CONTENTS

	<u>Page</u>
Message from the Dean Welcome Note Provisional programme	3 4 5-7
ROTEM/TEG IN THE MANAGEMENT OF HEMORRHAGIC SHOCK Prof Fathima Paruk	8
THE PRINCIPLE OF 1:1:1 BLOOD PRODUCT USE IN RESUSCITATION OF TRAUMA VICTIMS Prof Ken Boffard	9
REBOA – a new snake in the grass? Dr Timothy Hardcastle, Trauma Surgeon – IALCH/UKZN Controversies in Surgery 2016	10-14
INDUCED COMA FOR MANAGEMENT OF HEAD INJURY Prof Sam Mokgokong	15
VASCULAR STENTING FOR TRAUMA Prof Jay Pillai	16
ARTERIAL EMBOLIZATION TREATMENT FOR SOLID ORGAN TRAUMA Prof Samia Ahmad	17
MAGGOT DEBRIDEMENT THERAPY IN SOUTH AFRICA <u>H J C DU PLESSIS</u> M.B., Ch.B., M. Med (Surg) (Pret), FCS(SA), FACS Emeritus Professor of Surgery, University of Pretoria, and Director of Wound Care, Department of Surgery, Steve Biko Academic Hospital, Pretoria <u>Herman.duplessis@up.ac.za</u>	18-20
NON-OPERATIVE TREATMENT OF ACUTE APPENDICITIS- IS THIS APPROPREATE IN SOUTH AFRICA O.D. MONTWEDI, _Department Of Surgery University Of Pretoria	21-25
NON-OPERATION TREATMENT OF ABSCESSES-ARE THERE LIMITS OR LIMITATIONS Brandon Jackson, MB BCH, MMED (SURG), Department of Surgery, Kalafong Hospital and Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa.	26-30
EVAR FOR THORACO-ABDOMINAL AORTIC ANEURYSMS Prof TV Mulaudzi	31-35
ENDO VENOUS MANAGEMENT OF VARICOSE VEINS Dr MH Sikhosana	36-37

DRUG ELUTING BALLOONS AND STENTS IN VASCULAR SURGERY A.T.O. ABDOOL-CARRIM	38
MOLECULAR GENETICS IN THE MANAGEMENT OF BREAST CANCER	39
Maritna J Kotze Department of Pathology, Faculty of Medicine and Health Sciences, Stellenbosch University and National Health Laboratory Services, Tygerberg Hospital, Cape Town.	
THE SIGNIFICANCE OF LYMPH NODE MICROMETASTASES AND ISOLATED TUMOUR CELLS IN BREAST CANCER Carol Benn	40-45
NEW THERAPIES IN THE MANAGEMENT OF MALIGNANT MELANOMA IMMUNOTHERAPY	46
Dr Daniel A. Vorobiof, Sandton Oncology Centre, Johannesburg	
NEW THERAPIES IN THE MANAGEMENT OF MALIGNANT MELANOMA TARGETED THERAPY	47
Dr Daniel A. Vorobiof, Sandton Oncology Centre, Johannesburg	
LAPAROSCOPIC LIVER AND PANCREATIC SURGERY Martin Brand, Department of Surgery, University of the Witwatersrand	48-51
GASTRO-INTESTINAL FAILURE Prof JP Pretorius	52-55
THE USE OF OVER THE SCOPE CLIPS TO CLOSE GIT FISTULAE. Dr Adam Boutall	56-57
EXPERIENCE IN SINGLE INCISION PAEDIATRIC ENDOSCOPIC SURGERY (SIPES) Prof ML van Niekerk	58
USE OF "GLUES" FOR HERNIA REPAIR. <u>Ramsey Maluleke</u> , Department of Surgery,University of Pretoria and Steve Biko Academic Hospital.	59-63
BIOLOGICAL PLUGS AND ANTIBIOTIC BEADS IN THE TREATMENT OF ANORECTAL FISTULAE B.L. Khulu FCS (SA). Department of Surgery, Tembisa hospital & University of Pretor	64-70 ia
LAPAROSCOPIC LIVE DONOR NEPHRECTOMY Prof Zach Koto	71-74
THE CONUNDRUM OF DIFFICULT VENOUS ACCESS FOR HAEMODIALYSIS	75-77
	78
HIV POSITIVE DONOR ORGANS TRANSPLANTED TO HIV NEGATIVE RECIPIENTS – A LEGAL PERSPECTIVE Prof Magda Slabbert, College Of Law, University Of South Africa	79

MESSAGE FROM THE DEAN

It is my privilege to welcome you to the 20th Symposium on Controversies and Problems in Surgery.

This symposium provides an opportunity to share expertise and thereby advance surgical practice in our country. This is in line with the values of the University which are to foster an inquiry-led and evidence-based approach to creating knowledge; and academic citizenship, whereby we commit ourselves to harnessing our intellectual abilities in the interest of our nation and humanity.

The Faculty is honoured to host such a specialist group of surgeons. I believe that the discourse of the symposium will ultimately result in improved patient care and outcomes; thereby making each patient matter.

A special thank you to all my staff that have committed time and effort to organising the symposium.

Sincerely,

Prof Tiaan de Jager Acting Dean: Faculty of Health Sciences

Welcoming Note 2016

It gives me pleasure to welcome back the loyal attendees to this 20th Annual Controversies and Problems in Surgery and welcome the new comers and wish they too become loyals.

The theme this year is "New Techniques and Novel Solutions to Common Surgical Problems". We trust you will enjoy as well as learn from the menu we prepared for you. We have included an update on Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for advanced intraperitoneal cancer metastasis by Prof Kurt van den Speeten. CRS and HIPEC are giving new glimmer of hope for the otherwise devastating malignant process. I should express a special word of gratitude for his loyalty and support. He so respects his "alma mater" that he comes at his own cost to these symposia! Thank you Kurt. I should not overlook thanking all other presenters as well for their sterling efforts.

We also thought it is time we discussed the ethics of HIV positive donor organs in our environment. I look forward to opposing views and arguments on this vexed topic.

This symposium would not be possible without the support of the Trade. I should like to thank our traditional and loyal sponsors and welcome new ones, especially from non-traditional non-medical industries. I hope these too will find the adventure worth their while and return next year and more years into the future.

I should extend a word of appreciation for members of my staff both academic and support staff for the effortless preparation of the conference which makes my job altogether light and most delightful!

It is with fondness to reflect that I first organised the 2nd Annual Symposium which was a resounding success, even if I have to say so myself, and I am now organising the 20th Annual Symposium and my last! I trust it will also not disappoint. May I wish future organisers a very good luck.

Happy discourse and happy learning.

Professor Taole Mokoena.

October 2016

PROGRAMME 20TH ANNUAL CONTROVERSIES AND PROBLEMS IN SURGERY 8th AND 9TH OCTOBER 2016

Venue:

Date:	Saturday 08 October 2016	
07h15:08h00	Registration	
08h00-08h05	Introduction and Welcome	Prof Taole Mokoena
08h05-08h15	Opening address by the Dean	
TRAUMA		Chairman: Dr Steve Moeng
08h15-08h35	Use of ROTEM 1 TEG in management of haemorrhagic shock	Prof Fathima Paruk
08h35-08h55	The principle of 1:1:1 blood product use in resuscitation of trauma victims	Prof Ken Boffard
08h55-09h15	REBOA in Trauma	Prof Tim Hardcastle
09h15-09h35	Induced coma for management of head injury	Prof Sam Mokgokong
09h35-09h55	Vascular stenting for trauma	Prof Jay Pillai
09h55-10h15	Arterial embolization treatment for solid organ trauma	Prof Samia Ahmad
10h15-10h35	ΤΕΑ	
SEPSIS		Chairman: Prof Jan Pretorius
10h35-10h55	Maggot therapy revival	Prof Herman du Plessis
10h55-11h15	Non-operative treatment of acute appendicitis – is this appropriate in South Africa	Prof Daniel Montwedi
11h15-11h35	Non-operative treatment of abscesses – are there limits or limitations	Dr Brandon Jackson
VASCULAR		Chairman: Dr Christopher Tsotetsi
11h35-12h05	Use of EVAR in Thoraco-	Prof Dirk du Plessis
	abdominal aneurysm disease	Prof Thanyani Mulaudzi
12h05-12h25	Endovascular treatment of varicose veins – a day case procedure	Dr Boki Sikhosana
12h25-13h00	Drug eluting balloons and stents in vascular surgery	Prof ATO Abdool-Carrim
13h00-14h00	LUNCH	

ONCOLOGY		Chairman: Prof Meshack Ntlhe
14h00-14h30	Application of molecular genetics in the clinical management of breast cancer	Prof Maritha Kotze
14h30-14h50	The significance of lymph node micrometastases and isolated cells in breast cancer	Dr Carol Benn
14h50-15h10	New therapies in the management of melanoma	Dr Daniel Vorobiof
15h10-15h30	Immunotherapy and targeted treatment	Dr Daniel Vorobiof
15h30-16:00 TEA		
		Chairman: Prof Taole Mokoena
16h00-16h30	Surgical treatment of locally advanced pelvic malignancies	Prof Kurt vd Speeten
16h30-16h50	Cytoreduction surgery and hyperthermic intraperitoneal chemotherapy of disseminated intra-abdominal malignancies - update	Prof Kurt vd Speeten
18h00 for 18h30	GALA DINNER	

SUNDAY 9TH OCTOBER 2016

HEPATOPANCREATICOBILIARY		Chairman: Prof Martin Smith
08h00-08h30	Laparoscopic hepatectomy and pancreatectomy	Dr Martin Brand
08h30-08h50	Recent advances in management of pancreatic neoplasia	Dr Thomas Marumo
NEW TECHNIQUES		Chairman: Prof Zach Koto
08h50-09h10	Intestinal failure	Prof Jan Pretorius
09h10-09h30	Over the endoscope clipping system for GIT fistulae	Dr Adam Boutall
09h30-09h50	Single port laparoscopic surgery	Prof Martin van Niekerk
09h50-10h10	Natural Orifice Trans-endoluminal Endoscopic Surgery (NOTES)	Prof Hein vd Walt
10h10-10h20	Robotic surgery in RSA	Dr Marius Bongers
10h20-10h30	Use of "glues" for hernia repair	Dr Ramsey Maluleke
10h30-10h40	Biological plugs and antibiotic beads in treatment of anorectal fistulae	Dr Lawrence Khulu
10h40-11h00 BRUNCI	4	
TRANSPLANT		Chairman: Dr Ramsey Maluleke
11h00-11h20	Laparoscopic donor nephrectomy	Prof Zach Koto
11h20-11h40	The conundrum of difficult vascular access for haemodialysis	Dr Chris Tsotetsi
11h40-12h00	Transplant in HIV positive from HIV positive donor	Dr Elmi Muller
ETHICS AND MEDICO LE	GAL	Chairman: Dr Elbashir Osman
12h00-13h00	Is it not time to transplant HIV positive donor organs to HIV negative recipients in the HAART era?	Dr Zubair Asmal Dr Elmi Muller Prof Mariana Kruger Prof Magda Slabbert
13h00-13h05.		

ROTEM/TEG IN THE MANAGEMENT OF HEMORRHAGIC SHOCK <u>Prof Fathima Paruk</u>

The interest in and the use of visco-elastic point of care testing devices such as rotational thromboelastometry (ROTEM) and thromboelastography(TEG) has increased pari passu with our understanding of the coagulopathies in trauma. An evidence-based overview will address the following issues:

- 1. Rationale for their use
- 2. Interchangeability of the different devices
- 3. Advantages over standard laboratory tests
- 4. Limitations
- 5. Impact
 - a. Transfusion practices
 - b. Clinical outcomes
 - c. Cost
- 6. Current role of POC devices integrated into algorithms

THE PRINCIPLE OF 1:1:1 BLOOD PRODUCT USE IN RESUSCITATION OF TRAUMA VICTIMS Prof Ken Boffard

REBOA – a new snake in the grass? <u>Dr Timothy Hardcastle</u>, Trauma Surgeon – IALCH/UKZN

Controversies in Surgery 2016

Introduction

It said by Solomon in Ecclesiates "there is nothing new under the sun". This is never more true than in trauma care where the wheel is often re-invented (pelvic packing, liver packing etc.). This "new" development called REBOA (resuscitative balloon occlusion of the aorta) is a rediscovery of a technique originally described in the 1950's. In 1954 Lt. Col. Carl Hughes (US Army medical corps) reported in Surgery¹ on two cases where he had attempted to stem uncontrolled intra-abdominal haemorrhage with an intra-aortic balloon tamponade. While both cases demised he did report clinical efficacy in terms of control of the bleeding and in the one case blood pressure was restored.

The alternative technique that gained acceptance over the past 50 years was a left anterolateral-thoracotomy with transaortic cross-clamping, a morbid procedure carrying a high mortality, depending on the indication for the use thereof². Thereafter there is a distinct paucity of any reference to intra-aortic vascular control in the trauma population until Gupta and coworkers report briefly on a multi-centre series of 23 cases from 1989. They noted high complication rates in 8 of the 23 cases³.

Definition

So what is this REBOA thing in actual fact? It is the resuscitative use of a balloon-occlusion catheter placed via a femoral sheath access, aiming to inflate the balloon in the aorta at either anatomic level Zone I or III to enable proximal control of non-compressible bleeding in a patient rapidly deteriorating, or in cardiac arrest, after suspected non-compressible intraabdominal or pelvic haemorrhage⁴ (see fig 1). Quassim also highlights that the work of Greenberg and Malina in control of ruptured AAA's has been extrapolated to the trauma population⁴.

Figure 1: Zones of the aorta



Literature overview

Much of the technical aspects and early reports come from the Rasmussen group based in San Antonio TX⁵⁻⁸, who have reported the current indications and evaluated the technical aspects and their initial experience, while courses in the techniques have sprung up in the USA, the UK, Sweden and Norway, as well as in Israel. On the other side of the world, there is a fair experience with REBOA from Japan⁹.

What is the current evidence? Most publications are from within the immediate past 5 years and mostly report case series or small studies, with two larger multi-centre studies^{10,11}, both with less than 150 patients and some overlap of included patients. The grade of evidence and level of evidence is therefore at best Level III. However, more surgeons are technically adept at catheter-based therapies today than in the past.

Indications

Non-compressible bleeding in the abdomen (Zone 1 occlusion) or the pelvis/lower extremities (Zone 111 occlusion) in patients in extremis or in cardiac arrest. Zone 11 is the visceral zone and should be avoided during occlusion⁸.

<u>Technique</u>

Technically the device is placed via an arterial access usually in the proximal femoral artery using a Seldinger-type technique, with placement of an "introducer-sheath" device, which serves as the pathway to introduce the occlusion balloon. A metal guidewire is then placed though the sheath, advanced under fluoroscopic control to the correct level of either zone 1 or 111 in the aorta, and the appropriately selected balloon-occlusion catheter is deployed over the wire. The balloon is inflated with a mix of 50:50 saline and contrast and is then inflated, once the covering sheath is withdrawn. The device is manually secured at the insertion point to prevent movement and then the clinical picture of the patient is reviewed⁵. Deflation is accomplished after proximal and distal control and the device is removed with transverse arteriotomy closure in standard technical fashion.

Recommendations from the current literature suggest a maximum occlusion time of 40 minutes to definitive care to avoid complications⁸.

Experience to date in Trauma

The first small series reported in the recent literature was from the Gupta group in 1989, who reported on 23 patients, of which they contributed 14 cases. They reported feasibility but cautioned about high complication rates, with 3 cases each of aortic-catheter extrusion and limb ischaemia and one case of paraplegia. Two patients required surgical intervention to correct these complications acutely³.

The next series of 6 cases from Rasmussen's group had a 66% survival and all cases had achievement of haemostasis and a doubling of the systolic pressures⁷. All but 1 were cases of blunt trauma with major pelvic injury. No complications were reported. Using registry data Moore compared thoracotomy to REBOA and found that more thoracotomy patient demised early (62% in ED) while the patients who got a REBOA only had a 16% ED mortality. Overall mortality was almost 90% for the thoracotomy group compared to 63% for the REBOA group¹⁰. Again, no REBOA-relate complications were reported.

Using the Japanese Trauma Registry Norii and coworkers¹² determined that only 1% of all trauma patients warrant the use of REBOA and that those who received a REBOA were more severely ill, however with a higher mortality than matched controls who were not given

a REBOA. They comment that REBOA has been a standard of care there for many years. They mention that to qualify as an emergency doctor each person has to do 3 REBOA's. In light of these comments and the worse outcome, caution was advised and a prospective RCT recommended. No comment was made about complications.

In similar fashion Saito and coworkers⁹ reported on 24 patients out of over 5200 trauma cases in Japan, with a 30% survival at 30 days. Average inflation time was under 40 minutes. They also reported a 36% AKI rate and a 36% MOF rate, but more concerning was a 12% amputation rate due to limb-vascular compromise. While reporting that REBOA was feasible, they again caution against the overuse, given the high morbidity rates and high mortality. Importantly of their total of 24 cases, 14 survived longer than 24 hours, with the 9 sets of complications recorded in this subset of patients.

Given the relative contra-indications listed in the recent review, by Rasmussen's group⁸, namely non-compressible bleeding in the head and neck, a recent case report from Japan is pertinent to mention. They used REBOA to control a major pelvic bleed, however the raised supra-diaphragmatic blood pressures increased the size of a non-operable intra-cranial bleed leading to brain-death¹³.

Biffl provided an opinion piece in the Journal of Trauma¹⁴, where he emphasizes that this technique must be evaluated rigorously and transparently before widespread adoption. They also make the point that this is a tool in a spectrum of interventions for active non-compressible bleeding. They conclude with 8 pertinent questions for further evaluating REBOA, as listed here.

1. Is there a role for REBOA in the setting of thoracic trauma?

2. If thoracic injury can be excluded with reasonable certainty, should REBOA replace RT in the setting of blunt trauma arrest?

3. How does REBOA compare with RT for the patient in extremis with abdominal trauma?

4. How does REBOA compare with RT for the patient in extremis with pelvic trauma?

5. Does REBOA offer benefit in a patient with severe shock (SBP, 60Y80 mm Hg) after abdominal trauma or should LAP be undertaken without delay?

6. Does REBOA offer benefit in a patient with severe shock (SBP, 60-80 mm Hg) after pelvic trauma or should pelvic packing/external fixation/angioembolization be undertaken without delay?

7. Do new low-profile devices offer significant advantages in terms of improving the riskbenefit profile of REBOA, allowing more rapid deployment and potentially fewer vascular complications?

8. Who should be performing REBOA? What should be the standards for training, credentialing, and competency?

In answer to some of the questions the recently completed AORTA trial¹¹ may provide some of the answers. This multi-centre, prospective study (8 sites) included 114 patients who had a procedure to occlude the aorta, 46 of these were REBOA. Most (73%) were done in the ED, with no limb ischaemia reported, although there were embolic and pseudoaneurysmal complications. Thirty-six percent had improved haemodynamics. Median blood requirements were 15 units! Overall survival was 21% and there was no difference between the open or REBOA groups, with the conclusion that REBOA was again feasible, but more follow-up and cases were required to assess the real outcome benefits. Those who survived were mostly GCS 15/15, however overall mortality was almost 80%, with survivors having an overall incidence of AKI of 3,5%, pneumonia or ARDS 6% and MOFS 6%. While the mortality differences were not marked, a majority of patients having open thoracotomy were receiving CPR on arrival! The majority of REBOA deaths were in the ED or OR, while the majority of open deaths were in ICU, suggesting either early care limitation for futility in the REBOA group or a real better initial survival from the open procedure. In their discussion they do

highlight the advantages of REBOA as "less invasive" viable alternative which is potentially gentler than open procedures.

Where to from here?

There has been a recent review about the use of technology for prehospital control of haemorrhage¹⁵ that proposed REBOA as a prehospital procedure. There has been, to date, one case report of a successful London HEMS prehospital REBOA and a recent editorial in The Surgeon, from Scotland, proposing that within a doctor-staffed prehospital service REBOA was feasible as a "bridge to definitive haemorrhage control"¹⁶. A recent manikin-based study from Scandinavia has demonstrated that timely and effective control of bleeding is possible in the prehospital scenario, with insertion time under 5 minutes¹⁷.

The bigger issue for us in South Africa is whether this is a procedure for implementation in this country, given the high rates of trauma and particularly penetrating trauma¹⁸. The challenge is that with limited ICU access, limited access to long-term rehabilitation services and limited acute transfusion services, and with long transfer times from rural areas, if this procedure is really of importance outside selected specialized urban centres, such as Johannesburg, Cape Town and Durban/PMB? Given the estimates of the need for REBOA in a developed country¹⁹, such as the UK, of only 3-6 cases per year per major trauma centre, it is a question we will have to answer in light of the medical skill-set available to this country.

Conclusion

Watch this space – as more information is revealed about the indications, complications and outcomes of REBOA and where it is best-fit, we will see it is as another weapon in the fight against the grim reaper. It will, most likely, be a procedure of selected use in urban-trauma cases and may have a place in prehospital care in HEMS services. For the rest, it is not for now!

References

- 1. Hughes CW. Use of an Intra-Aortic Balloon Catheter Tamponade for Controlling Intra-Abdominal Hemorrhage in Man. Surgery, 1954; 36: 65-68
- Biffl WL, Moore EE. Resuscitative Thoracotomy. Op Tech Gen Surgery, 2000; 2(3): 168-175
- 3. Gupta BK, Khaneja SC, Flores L, et al. The role of intra-aortic balloon occlusion in penetrating trauma. J Trauma, 1989; 29(6): 861-865
- 4. Quassim Z, Brenner M, Menaker J, Scalea T. Resuscitative endovascular balloon occlusion of the aorta. Resuscitation, 2015; 96: 275-279
- Stannard A, Eliason JL, Rasmussen TE. Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) as an adjunct for hemorrhagic shock. J Trauma, 2011; 71: 1869-1872
- 6. Morrison JJ, Percival TJ, Markov NP, et al. Aortic balloon occlusion is effective in controlling pelvic hemorrhage. J Surg Res, 2012; 177: 341-347
- Brenner ML, Moore LJ, DuBose JJ, et al. A clinical series of resuscitative endovascular balloon occlusion of the aorta for hemorrhage control and resuscitation. J Trauma, 2013; 75: 506-511
- Belenkiy SM, Batchinsky AI, Rasmussen TE, Cancio LC. Resuscitative endovascular balloon occlusion of the aorta for hemorrhage control: Past, present and future. J Trauma, 2015, 79(4) Suppl 1: S236-S242

- Saito N, Matsumoto H, Yagi T, et al. Evaluation of the safety and feasibility of resuscitative endovascular balloon occlusion of the aorta. J Trauma, 2015; 78(5): 897-904
- 10. Moore LJ, Brenner M, Kozar RA, et al. Implementation of resuscitative endovascular balloon occlusion of the aorta as an Iternative to resuscitative thoracotomy for noncompressible truncal hemorrhage. J Trauma, 2015; 79: 523-532
- 11. DuBose JJ, Scalea T, Brenner M, et al. The AAST Prospective Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) Registry: Data on contemporary utilization and outcomes of aortic occlusion and resuscitative balloon occlusion of the aorta (REBOA). J Trauma, 2016 (IN PRESS)
- 12. Norii T, Crandall C, Terasaka Y. Survival of severe blunt trauma patients treated with resuscitative endovascular balloon occlusion of the aorta compared with propensity score/adjusted untreated patients. J Trauma, 2015; 78: 721-728.
- 13. Ochino H. "REBOA" Is it really safe? A case with massive intracranial hemorrhage possibly due to REBOA. AJCR, 2016 IN PRESS
- 14. Biffl WL, Fox CJ, Moore EE. The role of REBOA in the control of exsanguinating torso hemorrhage. J Trauma, 2015, 78(5): 1054-1058
- 15. Chaudery M, Clarke J, Wilson MH, et al. Traumatic intra-abdominal hemorrhage control: Has current technology tipped the balance toward a role for prehospital intervention? J Trauma, 2015; 78: 153-163.
- Morrison JJ, Jansen JO. Resuscitative endovascular balloon occlusion of the aorta (REBOA): A bridge to definitive haemorrhage control for trauma patients in Scotland? The Surgeon, 2014; 12: 119-120
- 17. Andersen NG, Rehn M, Oropeza-Moe M, Overland NP. Pre-hospital resuscitative endovascular balloon occlusion of the aorta. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2014, 22(Suppl 1): P19
- Hardcastle T, Oosthuizen G, Clarke D, Lutge E. Chapter 15: Trauma, a preventable burden of disease in South Africa: review of the evidence, with a focus on KwaZulu-Natal. In. Padarath A, King J, Mackie E, Casciola J, editors. South African Health Review 2016. Durban: Health Systems Trust; 2016: 179-189. URL: <u>http://www.hst.org.za/publications/south-african-health-review-2016</u>
- 19. Barnard EBG, Morrison JJ, Madureira RM, et al. Resuscitative endovascular balloon occlusion of the aorta (REBOA): a population based gap analysis of trauma patients in England and Wales. Emerg Med J, 2015; 32: 926-932

INDUCED COMA FOR MANAGEMENT OF HEAD INJURY Prof Sam Mokgokong

VASCULAR STENTING FOR TRAUMA

Prof Jay Pillai

ARTERIAL EMBOLIZATION TREATMENT FOR SOLID ORGAN TRAUMA Prof Samia Ahmad

MAGGOT DEBRIDEMENT THERAPY IN SOUTH AFRICA

<u>H J C DU PLESSIS</u> M.B., Ch.B., M. Med (Surg) (Pret), FCS(SA), FACS Emeritus Professor of Surgery, University of Pretoria, and Director of Wound Care, Department of Surgery, Steve Biko Academic Hospital, Pretoria Herman.duplessis@up.ac.za

INTRODUCTION

Maggot therapy was well known and mentioned in historical papers by surgeons caring for injured soldiers. The first intentional use of maggots only started after World War 1 in the USA when an orthopaedic surgeon, Dr William Baer, used maggots in patients with chronic wounds and osteomyelitis. His experience was published in 1931 and this started the widespread use of maggots in the USA. Maggot therapy became so popular that within 10 years more than 300 hospitals in North America used it and more than 100 scientific papers were published on the subject.

With the development of antibiotics maggot therapy fell into disuse for about 40 years. Interest in their use was stimulated again by Dr Ron Sherman of California, when he treated patients with leg ulcers in the VA hospital in Long Beach. This publication lead to renewed interest in the use of maggots to clean wounds. Maggot therapy has been registered by the FDA as a therapy in the United States, and the maggots are produced by Monarch labs for commercial use. Other countries followed this development, and currently it is used in the UK, USA, Canada, Europe, Israel, Thailand and Japan. Dr Frans Cronje started a maggot colony in the late 1990's at Eugene Marais hospital, and this colony was donated to the Department of Surgery at Steve Biko Academic Hospital in 2007. Debridement therapy was mainly utilised for patients in the hospital. ¹

MAGGOT PRODUCTION

The fly species used for MDT is mainly *Lucilia sericata*, which feeds only on dead tissue. Other species like *Lucilia cuprina*, may also feed on live tissue, but has been used for MDT ². Flies are kept in closed containers and fed on either glucose or whey protein, and water. When maggots are needed the flies are stimulated to lie eggs by feeding them chicken liver. The eggs are isolated and sterilised before hatching (within 24 hours) and the first instar maggots are the placed on the wound that needs debridement. They can be used as free roaming in the wound or isolated in a nylon bag. They secrete digestive enzymes that liquefies the dead tissue, and then feed on the liquid. Within 24 hours they develop in the second instar, and in a day the third instar maggot, and grows from 2-3 mm to 10-12 mm. They are left on the wound for 3-4 days, after which they are removed and handled as infective waste. If there are still slough remaining on the wound the process is repeated. In nature the maggots develop into pupae after 7-10 days, and out of this new flies will come if circumstances are optimal.

MECHANISM OF ACTION

The maggots clean wounds with 3 mechanisms, namely debridement of dead tissue with proteolytic enzymes, bactericidal action on micro-organisms, and stimulation of wound healing.

The *debriding action* is caused by the secretion of digestive enzymes, containing carboxypeptidases A and B, leucine amino-peptidase, collagenase, serine proteases and other metalloproteinases, each breaking down different components of the necrotic tissue.

The *bactericidal action* is caused by the secretion of allantoin, urea, phenyl-acetic acid, phenylacetaldehyde, calcium carbonate and other enzymes which are antimicrobial against *Staphylococcus aureus*, MRSA, and other skin organisms. It also disrupts the biofilm created on wounds by *Staphylococcus epidermidis* and other micro-organisms present on the wound.

Wound healing is promoted by the secretion of ammonium bicarbonate creating an alkaline environment that stimulates the formation of granulation tissue. The secretion of ammonia, urea and allantoin also stimulates the secretion of host epidermal growth factor and interleukin 6, which in turn promotes the growth of fibroblasts, chondrocytes, type II collagen and the formation of granulation tissue. These substances has a vasodilatory effect on the blood vessels near the wound, thereby improving the blood supply, oxygenation and venous drainage, and decreasing wound edema.

PRACTICAL APPLICATION

As the maggots only live and grow for 4 to 6 days, they need to be replaced every 3 to 4 days. We usually apply them on a Tuesday and Friday. We mostly apply them as free roaming in the wound, but create a dressing to contain them on the wound area. They are covered with an absorbable dressing that allows oxygen through and sealed with a sticky dressing. If the wound exudes excessively, absorbable material is added over the dressing until it is time for a change. When dressings are removed it is handled as infective waste for disposal. If the wound still contains slough, another batch of maggots is applied. When the wound is clean, the treatment is changed to some other dressings to promote healing, or skin grafting can be performed.

INDICATIONS

The registered indications in the USA is for "debridement of non-healing necrotic skin and soft tissue wounds, such as pressure ulcers, neuropathic foot ulcers, chronic leg ulcers, and non-healing traumatic or post-operative wounds"³. Another indication is for "any wound that failed two or more conventional treatments". Relative contra-indications are osteomyelitis and vascular insufficiency.

We have used MDT in Pretoria on selected wounds that needed debridement. We have used it on diabetic feet, post amputation sepsis, varicose vein ulcers, and decubitus ulcers, and even post irradiation ulcers. It is especially useful in patients who are poor anaesthetic risks because of co-morbidities, and in patients who can be treated as out patients because of shortage of beds in the hospital. A large amount of our patients are diabetics that can be treated as outpatients at the wound clinic.

RESULTS

During the past ten years we have treated at least 150 patients, with 363 treatments, with an average of 2.6 treatments per patient (varying between 1 and 8 treatments). Our success rate is almost 80%, meaning that the wound was cleared of slough and can proceed with other dressings.

This compares well with published figures ⁴. Our failures had to undergo surgical debridement or more proximal amputation because we could not clear the wound. One important contributing factor for failure was patients who continued smoking during treatment.



AVAILABILITY

We only produced maggots on a small scale for our own use. We did donate maggots to some private patients with good results. A private company, Inqaba Biotec ⁵, showed interest to collaborate with us in producing maggots for commercial use. An agreement was signed in April 2016, and we work together to make maggots available to more patients in South Africa under the name of *SURGIMAGGS*. This is done in collaboration with our maggot laboratory at Steve Biko Academic Hospital, and the University of Pretoria.

CONCLUSION

We have a unique asset in the maggot laboratory, which can now be utilised on a much wider scale to the benefit of patients in South Africa

REFERENCE

- 1. Du Plessis H J C, Pretorius J P. The Utilisation of maggot debridement therapy in Pretoria, South Africa. Wound Healing Southern Africa 2011;4(2):80-83
- 2. Paul A G et al. Maggot debridement therapy with Lucilia cuprina: a comparison with conventional debridement in diabetic foot ulcers. International Wound Jnl 2009; 6: 39-46
- 3. Monarch labs. <u>www.monarchlabs.com/</u>
- 4. Sun X, et al. A systematic review of maggot debridement therapy for chronically infected wounds and ulcers. International Jnl of Infectious Diseases 2014; 25:32-37.
- 5. Maggot debridement therapy is coming near you. www.inqababiotec.co.za/

NON-OPERATIVE TREATMENT OF ACUTE APPENDICITIS- IS THIS APPROPREATE IN SOUTH AFRICA

O.D. MONTWEDI, Department Of Surgery University Of Pretoria

INTRODUCTION

Acute appendicitis is the most common surgical emergency. Approximately 300 000 appendectomy are performed annually in the USA.

• The estimated lifetime incidence of appendicitis ranges from 7 to 14% depending on life expectancy and precision of diagnosis (1). In South Africa the incidence is low but with very high complications (2).

THE AETIOLOGY REVISITED

- The aetiology of acute appendicitis is a matter of great debate.
 - Obstruction theory: This theory proposes that Appendix gets obstructed commonly by feacolith which leads to stasis and enlargement with increased intraluminal pressure, Bacterial proliferation with recruitment of neutrophils and other inflammatory cells with pus formation. This high pressure leads to wall ischemia, necrosis and perforation.
 - Non obstructive theory: This is characterised by initial mucosal and submucosal inflammation. The probable cause of this condition is bacterial invasion of lymphoid tissue in the appendix wall, since the lumen is not obstructed this does not progress to gangrene, and in many instances process resolves spontaneously. It may happen in other cases that the swelling of lymphoid tissue in the appendix wall may lead to obstruction.

DIAGNOSIS

- The diagnosis is clinical with occasional need for diagnostic aids by laboratory or radiological imaging. Different scoring systems which incorporates both clinical and laboratory data for diagnosis have been designed.
- The most commonly being the Alvarado and Appendicitis inflammatory response score (AIR). Although the Alvarado is mostly used, the AIR seems to be more accurate than Alvarado (3).

COMPLICATED APPENDICITIS

- The duration of symptoms seems to be a predictor of complications rather than in hospital delay to initiate treatment. Rate of perforation especially in South Africa is much higher than elsewhere in the world 38% (2).
- There seems to be association of complications with health insurance status, poor health services utilization and service of health care delivery in general. This could be indicative of the quality of health care for a particular country.
- Time to presentation in the USA (United States of America) is 57.2 hours for Ruptured appendicitis and less than 24 hours in non-ruptured appendicitis. The average time in South Africa is 88.8 hours, with 64.8 hours for non-ruptured and 105.6 hours for ruptured appendicitis (2).

SPONTANEOUS RESOLUTION

It is possible that cases presenting to hospital have selected themselves from appendicitis that spontaneously resolved on its own and not even presents to hospital. The so-called early appendicitis that resolves after few hours of antibiotics may represent the spectrum of this disease (5).

TREATMENT

- Traditionally early appendectomy has been advocated to prevent incidence of complications, since the classical paper by R. Fitz in 1886 on 247 patients with pelvic sepsis following ruptured appendicitis. The mortality following appendectomy is reported to be less than 1 percent. The morbidity of wound surgical site infection and intra-abdominal abscesses cannot be ignored. The risk to anaesthesia although small is forever present.
- Reports on antibiotic treatment started surfacing. Coldrey in 1959 reported 471 patients who were treated with antibiotics with high success rate and only 7 percent recurrence rate.
- This treatment was also reported in US submarines where surgical facilities were not available (4). The interest in antibiotic first treatment started growing.
- This notion of antibiotic treatment was tested in 3 RCT (Randomised controlled trial) by Styrud et-al (2006) (4), Hansson (2009) (5) and Vons (2011) (11).
- These trials showed conflicting results, whilst the reported success rate with antibiotics treatment was high, the recurrence seem to be the issue.
- There were, however limitations to these trials. Styrud trial excluded female patients and the primary endpoint was unclear.
- Hansson trial had a high crossover from antibiotics to surgery group (52.5%)
- Vons included complicated appendicitis and not only acute uncomplicated appendicitis.
- The APPAC (Appendicitis Accuta) trail (6) attempted to overcome this limitation by conducting multicentre, open label, non-inferiority RTC comparing antibiotic with appendectomy for uncomplicated appendicitis.
- Primary endpoint for antibiotics group was resolution resulting in discharge from hospital without need for surgery in the next 12 months.
- The success in surgery group was defined as successfully undergoing appendectomy with no serious adverse effects.
- The study concluded that antibiotics treatment did not reach a prescribed non inferiority compared to appendectomy.

The Observational NOTA (Non Operative Treatment of Acute appendicitis) study (7) treated 159 patients with suspected appendicitis with antibiotics. Mean sick leave was 5.8 days, mean hospital day 0.4 days. Short term failure rate was 11.9%. The long term recurrent rate was 13.8%. The efficacy was deemed to be same as appendectomy group with other benefits favouring non operative treatment.

Svensson (5) included 50 paediatrics patients, 24 to antibiotics group and 26 to appendectomy group with 92% success rate in non-operative group. 8% short term failure and 38% long term failure were reported. There were no safety issues but conclusion was not to recommend non operative treatment in paediatrics until large trials are done.

Varadhan (8) et al performed a meta-analysis including four randomised controlled trials with total of 900 patients (470 in the antibiotics group and 430 appendectomy group). The antibiotic group had 63% success rate at 1 year and lower complication rate. The outcome was essentially similar between the two groups.

The world congress on emergency surgery held in July 2015 in Egypt concluded that: Antibiotics can be successful in selected patients with uncomplicated appendicitis who wish to avoid surgery and accept the risk up to 38% recurrence (9).

COMMON FICTURES OF RTC

- The consenting adults should not be pregnant. All immune compromised patients were excluded
- Uncomplicated appendicitis was not part of these studies.
- No sepsis on examination should be present for this treatment.
- Intravenous antibiotics were administered for 48 hours.(Choice of antibiotics dependant on treating team)
- Continuous assessment 6-12 hours was conducted to monitor the patient's response or lack thereof.
- Discharge if patient is better after 48 hours and oral antibiotics continued for 7-8 days.
- If no improvement in 48 hours, patient would be taken for appendectomy.
- Confirmation in unclear diagnosis was necessary with radiological imaging before starting antibiotic treatment.

ADVANTAGES OF NON OPERATIVE MANAGEMENT

- Less pain. (Visual pain score). The score was better at discharge compared to surgery group.
- Negative appendectomy eliminated. Negative appendectomy is associated with high long term complications compared to inflamed appendectomy.
- Less hospital stay
- Fewer days of sick leave.
- Morbidity and mortality not necessarily increased.
- No complications associated with surgery, anaesthesia, and wound sepsis.
- Financial cost is cheaper than surgery group.
- Efficacy is similar to surgery group.

DISADVANTAGES

- Antibiotics resistance: Introducing antibiotics to so many patients might lead to wide spread resistance.
- Recurrence: The rate of recurrence up to 38% in some situation has been reported
- **Missing other pathology (carcinoid):** The incidence of colon cancer with appendicitis is rare, but the possibility does exist. Surgery offers an opportunity to look inside the abdomen
- Allergic to antibiotics.

SOUTH AFRICA

- Late presentation; many patients present late with complicated appendicitis (38%) and those with acute appendicitis have already selected themselves for surgery as evidenced by non-improvement during waiting period for theatre time even with antibiotic cover albeit not intention to treat.
- No readily available imaging to confirm the diagnosis so the diagnosis in many situations is clinical based.
- The setup in district hospital is such that there is no expertise and human resource capacity available to always do the necessary monitoring.
- Antibiotics first seem attractive in outlying hospital where surgical services may not be immediately available, but weather the medical officers in those areas will be willing to take the risk is doubtful. There is already reluctance to perform certain procedures as stipulated in the District Hospital Service Package (10) citing fear of complications.
- Availability or lack of antibiotics could hamper this form of treatment.
- Follow up of this patients is crucial and this is a great challenge in many patients in South Africa for various reasons
- HIV is common in S.A and therefore a large number of patients with appendicitis could have HIV, this has never been included among trails for non-operative treatment.
- The role of antibiotics treatment for acute appendicitis is not relevant yet in South Africa.
- The antibiotics are safe only as a bridge to operative surgery. We need appropriately constructed and adequately powered RCT with Standardised inclusion criteria.
- Suitable diagnostic methods should be devised . Analysis on intention to treat to determine benefit of this procedure is needed.
- Gold standard should remain appendectomy, mortality is low, and morbidity of wound sepsis is reasonable and manageable.

REFERRENCES

- 1. Flum DR. Clinical practice. Acute appendicitis- appendectomy or the "antibiotic first" strategy. N. Engl j med 2015;372:1937
- 2. E Yang,D Kahn, C Cook; Acute appendicitis in South African: A systematic review. South African Journal of Surgery Vol.53
- 3. D Kollar.D.P.Macarten. M. Bourke. K.S cross.J. Dowdall: Predicting acute appendicitis? A comparison of Alvarado score, the appendicitis inflammatory response score and clinical assessment, world J Surg (2015) 39:104-109
- Styrud J, Eriksson s, Nilsson I, et al. Appendicectomy versus antibiotics treatment in acute appendicitis. A prospective multicentre randomised controlled trial. World J Surg 2006; 30: 1033
- 5. Anderson RE. The natural history and traditional management of appendicitis revisited: Spontaneous resolution and predominance of prehospital perforation imply that a correct diagnosis is more important than an early diagnosis. World J Surg 2007;31:86-92
- 6. P.Salminen et al: Antibiotic therapy vs appendicectomy for treatment of uncomplicated acute appendicitis(APPAC TRAIL): JAMA 2015;313 (23): 2340-2348
- 7. Di Saverio et al: non operative treatment of acute appendicitis; Ann Surg. 2014 Jul: 260 (1): 109-117 NOTA STUDY
- 8. Varadhan KK. Neal KR. Lobo DN. Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis. Meta- analysis of randomised controlled trials. BMJ 2012; 344:e2156

- 9. Di Saverio et al; WSES Jerusalem guidelines for diagnosis and treatment of acute appendicitis: World J emergency surgery (2016) 11:34
- 10. The primary healthcare package for South Africa: a set of norms and standards. Part 3: norms and standards for district hospitals. Pretoria: Department of health, 2002.
- 11. Vons C et al: Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. Lancet 2011; 377:1573-9

NON-OPERATION TREATMENT OF ABSCESSES-ARE THERE LIMITS OR LIMITATIONS

Brandon Jackson, MB BCH, MMED (SURG), Department of Surgery, Kalafong Hospital and Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa.

Introduction

The management of abscesses is to gain source control in order to reduce the production of endotoxins. The mediators already released also need to be managed¹. Antibiotics and drainage of abscesses in general is the usual standard. Incision and drainage, washout, releasing the abscess cavity loculations and leaving the abscess cavity open used to be the operative standard for almost all types of abscesses.

Percutaneous catheter drainage (PCD) has added to the options available in managing abscesses. PCD prevents the morbidity of an operation. PCD is considered successful if > 90% of the original abscess size is diminished and if septic patients recover from the sepsis².

Some abscesses have been successfully treated non-operatively with only antibiotics; antibiotics and needle aspiration; and others with antibiotics and PCD. Non-operative treatment unfortunately is not always successful and does not allow the performance of a biopsy for histological and cytological investigation of an underlying cancer. There are certain limiting factors that will allow the surgeon to manage abscesses non-operatively or operatively.

Type and Site of abscesses

PCD is not always suitable due to the abscesses lying in difficult locations such as intra-abdominal abscess, particularly in the presence of intra-mesenteric, interloop or multiloculated abscess³. Diverticular abscesses usually have small-bowel loops in contiguity with the fluid collection resulting in an increased risk of small bowel perforations when inserting the PCD. Diverticular abscesses when amenable to PCD still has a reported failure rate of 15 to 30 percent⁴. PCD of renal abscesses also has risks of pyopneumothorax, bacteraemia, and fistula in the gastrointestinal tract⁵.

In a retrospective chart review of 114 patients with intra-abdominal abscesses. Only three percent underwent urgent operative management within 48 to 72 hours which was due to progression of symptoms or complications of the abscess. Antimicrobial therapy without drainage was successful in 86 percent of cases. The rate of percutaneous drainage or surgical intervention for pelvic abscesses were no different than abscesses in the other locations although previous studies showed pelvic abscesses were associated with a worse prognosis and often required surgery⁶.

Muscle abscesses (e.g. psoas muscle) can usually be treated conservatively, but the presence of concurrent bone involvement limits the successful rate. A retrospective study of 94 patients showed the success of conservative management for muscle abscesses alone, however musculoskeletal infection was statistically significantly more likely to undergo surgery (p =0.0001). The presence of skeletal infection (osteomyelitis, diskitis, and epidural abscess) (p = 0.0001) was associated with drainage failure².

Skin abscesses and be managed with needle aspiration which does have limited clinical indications but is especially useful in situations where immediate incision and drainage is less desirable, such as facial abscesses. Skin abscesses are not usually treated successfully with non-operative intervention. A prospective study of a total of 101 patients with skin abscesses where 54 were randomized for incision and drainage and 47 ultrasonographically guided needle aspiration. All patients had a sonar at initial presentation, 60% of needle aspirations yielded little or no purulence, despite sonographic visualization of an abscess cavity and sonographic guidance during the procedure. The overall success of ultrasound guided needle aspiration was 26% compared with 80% success in patients randomized to incision and drainage⁷.

Size of the Abscess

Intra-abdominal abscesses greater than 5cm has a less favourable outcome with only antibiotic treatment. According to the study by Kumar, patients with large intra-abdominal abscesses (>6.5 cm) and a temperature >38.4 degrees are associated with higher likelihood to failing conservative management with antibiotics alone and requires percutaneous drainage⁶.

Table 1⁶

Factors Associated With Failure of Conservative Management of Intra-abdominal Abscesses				
	Clinical Improvement With Antibiotic Management	Failed Conservative Management	P Value	
No. of patients	61	50		
Age (yr)	39 (25-48)	39 (29-50)	0.5694	
Tmax-Admission (F)	100.8 (99.3-101.5)	101.2 (100.6-101.9)	0.0067	
Admission WBC (×10 ³ /µl)	13.7 (10.7–16.8)	15.2 (13.1–18.5)	0.0622	
Maximum abscess diameter (cm)	4 (3–6)	6.5 (5-10)	< 0.0001	

WBC = white blood cell.

For patients with Crohn's disease, Carvalhoa recommends that abscess greater than 4 cm usually would not respond to medical treatment alone and require drainage. The American College of Radiology recommends imaging-guided PCD for Crohn's disease related abdominal fluid collections greater than 4 cm³.

A few studies have shown the success of sonar guided needle aspiration of lactating breast abscesses. However if the abscess is larger than 3cm to 5cm, needle aspiration is unlikely to be successful and will require PCD under sonar guidance⁸. A larger than average volume of pus is a risk for failure to treat with needle aspiration. Eryilmaza reported from a prospective study that the mean volume of pus from successful needle aspiration was 44.3ml and in the unsuccessful aspiration was 70.55ml⁹.

For Renal abscesses the 3cm to 5cm is the maximum diameter between treating with antibiotics only or a drainage procedure (percutaneous or surgical). Some authors divide this limit further into <3cm (antibiotics only), 3cm to 5cm (antibiotics only or antibiotics with drainage) and >5cm (antibiotics and drainage)⁵.

<u>Table 2⁵</u> <u>Reported Primary Treatment of Renal or Perinephric Abscesses by Size</u>

Investigator	Country	Year	n		Mean abscess size		Mean hospital stay
				< 3 cm	3 - 5 cm	> 5 cm	(days)
Siegel, et al.4	United States	1984 - 1993	51	Antibiotics alone	PCD	PCD	20 - 21
Dalla Palma, et al. ⁵	Italy	1984 - 1997	16	Antibiotics alone	Antibiotics	-	-
Shu, et al.10	United States	1991 - 2002	26	Antibiotics alone	PCD	PCD	11
Coelho, et al.11	Brazil	1992 - 2002	65	Antibiotics alone	PCD or SD	SD	-
Lin, et al.9	Taiwan	2001 - 2006	73	Antibiotics alone	Antibiotics alone	PCD or SD	21 - 24
Present study	Korea	2001 - 2008	41	Antibiotics alone	Antibiotics alone	PCD	15.3

PCD, percutaneous drainage; SD, surgical drainage.

Type of infections: MRSA

Antibiotics are thought to penetrate abscesses poorly and have poor activity in this environment in which bacteria are not rapidly dividing and phagocytic activity is impaired⁶. Treating abscesses with medical therapy without a diagnostic drainage has another disadvantage that empirical regimens are used without knowledge of the infective organisms and their antimicrobial susceptibilities⁵.

The type of bacteria contained in the abscess influences the management. A multivariate analysis showed that Methicillin-resistant Staphylococcus aureus (MRSA) is an independent risk factor for failure of therapy regardless of the drainage procedure. However Gaspari reported in a prospective study of superficial abscesses that ultrasonographically guided needle aspiration of abscesses with MRSA were even less likely to be successful compared to incision and drainage 8% versus 61%⁷.

Concurrent use of other medications: corticosteroids

Concurrent use of medications that may influence the immunological response to infection also influences the treatment options. Retrospective studies on patients with Crohn's disease associated abscesses have reported success rate of 60% using parental antibiotics alone. Unfortunately, over 50% of those patients eventually required operative drainage. These patients were on corticosteroid treatment for their inflammatory bowel disease³.

Another study by Cronin on muscle abscesses also demonstrated a higher failure rate with PCD when the patients were on chemotherapy².

Characteristics of abscesses: viscosity and loculations

There are specific characteristics of the abscess that does not allow for percutaneous drainage, such as thickened abscess contents, i.e. increased viscosity (hematoma, pus)⁶. Washing out of the abscess cavity to decrease the viscosity of purulent discharge may improve the flow from PCD using normal saline or sterile water. Studies have compared normal saline and lytic agents, specifically urokinase, to increase PCD flow. There was no difference in the success or failure of the draining abscess².

The size of the PCD also influences drainage, small-caliber catheters may be easily obstructed by necrotic tissue, blood coagulates and thick purulent fluid in the abscess cavity³.

Compartmentalization of the abscess cavity can also influences drainage of the abscess with a PCD. Loculations or septations even with the use of ultrasound-guided needle aspiration may fail^{7, 10}. A

disadvantage of PCD placement is that, in multi-septated abscesses, the drainage may not access all of the individual compartments, thereby preventing a complete drainage¹¹.

Esther also demonstrated in patients with breast abscesses, **uncapsulated** abscesses are not usually adequately drained and requires the insertion of a PCD¹¹.

Hospital setting

The local expertise of the hospital influences management. Carvalhoa reported patients with intraabdominal abscesses that were admitted to a teaching hospital were associated with an increased likelihood of Percutaneous Drainage³.

Eryilmaza reported that delayed access to medical facilities is associated with a higher failure rate of needle aspiration for breast abscesses⁹.

Patient factors also influences outcome, age over 65 years, thrombocytopenia and underlying comorbidity such as Diabetes Mellitus is independently associated with poorer outcomes⁵. Worsening of sepsis when treating conservatively indicates that management needs to progress to operative treatment.

Distorted anatomy

PCD in patients with previous abdominal surgery now with intra-abdominal abscesses has a high risk of complication such_as bleeding, perforated viscus, and solid organ injury. Minor complications, including catheter obstruction and migration, occur more frequently⁶.

Complicated abscesses

Complicated abscesses that may indicate surrounding tissue damage is highly unlikely to be treated successfully with non-operative measures. Patients with Crohn's disease associated abscesses and complicated with strictures or fistulae were associated with an increased likelihood of operative intervention. Conversely, small abscess without concurrent fistula have a higher chance of respond to antibiotics alone. The presence of strictures and abdominal fistulas usually indicates the need of surgical treatment since there might be already an irreversible structural damage in the bowel wall³.

Conclusion

There are many factors that influences the most appropriate management of abscesses. The treatment of one abscess is not always the same for another. Health professionals need to be aware of the non-operative options available to manage abscesses and the limits and limitations thereof; and when to progress to operative management.

References

- 1. Seiler CA, Brügger L, Forssmann U, Baer HU and Büchler MW. Conservative surgical treatment of diffuse peritonitis. Surgery. 2000; 127 (2): 178-184.
- Cronin CG, Gervais DA, Hahn PF, Arellano R, Guimaraes AR and Mueller PR. Treatment of Deep Intramuscular and Musculoskeletal Abscess: Experience with 99 CT-Guided Percutaneous Catheter Drainage Procedures. American Journal of Radiology 2011; 196:1182–1188.
- 3. Carvalhoa ATP, Cathalá Esberarda B, Moreira ADL. Current management of spontaneous intra-abdominal abscess in Crohn's disease. Journal of coloproctology (rio j). 2016, 179; 1-6.
- 4. Brandt D, Gervaz P, Durmishi Y, Platon A, Morel Ph and Poletti PA. Percutaneous CT Scan-Guided Drainage vs. Antibiotherapy Alone for Hinchey II Diverticulitis: A Case-Control Study. Diseases of the Colon Rectum, 2006; 1533-1539.
- 5. Lee SH, Jung HJ, Mah SY, and Chung BH. Renal Abscesses Measuring 5 cm or Less: Outcome of Medical Treatment without Therapeutic Drainage. Yonsei Med J 51(4):569-573, 2010.
- 6. Kumar RR, Kim JT, Haukoos JS, Macias LH, Dixon MR, Stamos MJ, et al. Factors Affecting the Successful Management of Intra-Abdominal Abscesses With Antibiotics and the Need for Percutaneous Drainage. Dis Colon Rectum 2005; 49: 183–189.
- Gaspari RJ, Resop D, Mendoza M, Kang T and Blehar D. A Randomized Controlled Trial of Incision and Drainage Versus Ultrasonographically Guided Needle Aspiration for Skin Abscesses and the Effect of Methicillin-Resistant Staphylococcus aureus. Ann Emerg Med. 2011; 57:483-491.
- 8. Ulitzsch D, Nyman MKG and Carlson RA. Breast Abscess in Lactating Women: US-guided Treatment. Radiology 2004; 232:904–909<u>.</u>
- 9. Eryilmaza R, Sahina M, Tekelioglub H and Daldal E. Management of lactational breast abscesses. The Breast. 2005: 14: 375–379.
- 10. Elagili F, Abdullah N, Fong L and Pei T. Aspiration of Breast Abscess Under Ultrasound Guidance: Outcome Obtained and Factors Affecting Success. Asian J Surg. 2007; 30(1): 40–4.
- 11. Esther MF, Schwarzc I, Stadlmannb S, Singerb G, Hauserc Rahel N and Kubik-Huch A. Breast Abscesses: Diagnosis, Treatment and Outcome. Breast Care. 2012; 7:32–38.
- 12. Simillis C, Symeonides P, Shorthouse AJ, and Tekkis PP. A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon). Surgery 2010; 147:818-29.
- 13. Whiteford MH, Kilkenny J, Hyman N, Buie D, Cohen J, Orsay C, et al. Practice Parameters for the Treatment of Perianal Abscess and Fistula-in-Ano (Revised). Dis Colon Rectum. 2005; 48: 1337–1342.

EVAR FOR THORACO-ABDOMINAL AORTIC ANEURYSMS Prof TV Mulaudzi

Definition

TAAAs are localized dilatations in the thoracic and abdominal aorta secondary to weakening and subsequent expansion of the aortic wall. A TAAA by definition is a dilatation at least 1.5 times its normal value.

Defining these anatomic aortic sizes is critical to help identify pathologic aortic growth because TAAA diameter is the strongest predictor of rupture, with a reported mean aortic diameter of ruptured TAAAs of 6.1 cm

Normal Aortic Diameter and Length by Segment as well as Percentage of Thoracoabdominal Aortic Aneurysm Total by Segment

Mean Aortic Diameter (cm) Mean Aortic Length (cm) TAAAs (%)

Ascending aorta	3	5	40
Aortic arch	2.5-3.5	4	15
Descending thoracic aorta	2.3-2	NR	35
Thoracoabdominal aorta	1.7-2.6*	NR	10

NR, Not reported; TAAAs, thoracoabdominal aortic aneurysms.

Normal and Pathologic Aortic Size

The aorta normally enlarges as it progresses from the aortic root to the terminal aorta.In addition, gender, age, and body surface area influence aortic diameter.Even after adjustment for age and body surface area, mean aortic size is significantly smaller, usually 2 to 3 mm, in women than in men. Body surface area is reported to be a better predictor of aortic diameter than height or weight.

The growth rates of TAAAs are not predictable or linear. However, there is consensus that TAAAs, similar to AAAs, have growth rates that accelerate as they enlarge.For example, TAAAs larger than 5 cm expand at a growth rate of 0.79 cm/y, whereas TAAAs less than 5 cm experience growth rates of 0.17 cm/y. Dapunt and associates documented that patients with ruptured TAAAs experienced growth rates of 0.7 cm/y.

Normal Adult Thoracic Aortic Diameters by Gender

Thoracic Aorta	Range of Reported Mean (cm)	Assessment
Mid-descending, female	2.45-2.64	CT
Mid-descending, male	2.39-2.98	CT
Diaphragmatic, female	2.40-2.44	CT
Diaphragmatic, male	2.43-2.68	CT

CT, Computed tomography

Anatomic Classification

Evaluation of a patient with a TAAA as well as the technical performance of either open or endovascular repair is closely aligned with the Crawford classification. Classification of TAAAs also has important therapeutic implications for the operation to be performed as well as for the risk of specific complications.



Crawford Classification TAAA's

Type I TAAAs account for approximately 25% of all TAAAs; they involve the entire descending thoracic aorta and extend only to the upper abdominal aorta.

Type II TAAAs (approximately 30% of TAAAs) involve the entire descending thoracic aorta and most or all of the abdominal aorta.

Type III TAAAs (less than 25%) involve variable lengths of the descending thoracic aorta and extend into the abdominal aorta.

Type IV TAAAs (<25%) are limited to most or all of the abdominal aorta, including the visceral and renal arteries.

Recommendations for Repair of Thoracic and Thoracoabdominal Aortic Aneurysms Class I

- 1. 1.For patients with chronic dissection, particularly if associated with a connective tissue disorder, but without significant comorbid disease, and a descending thoracic aortic diameter exceeding 5.5 cm, open repair is recommended. (*Level of Evidence: B*)
- 2. 2.For patients with degenerative or traumatic aneurysms of the descending thoracic aorta exceeding 5.5 cm, saccular aneurysms, or postoperative pseudoaneurysms, endovascular stent grafting should be strongly considered when feasible. (*Level of Evidence: B*)
- 3. 3.For patients with thoracoabdominal aneurysms, in whom endovascular stent graft options are limited and surgical morbidity is elevated, elective surgery is recommended if the aortic diameter exceeds 6.0 cm, or less if a connective tissue disorder such as Marfan or Loeys-Dietz syndrome is present. (*Level of Evidence: C*)
- 4. 4.For patients with thoracoabdominal aneurysms and with end-organ ischemia or significant stenosis from atherosclerotic visceral artery disease, an additional revascularization procedure is recommended. (*Level of Evidence: B*)

From Hiratzka LF, et al; Writing Group Members: 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCA/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. Circulation 121:e266-e369, 2010.

Open versus Endovascular Repair for Thoraco-abdominal Aortic Aneurysms

Until recently, elective surgical therapy for TAAAs involved major surgery with a significant risk of perioperative mortality and morbidity. Centres of excellence in this procedure report

elective mortality and paraplegia rates of 4.8% and 4.6%, respectively.Mortality after surgical treatment of ruptured TAAA is extremely high, even though rates of 26% have been reported. In contrast, national mortality rates before the introduction of endovascular technology were 22%. Surviving patients experience many postoperative complications and have lengthy hospital stays. Given the continued high mortality and morbidity in contemporary surgical practice, it is not surprising that new techniques for repair were developed. Data suggest that TEVAR of isolated descending TAAs is a safe alternative to open surgery and is associated with lower mortality and morbidity. However, long-term (>10 years) results are not yet available. In addition, no specific risk scoring system has been developed to predict mortality in patients undergoing TEVAR.

The decision about which therapy is appropriate for a particular patient is an evolving aspect of care of these complicated patients. There are few guidelines on indications for TEVAR versus open TAAA repair as determined in a prospective, randomized comparison. A Cochrane review comparing thoracic stent-grafting with surgery for TAAs concluded that although stent-grafting of the thoracic aorta is technically feasible and nonrandomized studies suggest reduction of early outcomes, such as paraplegia, mortality, and hospital stay, highquality randomized controlled trials assessing clinically relevant outcomes including open conversion, aneurysm exclusion, endoleaks, and late mortality are needed. However, three industry-sponsored comparative trials are now available. Stent-graft devices are approved to treat only degenerative aneurysm disease as well as aortic transections. In addition, there are no randomized, controlled prospective trials comparing open and endovascular TAA repair, even though industry-sponsored trials suggest clinical equipoise.

Industry-Sponsored Endovascular Graft Trials Long-Term Results

Long-term follow-up data from the preclinical Gore TAG trial were recently published. Makaroun and coauthors reported 5-year follow-up with the Gore TAG device in treating degenerative TAAAs and documented no difference in all-cause mortality between endovascular and open TAAA repair at 5 years (67% vs. 68%) Major adverse events at 5 years were significantly reduced in the TEVAR group (57.9% vs. 78.7%; P = .001). Endoleaks in the TAG group decreased from 8.1% at 1 month to 4.3% at 5 years. Five TAG patients have undergone major aneurysm-related re-interventions at 5 years (3.6%), including one arch aneurysm repair for a type 1 endoleak and migration, one open conversion, and five endovascular procedures for endoleaks in three patients. For the TEVAR patients, sac size at 60 months decreased in 50% and increased in 19% with respect to the 1-month baseline. At 5 years, there have been no ruptures, one migration, no collapses, and 20 instances of stent fracture in 19 patients, all before revision of the TAG graft. Although the authors acknowledged that the rates of secondary intervention were much higher in the stent-graft group, they concluded that stent-graft repair of TAAA is superior to open repair at 5 years. Even though this study is prospective, it was not randomized and not designed to help us determine which patients are best served by stenting versus open repair.

A meta-analysis reviewing open TAAA repair and stent-grafting by Walsh and colleagues included 17 eligible studies totaling 1109 patients and demonstrated that stenting was associated with a significant reduction in mortality (pooled odds ratio, 0.36; P < .0001) and major neurologic injury (pooled odds ratio, 0.39; P < .0001), with no difference in the major re-intervention rate after elective TAAA repair. Importantly, there was no effect on mortality in patients with thoracic aortic trauma or rupture. The authors concluded by suggesting that

endovascular TAAA repair reduces perioperative mortality and neurologic complications in patients undergoing elective TAAA repair, although they did suggest that there may be less benefit in other thoracic aortic conditions

Decision Making

Subpopulations benefiting from thoracic endovascular aneurysm repair

It is reasonable to conclude that patients older than 75 years, if anatomically suitable, should be directed towards stent grafting. A subset of patients with significant COPD is likely to benefit from stent-grafting when possible to avoid the attendant risks incurred from a thoracotomy. Patients with increasing pain or ruptured TAAA's should be considered for TEVAR as this can be performed more expeditiously than open repair if the anatomy is suitable for endovascular technique.

Indications and contraindications for TEVAR

Similar criteria should be used for both open and endovascular repair and include aneurysm size >6.0cm diameter, saccular configuration and symptoms, including rupture. The main consideration in the preferential choice of TEVAR over open repair include anatomy and comorbidities

- There should be adequate landing zone(>20mm) both proximally and distally to allow adequate sealing and exclusion of the aneurysm from the circulation
- Appropriately sized arterial access to deliver the stent-graft to the desired location
- Many aortic aneurysms impinge on a major arterial branch that must be covered for adequate sealing. In these circumstances the safety of branch sacrifice must be balanced against further observation of the aneurysm or open repair.
- Iliac artery : vessel calcification, lumen size(ideally >8mm) and tortuosity have profound impact on procedure
- Aortic channel : Tortuosity of the aorta associated with exaggeration and elongation of the normal curvature presents an anatomic hindrance to deliverance of the device
- TEVAR is contra-indicated when the anatomy of the aneurysm prevents safe and effective performance of stent graft occlusion.
 - Severe aortoiliac occlusive disease
 - Rapid taper of the aorta
 - Circumferential thrombus at the attachment sites
 - Severe angulation of the arch >60 degrees

Complications

1.Vascular:

These are related to the use of large sheaths in atherosclerotic arteries, and can be avoided by using prophylactic iliac conduits and endoconduits.

2.Neurological complications :

Stroke and spinal cord ischaemia occur at similar rates during open and endovascular repair(2-7%)

Deployment of the endograft proximal to the CCA shows a strong association with stroke Other factors identified as independent risk factors for stroke include female sex and prolonged procedure time(>160minutes)

Several risk factors have been linked to an increased risk of spinal cord ischaemia after TEVAR

Concomitant or previous open infrarenal aortic replacement

Extensive thoracic aortic coverage Intraoperative hypotension(systolic<80mmHg) Renal insufficiency Coverage of the hypogastric and left SCA

3.Endoleaks

Decreasing incidence of endoleaks reported with second and third generation devices which have design improvements to allow better conformability. Distribution of endoleaks variable with TAG study reporting majority type I and type II endoleaks and EVAR trial reporting more Type I and type III endoleaks

4.Sac Enlargement

Sac shrinkage is a good surrogate marker of successful repair of aneurysm

Sac enlargement indicates poor exclusion and pressurisation of the sac and may possibly allow traction in a large cavity leading to stent-graft kinking, migration or dislodgement.

5.Re-interventions :

Defined as all procedures performed on a patient referable to or as a consequence of the initial endograft procedure

Most re-interventions are for endoleaks and most re-interventions are treated endovascularly.

Branched and fenestrated endograft treatment

Fenestrated devices can be used to treat juxta-renal aneurysms with covered stents used for the renal and superior mesenteric position. Several fenestrated devices are available in various stages of development.

The most common initial configuration consisted of two renal fenestrations with a scallop for the SMA. As more experience achieved the number of incorporated visceral vessels in the repair increased. For custom made devices the number of fenestrations is not an issue as the fenestrations can be measured and placed accurately according to the patients anatomy. However there is a tendency to more 'off the shelf 'devices to accommodate variablility in patient anatomy.

Branched stent grafts are manufactured with branches preattached to the main body Both straight cuffs and helical limbs have been used effectively to bridge the aneurysmal aorta into the coeliac and SMA.

ENDO VENOUS MANAGEMENT OF VARICOSE VEINS MH Sikhosana

Introduction

Varicose veins (tortuous, dilated superficial veins >3mm in diameter) are one of the common lower extremity vascular conditions. Affecting about 20% of the population (30-35% females and 10-15% males). And they have been shown to negatively impact the patient's quality of life (poor cosmesis, leg heaviness, swelling, pain and bleeding).

Traditionally varicose veins have been treated with ligation of saphenous junctions with or without stripping and phlebectomy of the isolated varicosities. The success of the surgical treatment has been reported to be in the range of 80%. But with the risk of complications (bleeding, nerve injuries, post procedural pain, haematoma and infection). The other limitations of surgical treatment are the requirement of general anaesthesia, the longer post procedural recovery period and the 20-30% recurrence rate at 5 years.

Endovenous treatment

Endovenous modalities are proving to be at least as effective as the surgical treatment without the same complications, better cosmeis, can be done as out- patient procedures and quicker recovery period. The accepted endovenous treatment modalities are sclerotherapy, endothermal ablation procedures (radiofrequency and laser ablation) and non-thermal, non-tumescent techniques (ClariVein and Venaseal).

Sclerotherapy

Involves instilling a sclerosant(osmotic, alcohol or detergent) into the vein and applying compression resulting in fibrosis. Liquid sclerotherapy has poor occlusion rates as sclerosant is deactivated by blood contact. This has been corrected by the introduction of foam sclerotherapy (mixing of sclerosant with air in a ratio of 1:4). As foam increases the contact area between the sclerosant and the vein wall, increasing fibrosis and reducing thrombosis.

Radiofrequency

The Closure Fast catheter has a 7cm bipolar electrode at its distal end. The catheter is inserted into the greater saphenous vein just below the knee up to 2cm below the sapheno femoral junction. Tumescent anaesthesia (lidocaine, normal saline and sodium bicarbonate) is then injected around the vein to provide analgesia, separation of the vein from surrounding structures (protection from thermal injury) and improve contact of the vein with the electrode by causing external compression of the vein. Whilst applying external compression, the electrode delivers radiofrequency energy that results in the destruction of the endothelium, contraction of vein wall collagen and thrombus formation.

Laser

Similar to radiofrequency, difference being the catheter and the mechanism to ablate the vein. Laser uses a fiber to deliver laser energy and forms steam bubbles which destroy the endothelial lining, this causes an inflammatory reaction leading to thrombotic occlusion.

ClariVein
Is a hybrid system composed of rotating tip (causing endothelial damage) with simultaneous injection of liquid sclerosant.

Venaseal

The vein is accessed at the same level as for radiofrequency. Cyanoacrylate glue instillation and manual compression cause fibrosis.

Endovenous treatment options for telangiectasia (<1mm) and reticular veins (1-2mm)

With 30% telangiectatic matting occurring after sclerotherapy, cutaneous laser and intense pulse light are the other options.

Indications of ligation and stripping in the era of endovenous treatment

- 1. Superficial saphenous tributary
- 2. Saphenous aneurysm
- 3. Chronic thrombophlebitis
- 4. Excessive tortuosity

Conclusion

The high success rate, less complications, quicker recovery, good cosmetic outcome and possibility of out-patient procedure makes endovenous therapy the more attractive option to treat varicose veins.

DRUG ELUTING BALLOONS AND STENTS IN VASCULAR SURGERY A.T.O. ABDOOL-CARRIM

Balloon angioplasty and stenting have become very popular in the peripheral arteries and in some instances have replaced open surgery simply because they are less invasive and have less wound complications. However, the long term patency for the endovascular approach is much less compared to open surgery. The essential component of angioplasty is to rupture plaque and remodel the vessel, stenting was introduced to improve the outcomes of angioplasty ensuring adequate lumen, ensuring flow and reducing embolic load. Balloon angioplasty became popular in late 1980's and and subsequently stents were introduced initially stainless steel, cobalt chromium and nitinol stents. The arch enemy of stenting and balloon angioplasty has been neo-intimal hyperplasia leading to recurrent stenosis. More, recently bare metal stents that have a swirling flow technology have been introduced known as the biomimetics stents early results are encouraging. The advent of drug elution and coated stents have also greatly improved outcomes. The greatest challenge has been the superficial femoral artery where results have been disappointing with high restenosis rates.

Drug eluting technology initially was introduced in the coronary circulation; in the last decade this technology has been utilized to treat peripheral arteries. A number of drugs have utilized to decrease or arrest neo-intimal hyperplasia these include Paclitaxel and Serolimus. The main areas where drug coated balloons and stents have been used is the superficial femoral, popliteal and tibial arteries.

Many trials have been conducted for both drug coated balloons (DCB) and drug eluting stents(DES) in the superficial femoral and popliteal and tibial arteries. The 5 year results with the Zilver PTX DES revealed better primary patency (66.4% vs 43.4%) than plain balloon angioplasty and bare metal stents.

The drug coted balloons Lutonix Paclitexal DCB showed primary patency at 12 months was 73.5% vs 56.8% for plain balloon angioplasty.

The IN.PACT (DCB)SFA 11 trial showed superior results compared to standard balloons.

The trials for below the knee with both DCB and DES the drug eluting stents showed reduced restenosis rate than DCB (28% vs 57.9%).

The vexing problem is what to use DCB or DES, both have a role but it would appear that lesion morphology will dictate what to use to get the best result essentially predilate lesion with plain balloon if good result the DCB will give good outcome however if predilation is suboptimal (recoil, dissection or moderate to severe calcification) then use a DES.

Drug technology is improving and short term and longer term results are better than plain balloon and bare metal stent and their use will increase albeit they are costly interventions.

MOLECULAR GENETICS IN THE MANAGEMENT OF BREAST CANCER Maritha J Kotze

Department of Pathology, Faculty of Medicine and Health Sciences, Stellenbosch University and National Health Laboratory Services, Tygerberg Hospital, Cape Town.

Application of molecular genetics led to significant advances in the prevention, diagnosis and treatment of breast cancer. It is the most common neoplasm among Asian and Caucasian women in South Africa, and the second most common cancer among women of African descent and the Coloured population of Mixed Ancestry. Inter-ethnic variability in breast cancer risk is explained by a combination of genetic and environmental risk factors that contribute to cancer development and tumour gene expression. Familial susceptibility to breast cancer accounts for approximately 10-20% of all cases, with the majority of high risk familial cases due to mutations in the BRCA1 and BRCA2 genes. The detection of founder BRCA mutations underlying the majority of inherited breast cancer in South Africa led to development of cost-effective assays routinely applied in clinical practice. BRCA mutation screening is useful to identify high-risk individuals in affected families for implementation of effective risk reduction strategies. These include prophylactic surgery shown to reduce the risk of developing breast cancer by 95% in mutation carriers.

The finding that sporadic and BRCA2-related breast cancers more likely to be estrogen receptor (ER) positive than those with BRCA1 mutations, highlighted the importance of including histopathology assessment in the pre-screen algorithm used to select the target population most likely to benefit from genetic testing. To date more than 100 genes have been identified that can change a healthy breast cell into a cancer cell or affect treatment response. This supports the use of multi-gene risk assessment tools such as the 70-gene MammaPrint profile performed in conjunction with the 80-gene BluePrint assay for tumour subtyping into luminal A, luminal B, HER2-enriched and basal-type. The significant impact of breast cancer on the health economy sparked extensive research into the molecular pathways underlying these distinct tumour subtypes. BluePrint is increasingly used to subdivide HER2-positive breast cancer into the luminal B and HER2 enriched subtypes that differ in their response to Herceptin treatment.

Against this background, new era of personalized medicine was introduced in South Africa with the promise that pharmacogenomics will deliver the right treatment at the right time in patients with cancer and associated co-morbidities. However, population differences in drug metabolism considered to be of particular relevance in Africa due to a high level of genetic diversity, questions the feasibility of using commercially available genotyping platforms. For this reason, we linked genetic testing service delivery to the generation of a research database using an institutional review board approved protocol. Establishment of joint pathology and genomic facilities resulted in a new model for research translation termed pathology-supported genetic testing (PSGT). This approach was used to validate the MammaPrint pre-screen algorithm (MPA) developed as a cost-saving strategy in South African patients with early-stage breast cancer considering chemotherapy. Over a 9-year period, after introduction of the Food and Drug Administration (FDA)-approved MammaPrint test in 2007, more than 100 early-stage breast cancer patients in South Africa could safely avoid chemotherapy using the PSGT approach. This was confirmed by recent level 1A evidence from the prospective Microarray in Node Negative and 1 to 3 Positive Lymph Node Disease May Avoid Chemotherapy (MINDACT) study. Many challenges encountered during this process contributed to the development of a new framework for implementation of next generation sequencing (NGS) using germline or tumour DNA. Whole genome or exome sequencing now enabes the combination of diagnostic genetic testing with pharmacogenomics in a single test.

THE SIGNIFICANCE OF LYMPH NODE MICROMETASTASES AND ISOLATED TUMOUR CELLS IN BREAST CANCER Carol Benn

Introduction and Background

Axillary lymph node dissection (ALND) has historically represented a routine surgical component in the management of breast cancer. The traditional benefits of ALND¹ include the impact on disease control (ie, axillary recurrence and survival), prognostic value, as well as an important role in planning oncology treatment selection. This procedure is not however without morbidity.²

The axilla now represents one of the most important prognostic factors in the treatment of breast cancer. Whilst ALND remains the standard treatment for women who have clinically palpable axillary nodes or positive nodes confirmed by methods such as ultrasound and or ultrasound guided fine needle aspiration or core biopsy Formal axillary dissection has slowly been replaced by sentinel lymph node biopsies³ (SLNB) in the node negative axilla.

The sentinel lymph node is defined as the first regional lymph node that receives lymph flow from the primary tumour. It is the security guard (sentinel) that acts as the gatekeeper.

Pathology assessment of sentinel lymph nodes

Smaller volume of pathology tissue received during SLNs compared with an axillary dissection has prompted a more comprehensive lymph node analysis increasing detection of micrometastasic⁴ disease. Data analysis shows that many women previously classified as having a node negative axilla are now classified as having minimally node positive disease. As a result, our nodal classification and cancer staging have evolved to recognize a stratification of nodal tumour burden rather than a simplistic positive and negative.

The more sections we evaluate from SLNs the more metastases we identify

It may be impractical to expect the practicing pathologist to mount, stain, and microscopically examine every section through the SLN paraffin blocks, unless the data received will impact on treatment protocols and outcome.

Despite recommendations from the College of American Pathologists and the American Society of Clinical Oncology, there are still variations in the approach to SLN evaluation by pathologists necessitating a standardized evaluation protocol.

¹ Wexler, MJ. "Role of axillary lymph-node dissection in the management of breast ..." 2003. <<u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3211638/</u>>

² Schrenk, Peter et al. "Morbidity following sentinel lymph node biopsy versus axillary lymph node dissection for patients with breast carcinoma." *Cancer* 88.3 (2000): 608-614.

³ Veronesi, U. "Sentinel lymph node biopsy in breast cancer: ten-year results of a ..." 2010. <<u>http://www.ncbi.nlm.nih.gov/pubmed/20195151</u>>

⁴ Shiller, SM. "The sensitivity and specificity of sentinel lymph node biopsy for breast ..." 2011. <<u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3069509/</u>>

The most important aspect of the sentinel node examination is careful attention to slicing the SLN no thicker than 2.0 mm with correct embedding of all the slices to assure we identify all macrometastases (> 2.0 mm). A single section from blocks prepared in this manner will identify all macrometastases present but smaller metastases may be missed. The prognostic significance of these missed micrometastases(Mic) is under continual evaluation.

Numerous studies analysing the discordance between frozen section, imprint cytology at the time of the procedure demonstrate that best assessment of the sentinel lymph node pathology is determined in the laboratory by definitive histology.

Challenges with Micro-metastatic disease

Micrometastatic disease in the SLN was first described by Huvos⁵ in 1971

Although a continual subject of debate⁶;⁷; we have a better understanding of the clinical significance of micrometastases in breast SLNs. Micrometastases include all metastases ≤ 2.0 mm in greatest dimension. Isolated tumour cells (ITCs) are defined as cell clusters or single cells with no single cluster larger than 0.2 mm.

A systematic review of 58 studies⁸ (mainly from the pre-sentinel era showed a decreased survival in patients with micrometastatsic disease, even after all other prognostic factors were controlled for

The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER)⁹ national cancer database containing 209720 patients, from 1992-2003 looking specifically and LN disease showed that the presence of micromets is associated with a decreased survival and worse prognosis, than in patients with no nodal disease, but expectedly a better prognosis than those with macrometastatic disease,

So micrometastases is associated with an overall decrease in survival at 10 years with incrementally a worse outcome for T1, T2 t, and T3 tumours, compared to patients with no nodal metastases detected. This SEER analysis included data prior to the advent of the widespread use of SLN biopsy. The study showed that in women with a mammographically detected tumour <2.0 cm, there is little outcome significance associated with the presence of micrometastases. The study does suggest that for larger tumors, detection of micrometastases may be more relevant in terms of clinical outcome. Considering this is a population-based study, concerns

⁵ Huvos, AG. "Significance of axillary macrometastases and micrometastases in ..." 1971. <<u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1397119/</u>>

⁶ "The Breast: Comprehensive Management of Benign and Malignant Diseases." 12 Sep. 2016 <<u>https://books.google.com/books?id=1u4x_iGiHNEC&pg=PA462&lpg=PA462&dq=Huvos+AG,+Hutter+R_V,+Berg+JW.+Significance+of+axillary+macrometastases+and+micrometastases+in+mammary+cancer.+ Ann+Surg.+1971%3B173(1):44%E2%80%9346.&source=bl&ots=2uTbeT7LBQ&sig=7n65HxQ9Ivn-4DxDklvyo34EE0s></u>

⁷ de Boer, Maaike et al. "Breast cancer prognosis and occult lymph node metastases, isolated tumor cells, and micrometastases." *Journal of the National Cancer Institute* 102.6 (2010): 410-425.

⁸ de Boer, Maaike et al. "Breast cancer prognosis and occult lymph node metastases, isolated tumor cells, and micrometastases." *Journal of the National Cancer Institute* 102.6 (2010): 410-425.

⁹ Chen, Steven L, Francesca M Hoehne, and Armando E Giuliano. "The prognostic significance of micrometastases in breast cancer: a SEER population-based analysis." *Annals of surgical oncology* 14.12 (2007): 3378-3384.

as to how the nodes were sampled (with questions being that of the possibility of both micrometastases in larger tumors confirming aggressive intrinsic biology or alternatively suggesting undetected macrometastases deeper in paraffin blocks) must be considered.

A large retrospective analysis of pre-SLN era data from California and Massachusetts showed no impact on 15-year mortality in any tumour regardless of size category when only a single lymph node contained a metastasis. This study supports the hypothesis that the primary tumour biology has more prognostic importance than a minimal lymph node tumour burden.

When a SLNB is not successful or when clinically suspicious nodes are encountered in the axilla the surgeon should perform an axillary dissection (7 lymph nodes) for staging purposes and to ensure loco-regional control

Biology reigns supreme

The reclassification of breast cancer pathology has provided insight into the different behavioral characteristics of cancers.

The question remains as to whether the presence of micrometastatic disease in the sentinel lymph node with the understanding of tumour biology may in certain biological subsets predict more aggressive tumour behavioral traits

Understanding Occult Metastases

Occult metastases is the detection of metastatic disease in the sentinel lymph node that is not picked up on routine H&E staining. the NSABP-B32 ¹⁰,¹¹,study provided insight and information into the clinical significance of occult metastases in patients today with multidisciplinary oncological management. Occult mets were associated with age less than 50, tumour size greater than 2cm, and planned mastectomies

Significance of Micromets and tumour cells

Management of Sentinel lymph node metastases

Approximately 40 % of patients with a positive sentinel lymph node (SLN) will be found to have residual disease in the axilla

By definition as mentioned occult disease is not detected on routine H&E, but rather on IHC staining

1. Isolated tumour cells (ITC) are not considered an indication for further axillary surgery, radiation treatment or adjuvant systemic therapy. It should be noted that finding ITC in lymphatics as a result of iatrogenic displacement from core biopsy procedures has been documented and is not considered to be clinically significant

¹⁰ Krag, David N et al. "Technical outcomes of sentinel-lymph-node resection and conventional axillarylymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial." *The lancet oncology* 8.10 (2007): 881-888.

¹¹ Kell, Malcolm R et al. "Outcome of axillary staging in early breast cancer: a meta-analysis." *Breast cancer research and treatment* 120.2 (2010): 441-447.

2.Micrometastases — patients with micrometastases can be considered node positive and therefore it seems should result in a worse prognosis. Most studies, however show no change or only a small reduction in patient survival compared with those without micrometastases.

Pathologic evaluation of sentinel lymph nodes for occult metastases in a randomized trial of 3887¹² women who underwent SLNB alone or SLNB plus ALND for invasive breast cancer detected occult metastases in 16 % of patients (ITC clusters in 11 %, micrometastases in 4 %, and macrometastases in 0.4 %). The following findings were noted:

- Occult metastases were an independent adverse prognostic factor with an increased risk of distant disease and death.
- The risk associated with ITC was less than that of micrometastasic disease.
- Five years analysis showed small but statistically significant outcomes for patients with and without occult metastases with respect to overall survival (95 versus 96 %), disease free survival (86 versus 89 %), and distant disease free interval (90 versus 92 %).
- The presence of occult metastases was not a negative predictive factor; 85 % of women with occult metastases were alive without breast cancer recurrence at 5 years.

Results from the American College of Surgeons Oncology Group (ACOSOG) study Z0010¹³, a prospective multicenter study of 5210 patients with almost eight-year follow-up, confirm that IHC-detected metastases have no significant impact on overall survival. Thus, routine IHC or PCR is not recommended for the evaluation of SLNs in guidelines published by ASCO, and NCCN. Histologically negative nodes that are IHC or RT-PCR-positive are classified as pN0 disease in the TNM staging system for breast cancer.

Guidelines from ASCO and NCCN¹⁴recommending that routine completion ALND be carried out for micrometastases detected on SLNB with standard hematoxylin and eosin (H&E) examination, have recently been questioned particularly for women with less than three positive lymph nodes.

¹² Weaver, Donald L et al. "Effect of occult metastases on survival in node-negative breast cancer." *New England Journal of Medicine* 364.5 (2011): 412-421.

¹³ Olson, John A et al. "Impact of immediate versus delayed axillary node dissection on surgical outcomes in breast cancer patients with positive sentinel nodes: results from American College of Surgeons Oncology Group Trials Z0010 and Z0011." *Journal of Clinical Oncology* 26.21 (2008): 3530-3535.

¹⁴ "Recently updated NCCN Clinical Practice Guidelines in Oncology™." 2011. 12 Sep. 2016 <<u>https://www.nccn.org/professionals/physician_gls/recently_updated.asp</u>>

What are the controversies?

Current controversy

The SLN is the sole tumour-bearing node in up to 60 % of women who have a clinical and ultrasound node negative axilla and in almost 90 % of patients who harbour only micrometastatic disease

Completion ALND in patients with a positive SLNB showing micrometastases or macrometastases in less than three nodes is under continual review. Speculation that completion ALND may not be necessary in selected patients with a positive SLNB in less than three nodes because the need for systemic therapy is established has already been proven in the Z0011¹⁵;¹⁶ trial. The risk of an axillary recurrence appears to be low particularly in patients receiving WBR

The NCCN has only recently changed their guidelines and continues to recommend completion ALND for some women with positive sentinel nodes until additional randomized trial results are available. It is critical that the distinction can be made between isolated tumor cells, micrometastases, and macrometastases, is made in terms of clinical management, (at least a 22 % misclassification of sentinel node metastases has been demonstrated).

Omission of the ALND can be considered if the tumor burden appears low (cases with isolated tumor cells or micrometastases) when whole breast radiation with high axillary tangents is planned. Results from the two randomized trials studying the benefit of ALND for clinically node negative women with positive SLNs: the EORTC 10981-22023 AMAROS trial¹⁷;¹⁸; and Trial 23-01¹⁹, have shown that radiation can replace completion axillary dissection in the studied groups

Women who are having mastectomy rather than breast conserving therapy should be counselled that they will need completion ALND if the SLNB is positive or radiation, and postmastectomy radiation may impact their aesthetic outcome should prosthetics be used. This is a critical concept to understanding safety and low complication rate in reconstructive surgery

Another critical problem is in that women who underwent primary chemotherapy were excluded from the Z-011 trial, and therefore results of this trial could not be extrapolated to these patients.

¹⁵ Caudle, Abigail S et al. "Multidisciplinary considerations in the implementation of the findings from the American College of Surgeons Oncology Group (ACOSOG) Z0011 study: a practice-changing trial." *Annals of surgical oncology* 18.9 (2011): 2407-2412.

¹⁶ "Ten-year survival results of ACOSOG Z0011: A randomized trial of ..." 2016. 12 Sep. 2016 <<u>http://meetinglibrary.asco.org/content/170337-176</u>>

¹⁷ Donker, M. "Radiotherapy or surgery of the axilla after a positive sentinel node in ..." 2014. <<u>http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(14)70460-7/abstract</u>>

¹⁸ Donker, M. "[Axillary lymph node dissection versus axillary radiotherapy in patients ..." 2015.
<<u>http://www.ncbi.nlm.nih.gov/pubmed/26488192</u>>

¹⁹ Galimberti, Viviana et al. "Axillary dissection versus no axillary dissection in patients with sentinelnode micrometastases (IBCSG 23–01): a phase 3 randomised controlled trial." *The lancet oncology* 14.4 (2013): 297-305.

What should we as surgeons do

We need to understand that treatment of breast cancer today, is individualised, taking into account tumour biology, nodal involvement, genetic profiling in both node negative and positive tumours, with the added complexity that luminal A patients that are node positive may not be good candidates for chemotherapy, and that certain chemotherapeutic regimes may be more effective for certain tumour subtypes, and micrometastatic disease may play need to be managed differently in patients undergoing mastectomies without radiation, to patients undergoing breast conservation with radiation, and that depending on the type of adjuvant chemotherapy, the use of chemotherapy, and the type and length of endocrine therapy the outcomes may differ

Prognostic value of lymph node micrometastatic disease

So the prognostic value of micromets may be different for different tumour biologies, as well as having a different interpretation for members of the multidisciplinary team. This is why all these patients should be discussed in the MDM

Oncologist

The presence of micrometastatic nodal disease may guide an oncologist in terms of treatment., types of chemotherapy, as well as types of endocrine therapy, and suggestions as to the length of endocrine therapy

Luminal B breast cancers (with Ki between 15-25%) that have micrometastatic disease present, may convince oncologists to give chemotherapy

Radiation Oncologist

Micrometastatic disease is not a criteria for radiation per say

However if seen in a few nodes, or multiple areas of micrometastatic disease, this might suggest a higher nodal burden, and radiation may be suggested in the MDM.

Surgeon

Documentation of micrometastatic disease and discussion about the value of further axillary surgery in the MDM is essential for all these patients, particularly in those not receiving radiation therapy.

Conclusion

Due to the clinical significance of tumour behaviour and realizing today that the axilla is merely a prognostic indicator of disease behaviour, means that our understanding of micrometastatic disease and isolated tumour cells is not a linear one, but rather provides a complexity around options of further treatment both in terms of oncology and surgery. Whilst survival may not be altered significantly, and need for a completion ALND is no longer required; individual patient treatments may well be altered by the finding.

NEW THERAPIES IN THE MANAGEMENT OF MALIGNANT MELANOMA IMMUNOTHERAPY

Dr Daniel A. Vorobiof, Sandton Oncology Centre, Johannesburg

As mentioned in the previous abstract, the standard treatment of chemotherapy for advanced malignant melanoma has proven to be ineffective and unable to induce meaningful responses.

Immunotherapy, a treatment that boosts the immune system by reactivating inactive T cells (blocked by cancer cells) has undergone extensive research from bench to bedside over the past 10 years. Ipilimumab targets the CTLA4 molecule found on the surface of T cells, and is thought to inhibit immune responses. By doing that, it enhances the immune response to tumour cells.

International and local clinical trials have been conducted with ilpilimumab, and their results will be presented. Another group of immunotherapeutic drugs, anti-PD1 and anti-PDL1 (such as pembrolizumab and nivolumab) have also undergone extensive research, alone and in combination with anti-CTLA4 durgs, benefitting a larger group of patients with advanced malignant melanoma. This data will also be presented.

NEW THERAPIES IN THE MANAGEMENT OF MALIGNANT MELANOMA TARGETED THERAPY

Dr Daniel A. Vorobiof, Sandton Oncology Centre, Johannesburg

Treatment of Metastatic Malignant Melanoma continues to represent a considerable unmet medical need based on the ongoing worldwide incidence of the disease, and the poor efficacy and significant toxicities of available drugs.

The emergence of new therapies have considerably changed patient's outcomes. For longer than 20 years no effective new drugs were available.

The development of 2 new groups of systemic treatments have marked the beginning of a new therapeutic era.

The use of oral targeted therapies aimed at a specific gene mutation (BRAF) with vemurafenib or dabrafenib, alone or in combination with cobimetinib or trametinib, have been able to induce responses in more than 50% of the patients receiving it, and achieve a long term response in 10 - 15% of the patients.

A review of international and national clinical trials will be presented.

LAPAROSCOPIC LIVER AND PANCREATIC SURGERY Martin Brand Department of Surgery, University of the Witwatersrand

Index

Laparoscopic surgery for HPB pathology

Staging laparoscopy

Liver resection

Colorectal liver metastases

Hepatocellular carcinoma

Pancreas Resection

Distal pancreatectomy

Pancreaticoduodenectomy

Conclusion

References

Laparoscopic surgery for HPB pathology

The first laparoscopic cholecystectomy was performed 30 years ago, and since then we have rapidly progressed with few operations not being amenable to laparoscopic surgery. Some procedures have shown clear benefit to the patient such as two/three segment non-anatomical liver resections, and other have shown moderate benefit or equivalence, such as pancreaticoduodenectomies. Most benefit from less post operative pain, earlier mobilization, shorter hospital stay and improved cosmesis. However initially there were concerns regarding the extent of oncological resection, adequate lymph node staging, and peritoneal seeding as a result of the pneumoperitoneum. The cost of a laparoscopic procedure exceeds open surgery, however, the overall cost with fewer hospital days, earlier return to work and lower incidence of complications that require an operation such as incisional hernias are difficult to cost accurately. Intuitively when one considers all of these factors there may be cost equivalence.

Staging laparoscopy

When combined with intra-operative ultrasound staging laparoscopy becomes a powerful tool in staging certain malignancies, both for peritoneal disease as well as vascular involvement; however, with improved imaging techniques staging laparoscopy has specific indications.

In pancreatic adenocarcinoma (PDAC) laparoscopic staging metastatic identifies metastatic disease in border line resectable cancer in 30% of patients, and metastases in 10%-15% of resectable body and tail adenocarcinomas; in resectable gallbladder malignancies and T2/T3 hilar cholangiocarcinoma staging laparoscopy may reveal occult metastases in 40% of cases and vascular involvement in 10% of cases. (Gaujoux 2010) An uncommon indication is for colorectal liver metastases where the selective laparoscopic staging in patients with a clinical risk score more than two may identifies non-resectable disease in 20% of patients. (Jarnagin 2001)

Liver resection

Colorectal liver metastases

A recently published meta-analysis demonstrated improved safety and equivalent long term outcomes of LR liver resection. LR had less intra-operative blood loss, transfusion requirement, less complications, fewer hospital days, no difference in operative time and importantly no difference in 1-, 3-, and 5-year disease-free survival (DFS) or overall survival (OS) rates. (Schiffman 2015)

Hepatocellular carcinoma (HCC)

For HCC a meta-analysis demonstrated that LR was associated with significantly less intra-operative blood loss, shorter hospital stay, less post-operative liver failure; there were no differences in operative time, bile leak, pulmonary complications, positive resection margins and mortality. (Xiong 2012)

A meta-analysis assessing survival that included all hepatic malignancies either operated laparoscopically by open surgery demonstrated equivalence for the laparoscopic approach. Overall survival showed no difference after 1,3,and 5 years. Subset analyses of hepatocellular carcinoma and colorectal metastases demonstrated no difference in the 1-, 3-, and 5-year survival for HCC or in the 1-year survival for colorectal liver metastases, however interestingly, a survival advantage for colorectal liver metastases operated laparoscopically after 3 years (80% versus 67.4%). (Parks 2014)

Pancreas resection

Commonly performed laparaoscpic pancreatic procedures:

Diagnostic laparoscopy with or without biopsy; Pancreaticoduodenectomy; Tumor enucleation; Central pancreatectomy; and distal pancreatectomy with or without splenectomy. (Merchant 2009)

Distal pancreatectomy

Meta-analysis has shown that laparoscopic distal pancreatectomy is a superior procedure compared to open. Compared with open surgery, reports there was less blood loss, blood transfusions, postoperative time until oral intake, time to first flatus shorter hospital stay, and lower morbidity. There was no difference in postoperative mortality rate, and oncological outcomes were the same. (Sui 2012)

Pancreaticoduodencetomy (PD)

Laparoscopic PD remains controversial. A recent study compared matched LR to OR concluded that LR is associated with higher morbidity, primarily as a result of more severe pancreatic fistula and thus LR should only be considered only in patients with a low risk of pancreatic fistula. (Dokmak 2015)

A matched pair analysis performed to determine pathological outcomes indicated that LR was equivalent to OR in terms of R0 resection margins and lymph node yield. (Hakeem 2014)

Conclusion

Laparoscopic liver and pancreas resection have been shown to be oncologically equivalent to open surgery, and associated with less morbidity. Recently in a high volume center cost was also shown to be equivalent between laparoscopic and open surgery in a 2:1 propensity study, Median overall cost for LR was \$11,376 versus \$12,523 for open resection. (Bhojani 2012). However, laparoscopic liver resection and pancreatic surgery are complex procedures requiring adequate training and mentorship to be performed safely. A thorough understanding of open resection procedures is also required before undertaking the procedures laparoscopically.

References

Bhojani FD, Pitzul K, Gallinger S, Moulton CA, Okrainec A, Cleary SP. Clinical and Economic Comparison of Laparoscopic to Open Liver Resections Using a 2-to-1 Matched Pair Analysis: An Institutional Experience. J Am Coll Surg 2012;214:184–195.

Dokmak S, Ftériche FS, Aussilhou B, Bensafta Y, Lévy P, Ruszniewski P, Belghiti J, Sauvanet A. Laparoscopic pancreaticoduodenectomy should not be routine for resection of periampullary tumors. J Am Coll Surg. 2015 May;220(5):831-8. PMID: 25840531.

Gaujoux S, Allen PJ. Role of staging laparoscopy in peri-pancreatic and hepatobiliary malignancy. World J Gastrointest Surg. 2010 Sep 27;2(9):283-90. PMID: 21160897

Hakeem AR1, Verbeke CS, Cairns A, Aldouri A, Smith AM, Menon KV. A matched-pair analysis of laparoscopic versus open pancreaticoduodenectomy: oncological outcomes using Leeds Pathology Protocol. Hepatobiliary Pancreat Dis Int. 2014 Aug;13(4):435-41. PMID: 25100130.

Jarnagin WR, Conlon K, Bodniewicz J, Dougherty E, DeMatteo RP, Blumgart LH, Fong Y. A clinical scoring system predicts the yield of diagnostic laparoscopy in patients with potentially resectable hepatic colorectal metastases. Cancer. 2001 Mar 15;91(6):1121-8. PMID: 11267957

Merchant NB, MD, Parikh AA, Kooby DA. Should All Distal Pancreatectomies Be Performed Laparoscopically? Advances in Surgery 2009. 43(11) 283-300.

Parks KR1, Kuo YH, Davis JM, O' Brien B, Hagopian EJ. Laparoscopic versus open liver resection: a meta-analysis of long-term outcome. HPB (Oxford). 2014 Feb;16(2):109-18. PMID: 23672270.

Schiffman SC, Kim KH, Tsung A, Marsh JW, Geller DA. Laparoscopic versus open liver resection for metastatic colorectal cancer: a meta-analysis of 610 patients. Surgery. 2015 Feb;157(2):211-22. PMID: 25282529.

Sui CJ1, Li B, Yang JM, Wang SJ, Zhou YM. Laparoscopic versus open distal pancreatectomy: a meta-analysis. Asian J Surg. 2012 Jan;35(1):1-8. PMID: 22726557.

Xiong JJ, Altaf K, Javed MA, Huang W, Mukherjee R, Mai G, Sutton R, Liu XB, Hu WM. Metaanalysis of laparoscopic vs open liver resection for hepatocellular carcinoma. World J Gastroenterol. 2012 Dec 7;18(45):6657-68. PMID: 23236242

GASTRO-INTESTINAL FAILURE Prof JP Pretorius.

Gut on strike? Ileus? Feeding Intolerance? Intestinal failure?

The gastro-intestinal tract is far more than a place to deliver food too. It is seldom regarded as a true organ failure amongst the other major organs failing. The concept of "the gut as the motor of organ failure" proposed by Carrico et al in 1985, was the first attempt to consider the systemic or global importance of the gastro-intestinal tract in human pathophysiology during serious illness. Many researchers subsequently attempted to clarify the pathophysiology of gut failure: Alverdy et al. 2003: Interaction between host and bacterial pathogens lead to gut derived sepsis (at least partially independent of the pro-inflammatory response of bacteraemia)

Sousa et al. 2004: Germ free mice that entirely lack commensal bacteria have an improved survival rate following intestinal ischemia/reperfusion compared with conventional animals.

Deicht et al. 2006: Ligation of lymph duct after haemorrhagic shock prevents distant organ injury in a variety of animal species.

Reintam et al 2006: GIF seems to be a relevant independent clinical predictor of mortality in ICU. It significantly prolongs mechanical ventilation and ICU stay.

Reintam Blaser, Malbrain et al 2012: Created a Classification for AGI (acute gastro-intestinal injury)

Grade 1 = Increased risk of developing GI dysfunction (self-limiting condition) [following abdominal surgery]

Grade 2 = GI dysfunction (condition requires intervention) [Gastroparesis, ileus, IAH]

Grade 3 = GI failure (Function cannot be restored with interventions) [Progression of abovementioned with persistence or worsening of MODS]

Grade 4 = Dramatic manifestation of GI failure (condition that is immediately life threatening) [bowel ischaemia/necrosis, GI bleed \rightarrow shock, ACS, Ogilvie syndrome]

Reintam et al 2013: Using the above it was not possible to develop a valid GI dysfunction score that improved the accuracy of the SOFA score.

Full circle: Klingensmith, Coopersmith 2016: again "The gut as the motor of multiple organ dysfunction in critical illness"! Crit Care Clin 32 (2016) 203-212.

The gut has 3 broad functions – certainly absorption and nutrition comes to mind first, but also its endocrine and immune functions and lately the importance of the gut microbiome have drawn wide attention.

The gastro-intestinal tract plays a central role in critical illness from any origin.

GI dysfunction is a common problem in critically ill patients, yet it is not given the same consideration as other organ systems regarding scoring and predicting outcome in ICU. Some element of gut pathophysiology usually contributes to critical illness. This is related to disruption of the 3-way partnership between its epithelium, immune tissue and commensal bacteria or microbiome.

The initial theories of hyperpermeability of the gut resulting in bacterial translocation and subsequent inflammatory response proved to be too simplistic.

Alterations in the gut can lead to both local and distant insults via alterations in homeostatic processes and defense mechanisms as well as release of toxic mediators into mesenteric lymph as well as the systemic circulation.

The epithelium provides a large surface area for absorption. It is also an important barrier to entrance of pathogens from its lumen. It has four major cell types: a) enterocytes for nutrient absorption, b)mucus-producing goblet cells, c)hormone –producing enteroendocrine cells, d)defensin-producing Paneth cells.

The gut is the largest lymphoid organ, containing Peyers patches, the lamina propria, mesenteric lymph nodes and intraepithelial lymphocytes. This produces T and B cells, antigen recognition, presentation, amplification of antigen –specific response and production of cytokines and chemokines.

Normally there is a well-tolerated symbiotic relationship between the human host and its diverse microbiome. This understanding is still nascent. (Klingensmith and Coopersmith)

The clinical diagnosis is unfortunately nonspecific: Delayed gastric emptying

Alterations in intestinal motility

Mucosal ischaemia

Altered carrier and nutrient transporter proteins

Villus atrophy

Reduction in mucosal surface area

Loss of barrier function / altered permeability

Biomarkers show some promise – ie plasma citrulline and intestinal fatty acid binding protein which show an association with greater 28-day mortality.

Diagnosis of Gut Failure:

• <u>Clinical evaluation</u> =Bowel sounds: ?Clinical significance → lack of evidence. <u>Doesn't</u> <u>correlate with effective peristalses</u>

THEREFORE RATHER LOOK AT:

Abdominal distension/constipation/Diarrhoea/Abdominal pain/Vomiting/Gastro-intestinal bleeding

- <u>Gastric residual volume</u>
 - = WHICH VOLUME INDICATES GUT FAILURE?
 - → ASPEN and SCCM: GRV > 500ml

 \rightarrow EN feeding should not be stopped if drainage is < 500ml unless vomiting is present. GRV 250ml -500ml should raise concern. Poulard et al, 2010: Better to use vomiting as an indication to stop EN.

Pts who did not receive GRV monitoring , received larger volumes of EN, without an increase in VAP.

Thus - Each ICU should have a protocol for EN \rightarrow will ensure significant improvement of nutrient delivery.

Paracetamol absorption test

The drug is absorbed from small bowel. Good correlation between stomach emptying time and peak plasma concentrations. Drugs, upper GI operations, aspiration can influence results.

Management is also non-specific and supportive:

- Maintain visceral perfusion
 Early resuscitation and maintenance of APP > 50mmHg
- Strict glycaemic control Maintain macrophage function/improved antral function

Preserve LBM (improved protein metabolism)

- Correct acidosis and electrolyte abnormalities
- Minimize medication that alter bowel function
- Daily dialysis if indicated (correct fluid balance)
 = Better metabolic control improves bowel motility (excess water, acidosis, electrolytes)
- Probiotics, prebiotics and synbiotics can be used to target the microbiome.
- Selective decontamination of the gut can be used to minimize pathogenic enteral bacteria.
- Fecal transplants can be used to restore the gut microbiome.
- Nutrition plays an important role in mucosal health and has beneficial effects on gutassociated lymphoid tissue. EN should be started within 48 hours of ICU admission. Placement of enteral tubes to access the gut is a priority.
- Prokinetic drugs like metoclopramide and erythromycin are still used while the search is on for better prokinetics. May be used in combination.
- Opiate antagonists: Enteral Naloxone → reverses high GRV and may prevent aspiration pneumonia
- Acupuncture may be tried
- The Neely Catchpole regimen alpha blocker plus neostigmine
- Agonists of other hormones: Ghrelin → stimulates motility of bowel and promotes anabolic metabolism via growth hormone secretion.
- Experimental drugs showing promise a novel motilin agonist, camicinal

- TENS transcutaneous electrical nerve stimulation. Gate theory in spinal cord. Set according to individual experience.
- Chewing gum
- Early mobilization out of bed.
- Exercise all ERAS principles.

References:

- 1. Reitam Blaser A et al Intensive Care Med 2013; 39:899-909
- 2. Reitam Blaser A et al Acta Anaesth Scand 2014; 58:914-922
- 3. Klingensmith NJ, Coopersmith CM Crit Care Clin 2016; 32: 203-212
- 4. Rosenthal MD, Moore FA Surgical Infections 2016; 17(2): 167-172
- 5. Wischmeyer PE, McDonald D, Knight R Curr Opin Crit Care 2016; 22: 347-353

THE USE OF OVER THE SCOPE CLIPS TO CLOSE GIT FISTULAE. Dr Adam Boutall

The over the scope clip has been commercially available since 2008. The system consists of a Nitonol bear shaped clip, pre-mounted on a translucent cap, which is placed on the tip of the colonoscope or gastroscope. The delivery system is similar to the more familiar variceal elastic banders.

Over the scope clips (OTSC) can be used in 3 distinct clinical scenarios.

- 1. Endoscopic control of haemorrhage.
- 2. Endoscopic closure of acute GIT perforations.
- 3. Endoscopic closure of fistulae or anastomotic leaks.

OTSC are well established for endoscopic control of haemorrhage and the closure of acute perforations, with excellent results reported in the literature. The use of endoscopic clipping devices for the closure of GIT fistulae and anastomotic leaks, is more controversial with lower success rates.

Regardless of the method of closure of a fistulae certain basic principles need to be adhered to: **SNAP**

- **S**epsis needs to have been drained
- Nutritional supplementation to ensure that the patient is in an anabolic state.
- Anatomy of the fistulae should be defined
- **P**rotection of the peri –fistulous skin is vital. Help of a stoma therapist is an important component in the management of these patients

Factors in favour of fistulae closure include,

- A long thin tract,
- No associated abscesses,
- A patient who is nutritionally replete.

The well-known acronym 'FRIENDS' can be used to identify fistulae that will not close.

- 1. Foreign body
- 2. Radiation
- 3. Infection
- 4. Epithelisation
- 5. Neoplasia
- 6. Distal obstruction & active Disease
- 7. Steroids and a short tract

When considering a patient for use of an OTSC for closure of a fistulae tract, all of the above should be considered. The advantage of using an endoscopically placed clip to attempt to close a fistulae, is the reduction in "collateral damage" and a relatively low rate of complications. Unfortunately the results remain relatively poor especially in the lower GIT.

The role for endoscopic clips in the treatment of peri-anal fistulae is an emerging field with only a few series reported in the literature, and widely varying success rates. Peri-anal fistulae surgery has a long history of new techniques met with much enthusiasm, followed by clinical disappointment.

In conclusion OTSC is a relatively safe technique which is an excellent modality for endoscopic control of haemorrhage and closure of acute perforations. It can be used for closure of enterocutaneous fistulae, in suitable cases, with a moderate success rate. The high complication rate associated with the surgical closure of entero-cutaneous fistula, makes OTSC a very attractive option that is unlikely to harm the patient.

References

- Wedi et al. "One hundred and one over-the-scope-clip applications for severe gastrointestinal bleeding, leaks and fistulas" World J Gastroenterol 2016 February 7; 22(5): 1844-1853.
- 2. Verlaan et al. "Endoscopic closure of acute perforations of the GI tract: a systematic review of the literature" GASTROINTESTINAL ENDOSCOPY Volume 82, No. 4: 2015.
- 3. Gautier et al. "Easy clip to treat anal fistula tracts: a word of caution" Int J Colorectal Dis (2015) 30:621–624.
- Mennigen et al. "The OTSC proctology clip system for the closure of refractory anal fistulas" Tech Coloproctol (2015) 19:241–246.
- 5. Danatelli et al. "Closure of gastrointestinal defects with Ovesco clip: long-term results and clinical implications" Ther Adv Gastroenterol 2016, Vol. 9(5) 713–721.
- 6. Law et al. "Immediate technical and delayed clinical outcome of fistula closure using an over-the-scope clip device" Surg Endosc (2015) 29:1781–1786.
- 7. Field et al. "Endoscopic Management of Gastrointestinal Leaks and Fistulae" Clinical Gastroenterology and Hepatology 2015; 13:1714–1721.

EXPERIENCE IN SINGLE INCISION PAEDIATRIC ENDOSCOPIC SURGERY (SIPES)

Prof ML van Niekerk

Background and aim

Standard laparoscopic surgery has demonstrated significant benefits to patients. The natural evolution of laparoscopic surgery is towards fewer ports and smaller incisions. With SIPES, a single umbilical incision provides access for almost all abdominal paediatric operations, leading to virtually no visible scar.

Methodology

SIPES has been implemented in my practice since 2010. Standard straight instruments and no port devices are used for almost all operations. Depending on the target area, transverse or vertical umbilical incisions are used. In this presentation some technical aspects of the following procedures will be highlighted: Nissen fundoplication, Hirschprung's disease, imperforated anus, gastrostomy tube placement, Morgagni hernia and thoracoscopic sympathectomy.

Results

SIPES is feasible and safe. It gives excellent cosmetic results. It is more difficult than standard laparoscopic surgery because of loss of triangulation, limited visualisation and difficulties in tissue traction.

Conclusion

Surgeons will always work towards improving surgical techniques and developing new technology. Despite much criticism, there is great enthusiasm for the single incision approach.

USE OF "GLUES" FOR HERNIA REPAIR.

<u>Ramsey Maluleke</u>, Department of Surgery, University of Pretoria and Steve Biko Academic Hospital.

There are a number of options for mesh fixation in hernia repair. The options include the following.

- 1. Tackers/staples.
- 2. Stitches.
- 3. Glue.
- 4. Self-sticking mesh (e.g. parietex progrip mesh).
- 5. No Fixation

These measures prevent mesh graft displacement with consequent hernia recurrence.

Laparoscopic hernia repair is not devoid of complications. Some of the complications are due to the use of tackers and include sensory nerve entrapment with neuralgia, bleeding and haematomas and chronic unexplained pain. As a result of complications associated with fixation with tackers, efforts have been directed at looking for an alternative method of fixation with less complications

FIBRIN GLUE

It is also called fibrin sealant. It is a commercial tissue adhesive containing fibrinogen and fibrin. It is a two component system from human plasma.

- 1. The first component contains lightly concentrated fibrinogen and fibrinectin and traces of other proteins.
- 2. The second component contains thrombin, calcium chloride and an antifibrinolytic agent such as aprotinin.

Fibrinogen is the most important component. The tensile or adhesive strength correlates directly with the fibrinogen content. Thrombin is the second most critical component. The rapidity of clot formation and the tensile strength of fibrin seal is a function of concentration of thrombin used to initiate the process.

The use of cyanoacrylate glue as an alternative for mesh fixation has been described. However local toxicity and carcinogenic effect have been reported in some studies. To date, no transmissible viral disease secondary to fibrin glue use has been reported.

When rapid clot formation (5 to 10 seconds) is desired, thrombin concentrations of 500 to 1000 NIH units should be used (e.g. Tisseel, Evicel). If slower clot formation is desirable (e.g. plastic surgery procedures when close approximation of tissue is sought) thrombin concentrations of 4 to 10 NIH units should be used (e.g. Artiss).

Mixing the two components leads to activation of fibrinogen and thrombin by calcium chloride \rightarrow this leads to formation and crosslinking of fibrin \rightarrow formation of polymerized fibrin chains duplicating the last step of the coagulation cascade. Thrombin is chemotactic \rightarrow enhances fibroblast proliferation and incorporation into the mesh. After application, fibrin glue is broken down by fibrinolysis and replaced by fibrotic layer.



Formation of polymerized fibrin chains

Fibrin glue has been found to incite a significantly stronger inflammatory response. Through its haemostatic property it has the advantage of decreasing the incidence of haematomas created during dissection of the extraperitoneal space. This may cause lifting or displacement of the prosthesis.

Technical consideration

The fibrinogen and thrombin components are kept separate prior to application. Fibrin sealant is applied using a two-syringe technique. Some commercial products (e.g. Tisseel and Evicel) come fully mixed and assembled in dual syringe applications with only a brief period of thawing required. In the operating room, the fibrinogen/factor XIII source is thawed, if necessary, and drawn into one syringe, and the thrombin/calcium chloride into the other.

Depending upon the clinical application one would choose either the needle-tip or the spray applicator.

Physical properties of fibrin glue include the following:

- 1. Completely biodegradable within 6 weeks.
- 2. No foreign body reaction.
- 3. Adequate mechanical stretch properties.
- 4. Contains no toxic substances.
- 5. Underlying principle is that it mimics the natural stages of the coagulation process.
- 6. It is manufactured using stringent donar and blood screening protocols and validated production process, including viral inactivation procedures and quality control of each batch.

Contraindications to its use include the following: history of anaphylactic reactions to plasma products, patients with IgA deficiency and fibrin should never be injected intravenously because it causes thrombosis.

Evidence supporting the use of fibrin glue (sealant).

N.Katkhouda et al concluded that adequate mesh fixation in the extraperitoneal inguinal area can be accomplished using fibrin sealant. This method is mechanically equivalent to the fixation achieved by staples(tackers) and superior to nonfixed grafts. Biologic soft fixation with fibrin sealant will prevent early graft migration and will avoid complications associated with staple use.

				P Value		
	FS (n = 18)	Staples (n = 16)	No Fixation (n = 15)	FS vs. staples	FS vs. no fixation	Staples vs no fixatior
Graft motion (mm) Tensile strength (kg)	0 (0–2) 0.955 (0.25–3.2)	0 1.03 (0.09–4.5)	5 (0–10) 0.46 (0.16–2.64)	NS NS	<.01 <.01	<.001 <.01



Figure 3. Distribution of the grades of fibrous reaction in the three study groups.



Figure 4. Distribution of the grades of inflammatory response in the three study groups.

		Table 2.	HISTOLOGIC EVA	LUATION		
				P Value		
	FS (n = 33)	Staples (n = 31)	No Fixation (n = 28)	FS vs. staples	FS vs. no fixation	Staples vs. no fixation
Fibrous reaction* Inflammatory response†	1.94 ± 0.24 2	1.61 ± 0.49 1.67 ± 0.47	1.75 ± 0.44 1.85 ± 0.35	<.001 <.01	<.05 <.05	NS NS

FS, fibrin sealant.

Results expressed as the mean score ± SD.

* Grades of fibrous reaction: 1, mostly collagen aggregates, few fibroblasts; 2, mostly fibroblasts, little amount of collagen deposits. † Grades of inflammatory response: 1, little or no inflammatory response; 2, significant inflammatory reaction (dense lymphoid aggregates).

B.Novik et al in the first published study on the use of fibrin sealant for mesh fixation in laparoscopic hernia repair in humans concluded that fibrin glue seems to be a reasonable, feasible, and maybe even competitive alternative to the standard tissue penetrating mesh fixation. The results of the study justify lauding larger trials.

A meta-analysis of 5 randomized controlled trials by Nehal S. Shah et al comparing tissue glue with tack fixation in laparoscopic inguinal hernia surgery depicts a significant reduction in chronic pain with no increase in recurrence rates. Early post operative outcome is similar after both methods of mesh fixation, although larger randomized controlled trials are required, with long-term pain as the primary end point.

A study by Erwin Reider et al concluded that fibrin glue appears to be an appealing noninvasive option for mesh fixation in laparoscopic neutral hernia repair, but only if appropriate meshes are used. Glue can also serve as an adjunt to mechanical fixation to reduce the number of invasive tacks.

Currently the TISTA trial is ongoing. It started recruiting on 01/02/2013. This is a prospective, randomized, controlled, single-center trial with two-by-two parallel design.

TISTA stands for **TI**sseel vs **STA**ples.

References

- 1. Namir Katkhouda, Eli Mavor, Melanie H. Friendlander, Rodney J. Mason, Milton Kiyabou, Steven W. Grant, Kranti Achanta, Erlinda L. Kirkman, Khrishna Narayanan and Ralinla Essani. Use of fibrin sealant for prosthetic mesh fixation in laparoscopic extraperitoneal inguinal hernia repair. Annals of Surgery 2001;1:18-25.
- 2. B. Novik, S. Hagecorn, U.-B. Mörk, S. Skullman, J. Dalenbäck. Fibrin glue for searing the mesh in laparoscopic totally extraperitoneal inguinal hernia repair. Endoscopy 2006;20:462-467.
- 3. Nehal S. Shah, Catherine Fullwood, Ajith K. Siriwardena, Aali J. Sheen. Mesh fixation at laparoscopic hernia repair: A meta-analysis comparing tissue glue and tack fixation. World J Surg 2014;38:2558-2570.
- 4. Erwin Reider, Martin Stoiber, Verena Scheikl, BS, Marcus Poglitschg, Andrea Dal Borgo, Gerhard Prager, Heinrich Schina.2011; J Am Coll Surg 2011;212:80-86. Mesh fixation in laparoscopic incisional hernia repair: Glue fixation provides attachment strength similar to absorbable tacks but differs substantially in different meshes.

BIOLOGICAL PLUGS AND ANTIBIOTIC BEADS IN THE TREATMENT OF ANORECTAL FISTULAE

B.L. Khulu FCS (SA). Department of Surgery, Tembisa hospital & University of Pretoria

Introduction

Anal fistulae have been troubling mankind for a long time. Medical writings about anal fistulae dating back to 400B.C. have been found in the literature. Although Hippocrates wrote about the disease more than two thousand years ago, we are still trying to find the best operation to cure anal fistulae.

Anal fistulae affect all races and genders. The disease has no respect for social standing as we learn in history that Louis XIV (1638-1775), King of France was afflicted with the disorder. On 18 November 1686, Louis underwent a painful operation for anal fistula that was performed by the surgeon Charles Felix de Tassy, who prepared a specially shaped curved scalpel for the occasion. The wound took more than two months to heal. [1]

The challenges facing surgeons in treating anal fistulae revolves around healing time and morbidity associated with the perianal wound post fistulotomy, faecal incontinence as a result of surgery and recurrence rate. For this reason, there is a pursuit for more refined and less invasive sphincter sparing treatment modalities.

Current treatment options for anal fistulae

<u>Fistulotomy</u>, which involves lay- open of the fistula tract, is the procedure that has stood the test of time. This is done for low fistula-in-ano where less than 30% of the distal part of the external sphincter is divided in the process.

For fistulae that are higher, a <u>Seton</u> technique is used. More complex fistulae are managed with <u>mucosal advancement flap</u> technique or a combination of modalities.

Recently in order to avoid division of the anal sphincter complex, the technique of <u>Ligation of the</u> <u>Intersphincteric Fistula Tract (LIFT)</u> has been advocated.[2]

In a quest for a technique that has no wound complications, a quicker healing time and no risk of incontinence <u>biological plugs and fibrin glue</u> have been developed to deal with the problem of anal fistulae. This will be the focus of this discussion.

Fibrin glue/sealant for treatment of anal fistula

Fibrin glue was developed as a haemostatic agent during World War 1. The early experience with the use of fibrin glue for complex anal fistulae was described and published by Hjortup et al in 1991 [3]. It is a mixture of fibrinogen, thrombin and calcium ions. It is postulated to act via two mechanisms. As it is injected into the tract, the fibrinogen, thrombin and calcium ions react with factor XIII to form a clot. Secondly, the proteins within the glue promote the proliferation of fibroblasts and pluripotent endothelial cells within the tract. These cells lay collagen and extracellular matrix. The glue becomes replaced by fibrous tissue thus sealing off the tract [4]. The glue is available in two forms- an autologous preparation made from pooled human blood and a commercial preparation-the synthetic glue (cyanoacrylate glue) [4].

<u>Procedure</u> [4, 5]

- The external and internal openings of the fistula tract are identified.
- The fistula tract is thoroughly curettage to remove all granulation tissue and debris.
- A double barrelled (two chambered) syringe containing thrombin & fibrinogen within the respective chambers is used.
- Injection into the tract occurs via a single cannula attached to the syringe.
- Initially the cannula tip is inserted through the external opening and advanced through the tract to the internal opening.
- Once a blob of fibrin glue is noted in the internal opening, the cannula is slowly withdrawn while injecting the glue slowly.
- The fistula tract is filled completely from internal to external opening until a blob is seen outside.
- The glue is allowed to set for 30-60 seconds.

Advantages

- It is a simple procedure with no learning curve.
- It obviates creation of a wound.
- There is no risk of incontinence.
- It may be repeated
- It does not prevent or impair the use of other modalities of fistula treatment in case of failure. There is no burning of bridges.

Disadvantages

- Long term success rate is low compared to other modalities.
- There is risk of formation of new tracts and abscesses.
- Studies show a wide range of success- as low as 14% and as high as 74% [6].

Prospective randomised studies comparing fibrin glue to conventional surgical treatment for anal fistula are scanty. Fibrin glue remains a viable option for selected patients [7].

Antibiotic beads in the treatment of anal fistulae

Very little is published on the use of antibiotic beads/chains for treating anal fistulae.

This entails local implantation of gentamicin polymethylmethacrylate (PPMA) chains.

Kupferberg et al utilised this technique successfully in five patients who had recurrent high anorectal fistulae. The technique involves partial excision of the fistula, insertion of PMMA beads (Septopal) and primary closure of the wound, followed by gradual removal of the beads. Removal of the beads begins 7 days after operation and extends over at least 3 weeks [8].



The one end of the beads chain protrudes through the external part of the wound and is gradually pulled out on an ambulatory/outpatient basis.

The authors describe this technique as a safe, easily performed method and useful in combating infection, making healing of the fistula possible.

This method of treating anal fistulae has not been embraced widely as it is evidenced by the lack of publications.

FISTULA PLUGS

Fistula plugs have been developed as reasonable alternatives for treatment of anal fistulae. One such material is the Surgisis AFP Anal Fistula Plug (Cook Inc.). It is made from porcine small intestine submucosa. The material is of conical shape. When it is implanted in the fistula tract, there is invasion of host tissue cells and blood vessels into it. It provides a scaffold to allow infiltration of the patient's connective tissue. The procedure is minimally invasive, is sphincter sparing and thus avoids incontinence [9]

The Surgisis



A conicall shaped biomaterial.

<u>Technique</u>

- Pre operative bowel preparation is left to surgeon's discretion.
- A single dose of systemic antibiotic is recommended perioperatively.
- Anaesthesia can be conducted according to the surgeon's preference in consultation with the patient and the anaesthesiologist.
- Patient positioning may be prone jack knife or lithotomy according to surgeon's preference.
- The patient is preped and draped.
- Identify the external and internal openings of the fistula.
- Gentle probe the fistula to confirm the tract.
- Irrigate the tract with peroxide or saline.
- Debridement, curretage or vigorous brushing is not advised as this may render tract too wide for the plug to fit in snuggly.
- The plug is immersed in saline for two minutes to make it soft.
- The plug is then railroaded by its narrow end into the fistula tract through the internal opening.



Excess plug is trimmed at the level of the internal opening. The head of the plug is sutured and enchored to the internal sphincter with a 2/0 Vicryl suture or equivalent material. The plug must not protrude through the mucosa. It must be burried. The external opening should not be closed so as to allow drainage.

<u>Results</u>

1

Careful patient selection and proper surgical technique are critical to achieve success. Results are variable in different studies [6]. The cost of the plug in South Africa is roughly R10000.00.

Ref.	Type of study	No. Patients	Success rate	Follow-up (mo)
Johnson et al ^[41]	Prospective	15	87%	7
	Non-randomized			
	Controlled trial			in a state
Champagne et al ^[44]	Prospective	46	83%	12
O'Connor et al ^[45]	Prospective	20 (Crohn's)	80%	10
Van Koperen et al ^[46]	Prospective	17	42%	7
FIlie ^[47]	Retrospective	18 (5 rectovaginal)	88%	6
awee et al ^[48]	Retrospective	17 plug	66%	7.4
Laweserm		3 pug+flap		
Ku at a1[49]	Prospective	44 plug+flap	54.6%	6.5
Cy er ar	Prospective	19 (7 Crohn's)	61% overall	9
Schwandner er 4			45.5% cryptoglandular	
			85.7% Crohn's	
0	Prospective	21	71%	10
Sarg	Retrospective	47	43%	6.5
	Prospective	43	44%	11
hekkinkattii et al	Patrospective	35	14%	4
atar et al	Prospective	31 cryptoglandular:	20% (plug group)	12
Ortiz et al ^{ren}	Prospective Bandomized trial	-15 plug	87.5% (EAF)	
	Randoinized diai	16 endorectal-advancement	Statistics and the second second	
		flan (FAF)		
		1 map (EAL)	25%	74
I-Gazzaz et al	Retrospective	33	20 % E0%	105
Than et al	Prospective	Matan Ana 🏪 Malazara	30%	10.5
Cintron et al ^{ing}	Prospective	73	42.5%	15

Limura E et al. Modern management of anal fistula

GORE-BIO A Fistula Plug

This is a delayed absorbable synthetic plug. It is composed of a bio-absorbable monofilamentous compound with polyglycolic acid: methylene carbonate. It consists of a 16mm diameter circular disc with 6 arms of 9cm length attached to the disc. The disc makes it easier for the plug to be fixated to the internal opening. The 6 arms are withdrawn to protrude out of the external opening and trimmed accordingly. The disc and sutures must be covered with a mucosal flap [6].

<u>Results</u>

Ommer et al reported a success rate of 57.5% in a group of 40 patients who underwent GORE plug insertion[10] There was higher healing rate in patients who had transphincteric fistulae than those with supra sphincteric fistulae. The cost for the GORE plug was 500 Euros.



NEW DEVELOPMENTS

Autologous expanded Adipose- derived stem cells (eADSC)

Autologous ADSC are obtained with liposuction.

-The internal fistula opening is identified.

- The tract is curettaged adequately.

-Adipose derived stem cell solution is injected into the tract and into the walls of the fistula

-The internal opening is closed and the fistula tract sealed with fibrin glue

The ADSC are believed to supress inflammation and promote healing [6, 11]

Available data on this technique is limited and the technique has not taken off the ground.

CONCLUSION

The biologic alternatives in the management of anal fistula are attractive irrespective of their results, particularly in their sphincter preservation advantage. The cost of the plugs remains prohibitive to most patients. The plugs should be retained, improved and utilised as adjunct to current surgical techniques. There will always be that patient who will require nothing else other than a biological plug.

References

- 1. Wikipedia, free encyclopaedia- King Louis of France. <u>https://en.wikipedia.org/wiki/Louis</u> IVX of France.
- 2. Rojanasakul A. et al. Total anal sphincter saving technique for fistula- in –ano; Ligation of Intersphincteric tract. J.Med Ass. Thai. 2007; 90(3): 581-586.
- 3. Hjortup A. et al. Fibrin adhesive in the treatment of perineal fistulas. Dis. Colon Rectum 1991; 34: 752-754.
- 4. Sasank Kalipatnapa, Rajesh Selvakumar. J.Gen Practice Vol 4. Issue 1. 2016.
- 5. Malik A.I. Wilson R.L.Colorectal Disease.10, 420-430.
- 6. Limura E, Giordano P: W world J. Gastroenterology. 2015; 21(1): 12-20.
- 7. Lindsey I et al. Dis Colon Rectum 2003; 45:1608-1615.
- 8. Kupferberg A. et al. WJS 1984, 8: 970-973.
- 9. Amrami S et al. Gastro- enterology Clinique et Bioloque 32; 11: 946-948.
- 10. Ommer A. et al. Gore BioA fistula plug in the treatment of high anal fistulas- initial results from German Multicentre study. Ger Med Sci. 2012; 10:Doc13.
- 11. Scoglio D et al. Clin Colon Rectal Surg. 2014; 27:172-181.

LAPAROSCOPIC LIVE DONOR NEPHRECTOMY

Prof Zach Koto

Introduction

South Africa performs less than 300 kidney transplants annually according to the South African Renal Society. The major challenges are around the small donor pool in relation to the huge demands for organs. About 4 300 South Africans are awaiting kidney transplant according to the Kidney Transplant Foundation.

It is very clear that looking at these numbers, we will never be able to cope unless we look at innovative solutions to tackle this herculean challenge. What is needed is a significant paradigm shift

The traditional kidney source

The traditional organ source in South Africa has been cadaveric donors in the main and live donors have been a trickle considering what the potential is in South Africa.

The impact of HIV in South Africa has been huge. One is acutely aware of laudable work done by the Cape Town Group around HIV positive to HIV positive donation and transplantation to make an impact on this huge problem.

There is a need for Government, Society and all role players to have an indaba on how to address this massive problem. Cultural religious and ethnic issues need to be addressed urgently if we want to make an impact on this issue.

Live kidney donation

Live kidney donation is an important strategy towards addressing organ shortage. It is better than cadaveric donation and confers several advantages to the recipient:

- 1. Longer survival rates
- 2. Better quality of live
- 3. Immediate function of the graft
- 4. Better transplant survival
- 5. Possibility of transplanting pre-emptively

Reluctance of people to come forward

There has been reluctance of potential life donors to come forward because of potential morbidity of open donor nephrectomy and some of these concerns include the following:

- Long hospital stay
- Prolonged hospital stay
- Cosmetic concerns
- Slow recovery

Laparoscopic donor nephrectomy

The advent of laparoscopic surgery has changed many facets of surgery and live donor nephrectomy is no different. The first laparoscopic live donor nephrectomy was performed in

1995 by Drs Lloyd Ratner and Louis Kavoussi at John Hopkins hospital and over the years, John Hopkins Hospital has developed in one of the largest series of Laparoscopic donor nephrectomy.

Advantages of laparoscopic donor nephrectomy

Like all laparoscopic procedures the advantages of laparoscopic donor nephrectomy include the following:

Shorter hospital stay, less bleeding risks, less post-op pain, reduced surgical site infection and early return to work.

The minimal invasive techniques

- Standard laparoscopy
- Hand assisted retroperitoneoscopy
- Pure retroperitoneoscopy
- Robot assisted live donor nephrectomy

Challenges when deciding which kidney to choose

- Type of kidney
- Obese patient
- Donors with multiple arteries and veins
- Retroaortic left renal veins

Contra-indications to live donor nephrectomy

Amsterdam forum established guidelines to contra-indications (relative) to live donor nephrectomy

- Donors must have sufficient renal function (GFR >80ml/min)
- Normotensive (< ¹⁴⁰/₉₀ mmHg)
- No obesity (BMI < 35 kg/m²)
- No proteinuria
- No haematuria
- No stone disease
- Malignancy
- Urinary tract infection
- Minor CVA risk
- No alcohol or smoking

What are pre-op tests done for donors

Blood and urine screening
CXR, ECG

Radiographic assessment of the kidney and vessels

Psychological evaluation

Family history assessment

Laparoscopic donor nephrectomy (pure laparoscopic)

The safety of the donor is critical. The procedure must be done meticulously and safely. Expertise in laparoscopic surgery becomes very important.

The technique

Position of the patient.

The patient must be in a lateral decubitus position. We often take the left kidney unless there are contaminations in which case the right kidney can be taken. The reason for this is that it is easier technically to take the left kidney.

Ports are placed sub-costally, mid-clavicular line, anterior axillary line and posterior axillary line. The additional port is placed in the suprapubic area where the kidney is going to be extracted – we use the retrieval bag to retract the left colon medially.

The dissection starts with mobilization of the descending colon – it is important to mobilize the colon completely and we use the suprapubic port to retrack the colon medially.

We open Gerota's fascia. It is crucial at this point to identify the adrenal vein. The Adrenal vein is taken.

The gonodal vein is taken lower preferably to avoid devascularizing the ureter.

The ureter is dissected free and clipped at the level of the common iliacs.

Before starting the hilar dissection 25mg of mannitol is given.

The artery and the vein are skeletonized. Before we ligate the vessels it is important to liaze with the implantation team to ensure that they are ready to receive the kidney.

It is important that warm ischaemic time is minimized.

We use hem-o-lock clips to secure the renal pedicle.

The kidney is removed via a pfannenstiel incision.

Hand assisted laparoscopic donor nephrectomy

This technique is acceptable especially for surgeons less experienced in laparoscopic surgery. It gives one tactile feels and is very handy especially in the unlikely event of major bleed. Over 60% of laparoscopic donor nephrectomies have been hand assisted.

How do the two compare?

Most studies comparing pure laparoscopic live donor nephrectomy and hand assisted donor nephrectomy, have demonstrated shorter operation time and warm ischaemic time for hand assisted technique.

A recent meta-analysis showed that hospital stay was shorter with pure laparoscopic approach. Regular diet is resumed earlier with the pure laparoscopic group.

Conclusion

Laparoscopic donor nephrectomy results in shorter hospital stay and better quality of life for the donor.

It is hoped that this will increase the donor pool.

References

- 1. Nitin Gupta, Pampush Raina, Anat Kumar. Laparoscopic donor nephrectomy. *J Minim Access Surg*; 2005:155-164
- 2. Ratner L E, Hiller J, Sroka M, Sikorsky I, Montgomery R A, Kavoussi L R. Laparoscopic liver donor nephrectomy removes disincentives to live donation. *Transplant Proceedings* 1997; 29:340-3
- Jacobs S C, Cho E, Foster C, Liao P, Bartlett T S. Laparoscopic liver donor nephrectomy; the University of Maryland 6-year experience <u>J Urol</u> 2004 Jan;171(1):47-5

THE CONUNDRUM OF DIFFICULT VENOUS ACCESS FOR HAEMODIALYSIS

S.C Tsotetsi; Vascular Surgeon, Steve Biko Academic Hospital

In 1997, the National Kidney foundation – Kidney Dialysis Outcomes Quality Initiative (NKF – KDOQI) published clinical practice guidelines in an effort to increase the placement of autogenous arteriovenous (AV) access and prolong the use of such access by detecting dysfunction before thrombosis occurs. These guidelines stress the early identification of patients with progressive kidney disease, the identification and protection of potential native access sites by members of the health care team and patients. The guidelines recommend that patients be referred to vascular access surgeons for permanent dialysis access when their creatinine clearance is less than 25mL/min. Autogenous access should ideally be created 6 months before the anticipated need for dialysis. Prosthetic access should be delayed until 3 to 6 weeks before the initiation of dialysis because its patency is limited by the time of access placement.

Temporary Dialysis Catheter Access

<u>Short-term Dialysis catheters</u> are double-lumen, non-cuffed, non-tunnelled catheters that can be placed at the bedside without fluoroscopic guidance. These are placed on patients who require acute dialysis access and should be used for less than 3 weeks' duration. The subclavian vein should be avoided if possible to prevent central venous stenosis, which may have an impact on the future placement of ipsilateral AV access.

<u>Long-term Dialysis Catheters</u> are double-lumen, cuffed, tunnelled catheters that are placed with fluoroscopic guidance and are intended to be used for weeks to months. Ultrasound guidance has been shown to decrease the number of attempts at vein puncture and increase successful central vein cannulation to 100%. Owing to higher blood flow and lower complication rates, access through the right internal jugular vein with the distal catheter tip in the right atrium is preferred.

Complications of Temporary Dialysis Catheters

- 1. Central vein stenosis is seen in in up to 50% of patients with subclavian catheters in place for less than 6 weeks
- 2. Catheter thrombosis is seen in up to 25% of patients being dialysed through longterm dialysis catheters
- 3. Infections are higher with short-term catheters than long-term catheters and treatment constitutes catheter removal and antibiotics

A-V FISTULA CREATION

History and physical examination

History should document the patient's dominant extremity; any previous lines, previous access procedures. Physical exam includes Allan's test, peripheral pulses and evaluation of vein distensibility.

Arterial assessment

For optimal outcomes, no pressure gradient should be noted between the upper limbs, the arterial diameter should be greater than or equal to 2 mm throughout the extremity and the patent palmar arch should be present.

Venous assessment

Vein diameter of at least 2 mm although bigger is better. Central vein stenosis should be suspected if there are any prominent venous collaterals or oedema, a differential in extremity diameter, any history of previous central catheter placement.

Access Location

The AV access site is located as far distally in the extremity as possible, to preserve proximal sites for future access. Given its superior patency rate and lower complication rate, autogenous AV access should always be attempted before prosthetic AV access. The autogenous configurations include direct AV anastomosis and venous transpositions. Owing to easier access and lower infection rate, upper extremity access sites are used first

Prosthetic grafts

If no vein is available, an upper arm prosthetic AV access is performed.

Prosthetic lower extremity access

This is the preferred site once options in the upper extremity have been exhausted. The major disadvantage of the prosthetic lower extremity access is a higher infection rate compared with access in the upper extremity

HeRO graft

In most dialysis programmes there will be patients who have exhausted definitive access options due to central venous stenosis and are maintaining dialysis on a central venous catheter. Over the last few years, an alternative to central catheters for these complex patients has been proposed with the Hemodialysis Reliable Outflow (HeRO) graft (Cryolife Inc Company; Eden Prairie, MN, USA). Comprising two elements, a graft and venous outflow component, the graft is anastomosed to the ipsilateral brachial artery and tunnelled subcutaneously. The venous outflow component is placed percutaneously into the right atrium through the subclavian or internal jugular vein and superior vena cava. The HeRO graft has shown promise with 1-year primary and secondary patency rates of 21.9% (9.6e37.2%) and 59.4% (39.4e78%) respectively. Although these results are poor compared with a native AVF or AVG, in the general dialysis population, the cohort of patients having a HeRO graft placed are highly selected complex patients who have had multiple failed AVFs or AVGs.

Complications

Diffuse enlargement of an autogenous AV access.

Aneurysmal dilation and tortuosity is a unique feature that may develop in an autogenous AVF that has functioned for many years. The usual indication for intervention is compromise of the overlying skin. In addition, obstructive kinks and intraluminal thrombus may

compromise dialysis exchanges. Constructing a more proximal AV access using the arterialized vein end-to-end anastomosis after excision of redundant, or a prosthetic graft, can restore a functional access

VENOUS HYPERTENSION

Proximal, large vein obstruction is increasingly common (peripherally inserted central catheters [PICCs], defibrillators, pacemakers, and both permanent and temporary dialysis catheters). Subclinical venous obstruction is often unmasked by the increased flow of a well functioning AV access. Significance: Unilateral symptoms may reflect regional or central vein obstruction Superior vena cava obstruction may eliminate consideration of both upper extremities. Venous hypertension (V-HTN) may produce typical symptoms of venous insufficiency. Central venous stenosis/obstruction: Angioplasty with or without stent is preferable as initial therapy. Angioplasty alone is most appropriate for subclavian sites due to the potential for extrinsic compression. Surgical bypass is more durable but incurs considerably greater risk.

ARTERIAL STEAL SYNDROME

Management options; <u>Ligation</u>: Solves the problem, but requires sacrifice of the access; appropriate for severe symptoms; <u>IMN Banding</u>: More likely to succeed in high flow AV access, but often complicated by thrombosis rerouting of arterial inflow; Extension of the arterial anastomosis with or without brachial ligation (distal revascularization and interval ligation [DRIL]; revision using distal inflow [RUDI], and proximalization of the arterial inflow [PAI]) will retain a well-functioning AV access and resolve symptoms in most patients.

Graft Thrombosis

Despite the proven advantages of AVF over prosthetic graft access, both types of access eventually fail and contribute to multiple hospital admissions, complex surgical and endovascular interventions, and overall morbidity associated with chronic haemodialysis. Thrombosis is the principle cause of failure in both AVF and PTFE access, with approximately 85% as a result of venous stenosis secondary to neo-intimal hyperplasia.

Historically, management of a thrombosed access has involved surgical thrombetomy, frequently with revision to treat the causative stenosis; or placement of a new access at a different location. Endovascular techniques have since superseded surgery in this setting, incorporating the use of thrombolysis and/or thrombectomy, concomitant stenotic disease can be treated using angioplasty with stenting.

References

- 1. NKF-K/DOQI Clinical Practice Guidelines for Vascular Access: update 2006. Am J Kidney Dis 2006; 48(suppl):S176-247.
- 2. A Review on the Hemodialysis Reliable Outflow (HeRO) Graft for Haemodialysis Vascular Access J. Al Shakarchi
- 3. Vascular Access 2006 Work Group. Clinical practice guidelines for vascular access. Am J Kidney Dis 2006;48:S176e247.
- 4. Rutherford's Vascular Surgery, 7th Edition
- 5. The Society for Vascular Surgery: Clinical practice guidelines for the surgical placement and maintenance of arteriovenous haemodialysis access. Anton N J Vasc Surg 2008;48:2S-25S

Dr ZM Asmal Inc.

Prior to the adherence of HAART, transplant to HIV patient was unheard off.

With treatment for HIV the prognosis of these patients has significantly improved.

Transplant of these patients was done with good results. These transplants were initially done from HIV negative donors to HIV positive recipients. Subsequently HIV positive donors to HIV positive recipient also had relatively good outcome. The donation of HIV + donors to HIV – recipients is probably the next step. However this presents certain ethical dilemmas which need to be discussed.

This could be done using the principal of ethics nl: Autonomy Utility Justice

HIV POSITIVE DONOR ORGANS TRANSPLANTED TO HIV NEGATIVE RECIPIENTS – A LEGAL PERSPECTIVE

Prof Magda Slabbert, College Of Law, University Of South Africa

The transplantation of **HIV positive organs** to **HIV negatives patients** raises a few legal questions. It could be categorised into mainly three sections; consenting adults, children and research. Organ transplants are regulated by the Constitution of the Republic of South Africa, 1996, the National Health Act 61 of 2003 and the Regulations in terms of the Act. If all the different articles in the Acts and Regulations are scrutinised it is clear that the legal basis for any transplant is informed consent. For adults this poses no problem as they can give consent after being told of all the pros and cons of a transplant using a HIV infected organ. The problem comes when it is a child under the age of 12 years needing a transplant. The Children's Act 38 of 2005 also comes into play. Transplanting a HIV positive organ into a HIV negative patient is a new endeavour and therefore the legislative requirements for research using human participants will also be highlighted.