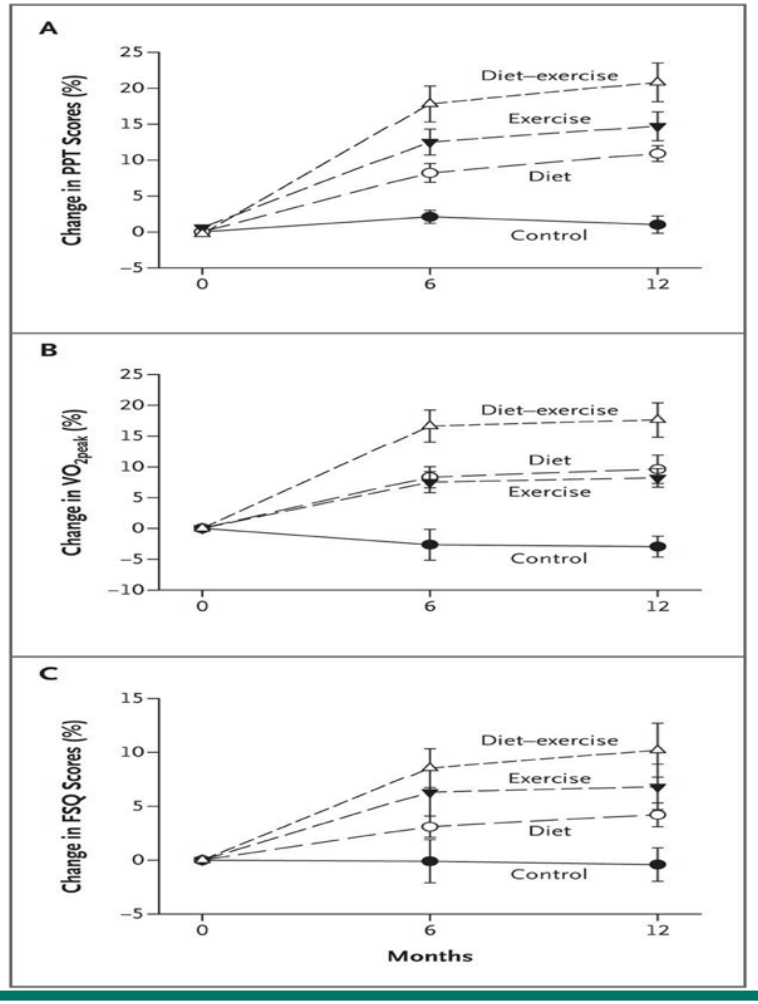


Image: M. Lee

*Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393-403.
*Wing RR, Hamman RF, Bray GA, Delahanty L, Edelstein SL, Hill JO,et al. Achieving weight and activity goals among diabetes prevention program lifestyle participants. Obes Res. 2004;12:1426-1434.
*Look AHEAD Research Group. Eight-year weight losses with an intensive lifestyle intervention: the look AHEAD study. Obesity (Silver Spring). 2014;22:5-13.
*Mathus-Vliegen EM. Obesity and the elderly. J Clin Gastroenterol. 2012 Aug;46:533-544.

Mean Percentage Changes in Objective and Subjective Measures of Frailty during the 1-Year Intervention.



*From New England Journal of Medicine, Villareal DT et al, Weight loss, exercise, or both and physical function in obese older adults, Vol 364, pp1218-1229. Copyright © 2011. Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Ethical Analysis

- Is obesity self-inflicted?
- If obesity is indeed self-inflicted, is this morally relevant?
- Treating obesity as a disease: what are the consequences?

Is Obesity Self-inflicted?

- Obesity is not a disease but an individual characteristic that is the consequence of choices for which the individual bears full responsibility

OR

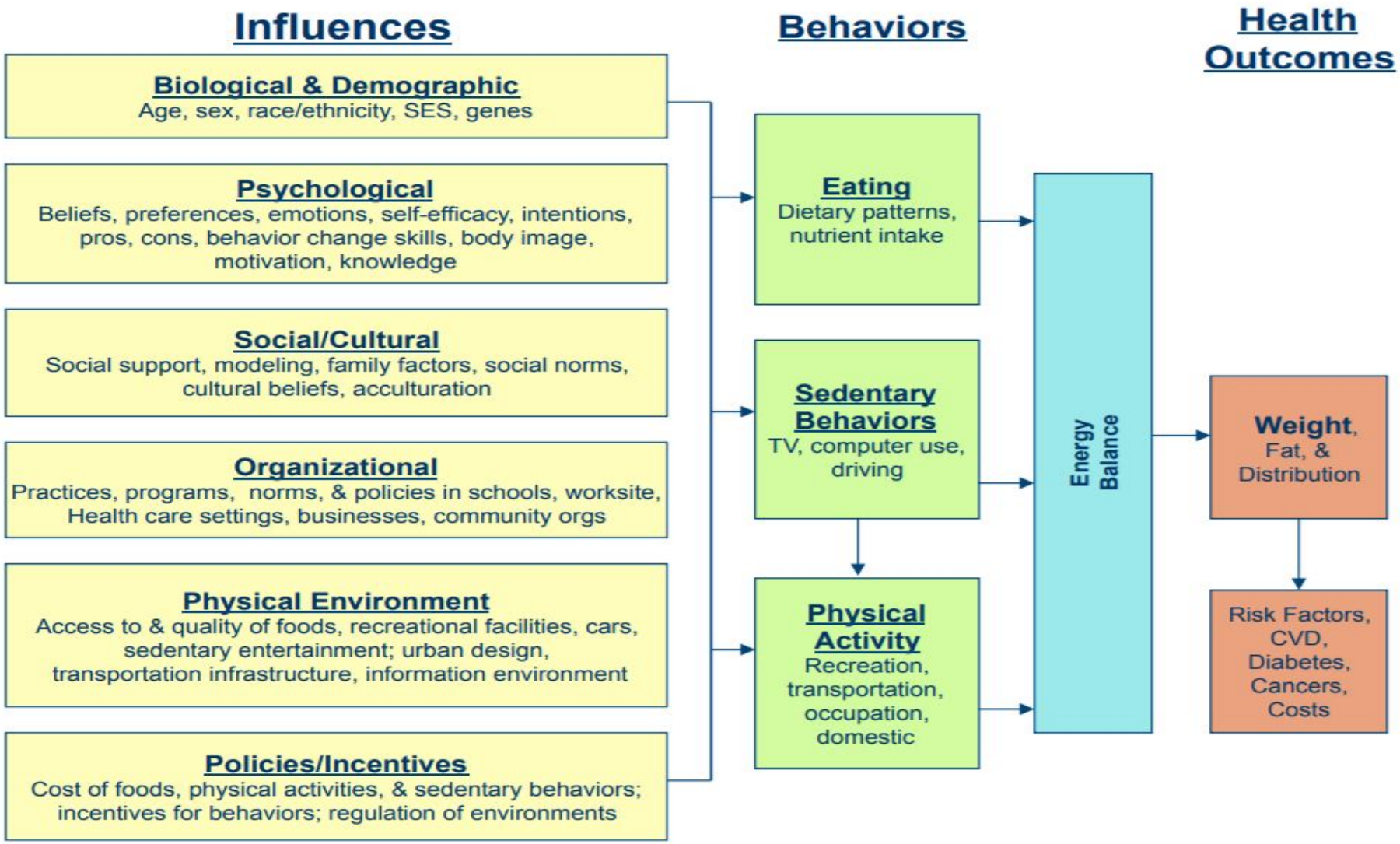
- Obesity is an illness, or at least a risk factor for illnesses, and should be treated as such

Value Judgment

- Related to ideas about aetiology & responsibility
  - (a) Weight control is assumed to be under individual control & responsibility
  - (b) Obesity is a negative phenomenon, so there is something lacking in self-control or the character of an obese person
  - (c) The lack of control correlates with other negative properties that characterize the whole person
    - Laziness, inefficiency, weak character & poor treatment adherence

An Ecological Model of Obesity

(NHLBI)



Developed for the NHLBI Workshop on Predictors of Obesity, Weight Gain, Diet, and Physical Activity; August 4-5, 2004, Bethesda MD

Image: NHLBI

Genetic Determinism

- Obesity-related genetic factors
  - Specific genes: FTO (fat mass and obesity related)
  - MC4R (melanocortin 4 receptors)
  - Thrifty genes

Credit: vchal/Shutterstock

Freedom of Choice?

- Obesity is bound to the habits and choices of the individual, but one can ask how freely people can choose their habits and what the living conditions that frame these choices are.
- Even if getting obese were socially determined or under individuals' control, it does not follow that losing weight is; loosing serious overweight very rarely succeeds with dieting (VIITE).
- One way of seeing this is to see the loss of control of weight as part of the "disease" of obesity
  - Saarni et al. Ethical Issues of Obesity Surgery—a Health Technology Assessment. OBES SURG (2011) 21:1469–1476

Advantages of Medicalisation

- The more disease-like a condition → stronger duty to provide treatments
- Discrimination based on disease or disabilities is usually not accepted → may advance the rights of the obese
  - Discrimination documented in many countries (work, relationships, health care, education, media)
  - Decreased by emphasizing that the causes of obesity are outside individual's control

Disadvantages of Medicalisation

- Makes all obese people sick, irrespective of the rest of their health status
- This “sick role” implies an expectation that the individual wants and tries to get cured from the disease
- Might be harmful for those obese who do not want to be sick, or who do not try to lose weight
  - Might increase the pressure to undergo bariatric surgery

Responsibility

- Health inequality that follows from free individual choices is less problematic than inequality that follows from social or random causes
- Should a problem that could be solved by the individual deciding to eat less and exercise more be solved by a publicly funded surgical operation?
- This breaks down to two questions:

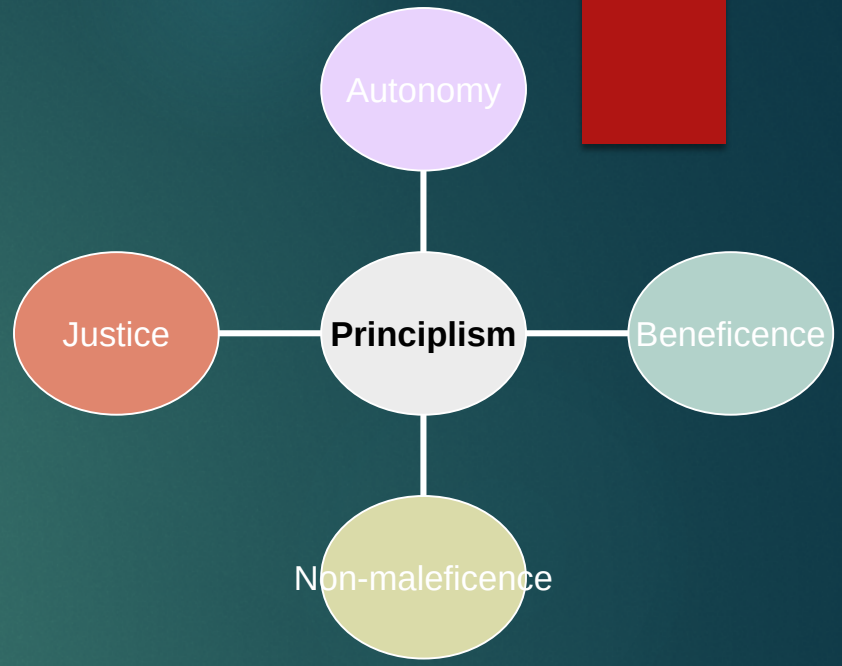
(a) Is obesity such a self-inflicted condition that the individual is responsible for it?

(b) If so, should this influence treatment or financing decisions regarding bariatric surgery?

Principles of Health Care Ethics

- Benefit
- Basic need or right
  - Unequal distribution is problematic
- Reason behind health problems less significant
- Many conditions where the individual has some responsibility, but which we routinely treat without questioning the merits of the individual (e.g., cholesterol, lung cancer, sports injuries, sexually transmitted diseases).
- So is there some specific and important reason for treating obesity differently?

Autonomy



- Informing patients is critical
  - Operation not immediately lifesaving
  - Uncertainties regarding efficacy
  - Need for revisional surgery
  - Irreversible (except gastric banding)
  - Treatment requires (and its success hinges on) permanently & significantly changing eating habits
  - Commercial interests
  - Societal prejudices
    - Saarni et al. Ethical Issues of Obesity Surgery—a Health Technology Assessment. OBES SURG (2011) 21:1469–1476

Informed Consent

- 80% of candidates for bariatric surgery have psychiatric disorders
- Most traumatized are those who experienced childhood obesity and its consequences
- Acceptance of bariatric surgery at any cost
- Difficult to observe dietary restrictions
  - Postoperative lack of alimentary discipline may lead to a disappointing weight loss, morbidity or even death
    - Sarwer DB, Cohn NI, Gibbons LM, Magee L, Crerand CE, Raper SE, et al. Psychiatric diagnoses and psychiatric treatment among bariatric surgery candidates. Obes Surg. 2004;14(9):1148- 1156.

Informed Consent

- Low educational level → partial comprehension of the benefits and risks of surgery → unrealistic expectations & poor decision making
- Patients undergoing bariatric surgery do not remember information on potential complications provided to them before surgery
- Internet information on bariatric treatment of variable content & quality
  - Patients accept and valorize anecdotic information found in online fora
    - Wee et al. Understanding patients' value of weight loss and expectations for bariatric surgery. Obes Surg. 2006;16(4):496-500.
    - Madan et al. Postoperative laparoscopic bariatric surgery patients do not remember potential complications. Obes Surg. 2007;17(7):885-888.

Informed Consent

- Choice of procedure should be made by a multidisciplinary team able to perform all approved procedures
- “Professionals and patients have interests that may go only partly in the same direction”
- Bariatric environment often regulated only by conscience & technical skill of the surgeon
  - Conflicts of interest - commercial companies providing products for bariatric surgery
  - Subjective influence: selection of patients, technique or supplying company
- The patient should not be advised to choose a procedure because the incision is smaller or restricted to a port, or because it may be cheaper or result in a shorter hospital stay
  - Willbanks OL. A plea for professionalism. Obes Surg. 1999;9(2):210.

Children & Adolescents

- Children and adolescents still developing physically & mentally → limited competency to consent
- Disharmonic family relations pose a series of challenges in assessing the best interest of children and adolescents
- Parents and adolescents who consider obesity as something that they can directly influence tend to be more in favour of non-surgical treatment
- Minors wanting surgery are less able to make an autonomous decision than minors who do not wish to undergo surgery
  - Bolt et al. Competence assessment in minors, illustrated by the case of bariatric surgery for morbidly obese children. Best Pract Res Clin Gastroenterol. 2014;28(2):293-302.

Who Should Pay?

- If seen as an effective treatment (or prevention) of significant and disabling disease → publicly funded
- If seen primarily as a psychosocial problem → status would be akin to aesthetic surgery → not publicly funded

Who Decides?

- Unclear who should set limits for BMI, age, family history of obesity and associated diseases
- Guidelines still in use were established in the early `90s in USA
- Variations regarding the obesity type, race, age, co-morbidities were suggested but not always applied
- Limits are often self-imposed, especially in private hospitals
  - NIH conference. Gastrointestinal surgery for severe obesity. Consensus Development Conference Panel. Ann Intern Med. 1991;115:956–961.

Risks to Justice

- Unequal access & distribution
  - Too strict inclusion criteria and guidelines
  - Unbalanced advertisement
  - Discrimination of gender, fitness, age and ethnicity
  - Self-payment
- Promotion of new and not validated procedures before the outcomes are fully explored
- Re-discovered techniques that skipped steps on way to clinical approval
- Industry pressure
- Academic ambitions

- Shikora SA. A call for maintaining ethical behavior in bariatric surgery. Obes Surg. 2012;22(6):849-850.
- Saarni et al. Ethical issues of obesity surgery--a health technology assessment. Obes Surg. 2011;21(9):1469-1476.
- Vartanian & Smyth. Primum non nocere: obesity stigma and public health. J Bioeth Inq. 2013;10(1):49-57

Pre-screening?

- Behaviourally induced weight loss is a mandatory step in presurgical preparation
- Loss of 15% excess body weight
- Check self-discipline and compliance.
  - Glenn et al. Mandatory weight loss during the wait for bariatric surgery. Qual Health Res. 2015;25(1):51-61.

Holistic Approach

- Beliefs, preferences
- Personal body image
- Motivation
- Knowledge
- Social, cultural influences
- Social, family support
- Stress, coping mechanisms
- Access, quality of foods
- Community programs, policies, incentives

Affect behaviors:

- Healthy eating
- Increased physical activity
- Healthy lifestyle

Image: World Health Organization

Conclusions

- Bariatric surgery not a panacea
- We are not only our genes
- Responsibility should be encouraged
- Holistic approach

Ethical considerations in bariatric surgery in a developing country

Obesity kills

According to the 2016 Global Burden of Disease (GBD) data (total number of deaths by cause for the world in 2019) we are being killed by non-communicable diseases (NCD'S). In ancient times we were nomadic hunter gatherers, we were killed by natural disasters, extremes of temperature and wild animals. Then we started settling, communities formed and industrialisation and urbanisation led to infective diseases (measles, mumps, more recently HIV, TB and malaria) and wars to be the biggest killers. But currently, we are being killed by NCD's and more specifically by strokes, myocardial infarcts and cancer.

The best long-term prospective data available on mortality risk associated with obesity, is from the Swedish Obesity Study (SOS) (Sjostrom L et al. NEJM 2007). It provides the most robust prospective data we have on long term outcomes after metabolic surgery. The main outcome for the study was mortality in individuals suffering from obesity and treated with best medical treatment compared to metabolic surgery. It revealed an almost 30% decreased mortality 13 years after metabolic surgery, and this is due to decreased myocardial infarcts, strokes and cancers.

The best evidence we have for the association between obesity and cancer risk is a recent BMJ umbrella review (Kyrgiou M et al. BMJ 2017). The researchers reviewed 204 meta-analyses to evaluate the current evidence for associations between seven adiposity indices and the risk of developing or dying from 36 primary cancers and their subtypes. strongly statistically significant results and no suggestion of bias. These associations were primarily between body mass index and malignancies of digestive organs (oesophageal adenocarcinoma and cancers of the colorectum (in men only), biliary tract system, and pancreas), hormone related cancers (such as postmenopausal breast in women who have never used HRT), premenopausal and overall endometrial cancer, kidney cancer, and multiple myeloma. The increase in the risk of developing cancer for every 5 kg/m2 increase in body mass index ranged from 9% (relative risk 1.09, 95% confidence interval 1.06 to 1.13) for rectal cancer among men to 56% (1.56, 1.34 to 1.81) for biliary tract system cancer. The risk of postmenopausal breast cancer among women who have never used HRT increased by 11% for each 5 kg of weight gain in adulthood (1.11, 1.09 to 1.13), and the risk of endometrial cancer increased by 21% for each 0.1 increase in waist to hip ratio (1.21, 1.13 to 1.29).

When we look at mortality figures such as that provided by the WHO, surgical mortality is often omitted. Examples include the morbidity and mortality associated with a patient suffering from obesity that presents with an incarcerated or strangulated ventral hernia. In these patients, wound infection, hernia recurrence or stomal complications can be expected at the very least, with life often threatened by anastomotic leak, deep vein thrombosis or pneumonia in the worst case scenario.

Obesity in South Africa

There is a lot of media hype around the obesity epidemic, so it is important to take an objective look at the numbers known for South Africa (SA). Obesity is not only a disease of the western world, but much more so it is a disease of developing countries. The 2013 GBD numbers for weight for SA are still the most recent, and this study indicates that 70% of women and 40% of men are overweight (Global, regional and national prevalence of overweight and obesity in children and adults 1980-2013. Lancet 2014). More recent Stats SA numbers (2017) found Type 2 Diabetes (T2D) to be the biggest killer of women in the western cape, with the other provinces not far behind (Mortality and causes of death in South Africa, 2015). The Society for Endocrinology, Metabolism and Diabetes of

South Africa in their 2017 Guidelines on the treatment of Type 2 Diabetes estimated T2D to increase by 140% by 2040. Currently Diabetes deaths exceed combined mortality from HIV & TB & Malaria in Southern Africa.

More concerning for South Africa are worldwide trends recently published in the journals Lancet and Nature. The burden of diabetes, both in terms of prevalence and number of adults affected, has increased faster in low-income and middle-income countries than in high-income countries. During the past four decades, the highest worldwide blood pressure levels have shifted from high-income countries to low-income countries in south Asia and sub-Saharan Africa. If post-2000 trends continue, child and adolescent obesity is expected to surpass moderate and severe underweight by 2022. BMI is increasing at the same rate or faster in rural areas than in cities in low- and middle-income regions.

What happens in a developing country is that there is a constant availability of affordable food that is high in fat, sugar, and salt (fast-foods). There is a high cost to fresh food, a more sedentary lifestyle, an increase in car ownership and city living, and less access to outside space. All these factors contribute to populations becoming overfed and undernourished.

Obesity can be treated

We now know that obesity can be treated. Treatment starts with lifestyle modification, can include medications, or can encompass metabolic surgery (indicated after failed lifestyle modification and medical management).

Evidence-based lifestyle therapy for obesity should include diet, exercise and behavioural modification. Healthy eating, physical activity and behaviour therapy should be first-line interventions in all individuals with a BMI ≥25 kg/m2 and they must be part of any weight-loss intervention. However, these interventions are not always sufficient to maintain weight loss.

Pharmacotherapy for obesity can be considered if lifestyle therapy does not provide sufficient clinical benefit for individuals with a BMI of ≥30 kg/m2, or ≥27 kg/m2 with obesity-related complications. Anti-obesity medications can act directly on the central nervous system, inducing weight loss by reducing appetite, or act peripherally and induce weight loss by interfering with absorption from the gastrointestinal tract.

Expected weight loss after lifestyle modification is 5%-10%, and after treatment with medication it is 10%. The biggest challenge after these two treatments however, is weight regain. Up to 90% of patients regain weight again. This is where metabolic surgery has proven to be able to keep weight off much more efficiently.

Bariatric procedures are the third-line intervention for obesity management, which is recommended in individuals with a BMI ≥40 kg/m2, or ≥35 kg/m2 with comorbidities. Bariatric surgery can be malabsorptive or restrictive, with each type requiring different lifestyle changes. The four most commonly performed metabolic surgical procedure are the laparoscopic adjustable gastric band (LAGB), the sleeve gastrectomy (SG), the Roux and Y gastric bypass (RYGB), and the duodenal switch (DS). LAGB is extremely safe to perform but up to 83% of patients needs revisional surgery at 15 years. At academic centres, procedures to remove gastric bands now outnumber placements. With the DS, efficacy comes at the expense of complications. Patients after DS in randomised controlled trials in 50% of cases required reoperation, and over 10% required hospital admission for malnutrition or micronutrient deficiencies. For this reason, DS now encompass < 1% of operations worldwide. Until 2013, RYGB was the most popular metabolic operation, with expected weight loss

just above 25%. In 2013, SG became the most frequently used procedure, with expected weight loss just below 25%. RYGB has the most robust long-term data, and is the gold standard for outcomes after metabolic surgery against which newer procedures can be measured. The SLEEVEPASS and BOSS trials are two RCT's comparing SG with RYGB that in 2019 published their 5-year outcomes.

Guided by the aforementioned knowledge, we have to view the obesity epidemic as a complex problem, in need of a framework grounded in ethics, to move us effectively into future policy design. Bariatric surgery is of particular interest, because it uses surgical methods to modify organs that appear healthy and because it does not remove the multifarious complex and in part unknown causes of obesity. It offers symptom relief, prevents other diseases, and prolongs life, but it provides no cure. Moreover, the disease that bariatric surgery is directed at alleviating is special in that it is often considered to be self-inflicted, resulting from lack of self-control, and is thus subject to prejudice.

Obesity as a disease – the scientific argument

This approach hinges upon two questions. What are the characteristics that define a disease? And what is the evidence that obesity possesses those characteristics? The scientific argument is challenging as there is a lack of a clear, specific, widely accepted, and scientifically applicable definition of 'disease.'

In simple terms the scientific cause of obesity, and often what initiates obesity in an individual, is a matter of physics – weight equals calories taken in (intake) vs. calories used (expenditure) – thus insinuates that obesity is a result of a lack of willpower or moral fibre. However, we now know that physiology is more than physics. Obesity is the result of a complex interplay between environment, culture, economics, genetics, biochemistry and neurology. We do not know which is the most important, but the brain seems to be at the heart of it.

Our bodies homeostatic system is about survival with the satiety centre situated in the nucleus tractus solitarius (NTS) in the hypothalamus. It is SUBCORTICAL and INVOLUNTARY.
When weight is lost, the body is flooded with Ghrelin, which heightens hunger and the desire to eat. At the same time the gut, pancreas and adipose tissue releases fewer satiety signals so the brain doesn't recognise feelings of fullness. Thus, you cannot simply think yourself slim.

The main arguments presented for declaring obesity a disease are:

- It leads to improvement in research into the causes of obesity
- It leads to improvement in methods to prevent and treat obesity
- It improves patient health and outcomes (prolongs life)
- It improves insurance coverage and reimbursement to providers for treating individuals with obesity
- It removes the stigma currently associated with obesity (i.e., it is not just a poor lifestyle choice). Obese individuals face various forms of prejudice due to their weight (Pomeranz 2008). There exists widespread negative stereotypes, e.g., that overweight and obese persons are lazy, unmotivated, less competent, non-compliant, sloppy, "willful deviants," and that they lack self-discipline (Cowan et al. 1999; Hell and Miller 2002; Puhl and Heuer 2009). Public stereotypes and paradigms prevail also among physicians, who consider obesity to be a weakness of the will, and members of the public regard obesity surgery as dangerous (Hell and Miller 2002).

The main arguments presented against declaring obesity a disease are:

- It is debatable (no scientific evidence) that a disease label would lead to better access to care and preventive measures, provide better legal protection, or that it would reduce discrimination or stigmatization.
- Obesity does not fit the definition of a disease (it has no symptoms, and it's not always harmful—in fact, for some people in some circumstances, it's been known to be protective rather than destructive (oesophageal squamous cell cancer). It was previously believed that some people with a BMI in the obese range are putatively 'healthy,' and some with a normal BMI have an excess of visceral body fat and are not healthy. This is also referred to as the 'obesity paradox' or the metabolically healthy obese'. It appears that some people with a BMI in the obese or overweight range have better short- and long-term health outcomes than those with a normal BMI. A recent study provides evidence that the "obesity paradox" is not true. This meta-analysis investigated the association of BMI, metabolic status, and cardiovascular events and total mortality. The result of this study was that obese individuals, regardless of their metabolic status (healthy or unhealthy) were at increased risk for adverse health outcomes, when compared to individuals of normal weight. This risk was seen only in the studies with more than 10 years of follow-up. Research suggests that the "obesity paradox" may have been due, in part, to the level of physical fitness of the individual. Those persons with a higher fitness level have the more favourable prognosis.
- Obesity as a disease makes doctors and industry rich and transforms otherwise healthy persons into patients, leading to overtreatment. This touches on the 'medicalisation of modern life', where it is argued that bariatric surgery is a way to correct unwanted moral behaviour, and that it transforms otherwise healthy persons into patients (de Vries 2007). It is maintained that the "obesity epidemic" has more to do with the various financial and political incentives of the weight loss industry, medical profession, and public health bureaucracy than with health consequences of excess weight (Oliver 2006). On the other hand, prejudices among physicians and lack of prestige of bariatric surgery in general may curb a push from bariatric surgeons. Furthermore, such claims have to be related to the level of severity; their relevance may be different (and much higher) in less severe cases of obesity than in extreme and morbid cases.
- It shifts the emphasis towards treatment with surgery/medications, and away from prevention efforts via lifestyle changes, including behaviour modification, diet, and exercise. Bariatric surgery can be seen as a conversion of an emotional, mental, or psychosocial problem to a physical one, and could enhance charges of somatization.
- A 'disease' label would categorically define the obese body as deviant. Bariatric surgery may increase attention to weight and the "obesity epidemic," and may further increase the burden of being obese (Oliver 2006). That is, when bariatric surgery becomes common, it may be harder to be obese by choice. It may lead to stigmatisation and discrimination as a result, thus negating the original intention.

The history of obesity and metabolic surgery – the forensic argument

This approach relies upon authoritative statements from respected organizations declaring that obesity is (or should be) considered to be a disease. The following is an exhaustive search of public statements.

1942 - Metropolitan Life Insurance Company defined BMI and ideal weight according to height, and overnight millions of people became overweight, obese and unhealthy.

1973 - the first International Congress on Obesity, held in Bethesda, Maryland, United States of America (USA).

1994 - SASSO (South African Society for Surgery, Obesity and Metabolism) is established, with membership only from the private sector.

1998 - The National Institutes of Health (NIH) declared obesity a disease. In 1998, the National Institutes of Health published Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults that stated, “Obesity is a complex multifactorial chronic disease.”

2002 – In early 2002, the Internal Revenue Service (IRS) issued a ruling that expenses for obesity treatment would qualify as deductible medical expenses. Later in 2002, the Social Security Administration (SSA) published an evaluation of obesity stating that “Obesity is a complex, chronic disease characterized by excessive accumulation of body fat.” This determination explicitly stated that obesity is a valid medical source of impairment for the purpose of evaluating Social Security disability claims.

2006 - In 2006, CMS (Centers for Medicare & Medicaid Services) issued a National Coverage Determination providing coverage for bariatric surgery under Medicare, a decision that followed as a natural consequence of the agency’s 2004 reassessment of obesity. NICE (National Institute of Health and Clinical Excellence) recommended weight loss surgery as treatment for obesity. The British and Welsh National Health Service (NHS) started covering metabolic surgery

From 2010 Discovery South Africa covers bariatric surgery only for SASSO accredited surgeons and only for patients on their most comprehensive plan.

In June 2013 in the Hyatt Regency Hotel in Chicago, the American Medical Association (AMA) recognized obesity as a “disease state”. They argued that labelling it a disease will ensure better coverage and thus treatment of obese individuals, and also further research funding into the causes of obesity. Hundreds of doctors were there on day three of the American Medical Association’s annual meeting, to vote on a list of organization policies. Resolution 420 was short and to the point: “That our American Medical Association recognize obesity as a disease state”. This issue had been under discussion for years, and months earlier the AMA asked its own Committee on Science and Public Health to explore the issue; the committee came up with a five-page opinion suggesting that obesity should not be officially labelled as a disease, for several reasons. The AMA membership didn’t agree with the committee; they passed Resolution 420 in an overwhelming voice vote. A number of other medical societies supported this idea, including the American Association of Clinical Endocrinologists, the Endocrine Society, the American College of Cardiology, the American College of Surgeons, and the American Heart Association.

2014 – The European Court of Justice ruled that obesity can be a cause of disability when it causes long-term impairment.

Currently Portugal is the only European country that recognises obesity as a disease. The rest of Europe prefers to refer to obesity as a risk factor. The main argument here is that ‘medicalization’ of obesity transforms otherwise healthy persons into patients, leading to overtreatment and making doctors and insurers rich. The European Association Society for the Study of Obesity (EASSO) holds the view that ‘obesity is a progressive disease, impacting severely on individuals and society alike, and that it is widely acknowledged that obesity is the gateway to many other disease areas.’

In 2019 a second accreditation system for performing metabolic surgery for both public and private sector South African surgeons and centres becomes available in South Africa.

The real world – the utilitarian argument (normative concept)

This approach is a logical analysis of the benefits and harms arising from considering obesity a disease. This argument moves to ethical reflection where we have to decide how to act in the real world, all things considered. This means ethical reflection must take into account all aspects of a proposed course of action, it must rely on good factual evidence and on an understanding of the social and legal contexts in which action has to take place. The main principles or ethical values in play are respect for self-determination, the pursuit of a good life, the promotion of the common good, the obligations between parents and children and justice.

Justice - just behaviour or treatment

Justice is a complex ethical principle involving fairness, equality, and equitable treatment. The principle of justice states that there should be an element of fairness in all medical decisions: fairness in decisions that burden and benefit, as well as equal distribution of scarce resources and new treatments, and for medical practitioners to uphold applicable laws and legislation when making choices.

In a certain perspective, the "obesity epidemic" can be viewed as an ideology-driven moral panic mediated by social relations of gender, class, and race (Aphramor 2005; Campos 2004; Campos et al. 2006; Gard and Wright 2005; Herndon 2005; Monaghan 2005; Monaghan 2005; Throsby 2007). Accordingly, bariatric surgery can become a tool for the politicization of body size, and its risk-benefit calculation presupposes moral disdain with obesity (Throsby 2007). Obesity is thus both a scientific and a political matter (Alverdy et al. 2009), rendering bariatric surgery a key element in the "politics of obesity." Obesity is as likely or more likely to afflict ethnic minorities and those of lower socioeconomic status (Saxena et al. 2004; Tjepkema 2008). If obesity is conceived of as an embodied inequality with severe health implications (Pomeranz 2008), bariatric surgery in the public health sector could reduce inequalities and discrimination. An additional argument to providing bariatric surgery to public patients would be to not discriminate by the assumption that patients will not be able to understand the implications of undergoing a procedure.

Only a small fraction of eligible persons are offered bariatric surgery, and those who gain access to bariatric surgery are not always those who are most affected (Flum et al. 2007). There may be many reasons for the unjust distribution of bariatric surgery. Restrictive guidelines comprise but one of these: "Medical insurers' and their agents' criteria, if excessively restrictive relative to the guidelines, may reflect an ingrained prejudice against the morbidly obese, manifesting itself in an unfair, unethical and immoral bias" (Cowan 1999, 69). Differentiating between morbid obesity and nonmorbid obesity, generates a moral divide with regard to entitlement to surgery.

Most health care systems intend to treat people's health problems independently of their causes (eg. lung cancer and smoking). However, resistance to bariatric surgery appears to challenge this ideal. For the first time in medicine we are at risk of withholding proven successful treatment options from patients due to the perception of self-inflicted harm.

Autonomy - the right or condition of self-government

Autonomy can be defined as the ability of the person to make his or her own decisions. In a medical context it is the right of patients to make decisions about their medical care without their health care provider trying to influence the decision. Patient autonomy does allow for health care providers to educate the patient but does not allow the health care provider to make the decision for the patient.

It can be argued that bariatric surgery is seen to support an existing social condemnation of fat (de Vries 2007) and supports existing aesthetic ideals of body and beauty (Stearns 1997). Patients should be free to choose whether they would be inclined to treat their weight at all. If choosing to opt for treatment, patients should be free to choose between different weight loss strategies (lifestyle modification, medication and bariatric surgery). While certain banding techniques are reversible (as the band can be removed), other procedures are permanent. Reversibility appears to be a morally relevant difference, especially as surgery does not cure the condition but only relieves its symptoms. Voluntariness may be jeopardized in bariatric surgery, for instance when preoperative dietary counselling is mandated by insurance payers before bariatric surgery.

Beneficence & Nonmaleficence - non-harming or inflicting the least harm possible to reach a beneficial outcome (some philosophers combine nonmaleficence and beneficence, considering them a single principle). Beneficence comes from the Latin word benefactum, meaning "good deed."

In particular, we should not cause avoidable, intentional or unintentional harm. This includes avoiding even the risk of harm. It is important to point out that this principle can be violated with or without intention. That is, you don't have to intend harm to violate this principle. In fact, you don't even have to cause harm. If you have knowingly or unknowingly subjected a patient or colleague to unnecessary risk, you have violated this principle (Munson, 2004). Beneficence may be considered to include four components: (1) one ought not to inflict evil or harm (sometimes called the principle of nonmaleficence); (2) one ought to prevent evil or harm; (3) one ought to remove evil or harm; and (4) one ought to do or promote good.

It is found that "do no harm" is relative to the cultural feasibility of the individual lens, and whether the greater harm is being done to society at large through increased expense of care of obese populations or psychological harm rendered through stigmatization of the obese populations. Every health intervention has potential to harm the recipient. There are many different precedents in medicine and research for conducting a cost–benefit analysis and judging whether a certain action would be a sufficient practice of beneficence, and the extent to which treatments are acceptable or unacceptable is under debate. Despite differences in opinion, there are many concepts on which there is wide agreement. One is that there should be community consensus when determining best practices for dealing with ethical problems. Obligations to confer benefits, to prevent and remove harms, and to weigh and balance the possible goods against the costs and possible harms of an action are all at play.

Cost and resource distribution

Bariatric surgery is costly (about USD7000) and has caused a significant rise in health care expenditure (Sturm 2002; Finkelstein and Fink 2003; Finkelstein et al. 2005a; Arterburn et al. 2005; Padwal and Sharma 2009). However, the health care costs of obese persons are 36–39% higher than for non-obese persons (Sturm 2002; Finkelstein et al. 2005), and persons with extreme obesity have 81% higher health care expenditures (Arterburn et al. 2005). An English summary in a recent Finnish report gives a 10-year average increase of per-patient cost with bariatric surgery of EUR 31,800 (USD45,530), at a gain of 7.05 QALY, compared to a cost of EUR 44,800 (USD 64,142) at a gain of 6.5 QALY without surgery, respectively (Ikonen et al. 2009).

The Discovery ObeCity Index (2017) evaluated body mass index (BMI) and waist circumference in six cities (PTA, JHB, CT, Durban, PE, Bloemfontein) and compared their health care spending. What was reported widely in the press was that Cape Town is SA's healthies city. Cape Town scores best with 53.5% of Capetonians having a normal weight status. Johannesburg and Durban came in at second

and third with 52.0% and 51.8%, respectively. Port Elizabeth and Bloemfontein have the worst weight status, with 48.8% of residents having a healthy weight status in both cities. What was not reported widely was the cost outcomes. Obesity costs the global economy R16.4trn, which is roughly equal to the impact of smoking and wars combined. It costs the South African economy R701bn. It impacts productivity, which costs the economy R109bn each year. Increased absenteeism costs the South African economy R47bn, according to the report. Other costs included increased medical spend, related to out-of-pocket healthcare costs, which amount to R124bn each year. Global figures show that daily expenses cost obese people an additional R31bn. Globally, statistics show that overweight women are predicted to earn 11% less than women of a healthy weight. People with an unhealthy bodyweight incur a direct increase in healthcare costs of approximately R4 400 per person per year.

We now know that for obese patients with type 2 diabetes, the upfront costs of bariatric surgery seem to be largely off-set by prevention of future health-care and drug use. This finding of cost neutrality is seldom noted for health-care interventions, nor is it a requirement of funding in most settings. The National Institute for Health (NIH) systematic review on cost-effectiveness (Picot et al. 2009) bariatric surgery was cost-effective in comparison to non-surgical treatment in the reviewed published estimates of cost-effectiveness. Surgical management was more costly than non-surgical management in each of the three patient populations analysed, but gave improved outcomes. For morbid obesity, incremental cost-effectiveness ratios (ICERs) (base case) ranged between £2000 and £4000 per QALY gained. They remained within the range regarded as cost-effective from an NHS decision-making perspective when assumptions for deterministic sensitivity analysis were changed. Usually, buying of health benefits at an acceptable cost (eg, £20 000 per quality-adjusted life-year in the United Kingdom) is the economic benchmark adopted by payers when new interventions are assessed. Bariatric surgery should be held to the same economic standards as other medical interventions. There is a robust body of evidence for the cost and cost-effectiveness of endovascular treatment (EVT) after ischaemic or thrombotic stroke. The cost analyses suggested that although EVT was associated with higher costs, it also resulted in improved patient outcomes. From the cost-effectiveness studies, EVT seems to be good value for money when a threshold of $50 000 per quality-adjusted life year gained is adopted. You can argue to rather prevent the cardiovascular catastrophe before it occurs by treating obesity and its comorbidies early.

Conclusion

The condition that bariatric surgery is directed at, obesity, is not a concise and clear concept, and its definition has changed over time. It seems to be a pragmatic concept, focusing on intervention in people considered to be in the need of help. Correspondingly, there is a debate on whether obesity is a disease qualifying for surgery. Some medical experts tend not to accept obesity as a disease, in the same manner as the World Health Organization (WHO) does. As members of The Obesity Society (TOS) point out, obesity is not a disease in a strict scientific sense, or in a forensic perspective, but as a normative concept; i.e., considering obesity as a disease can benefit the greater good. Even when obesity is accepted as a disease, there is little agreement on what kind of disease it is, e.g., whether it is a behavioral disorder (eating disorder) or a metabolic disease. So should bariatric surgery be recommended, as it appears efficient and the demand is growing? Many more questions remain. What is the opportunity cost of bariatric surgery, and what health services will receive less attention when bariatric surgery receives more? Which surgical procedure should be recommended? These and other morally pertinent questions are not addressed yet, as they depend on context.