Bristol Urological Institute
Improving care by advancing knowledge

The British Association of Urological Surgeons

Minimal Access Surgery for Cystectomy – Surviving the first year

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Factors affecting survival

- Disease – Cancer specific mortality
- Surgery – Death related to treatment

Cancer Survival

- Cystectomy
- Lymphadenectomy
- Herr PSM <10%, ≥9LNs

- Herr H, Lee C, Change S, Lerner S; Bladder Cancer Collaborative Group. J Urol 2004 May;171(5):1823-8; discussion 1827-8. Standardization of radical cystectomy and pelvic lymph node dissection for bladder cancer: a collaborative group report.

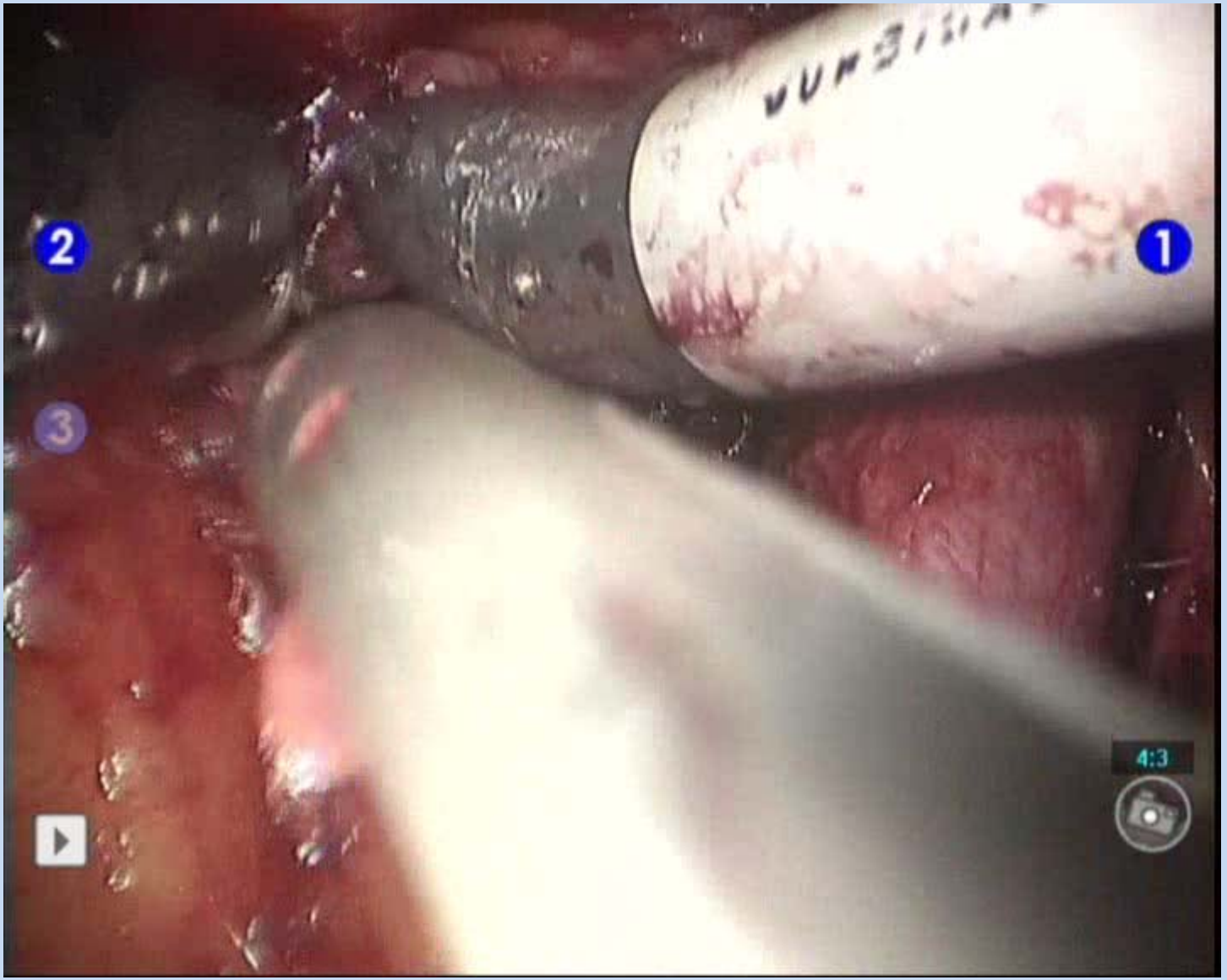
PSM Rates

	N=	Open	Robotic	Lap
Chade DC J. Urol 2010	Literature review 1998-2009	4-5% (8135 pts)	0-10% (184 pts)	0-5% (258 pts)
Richards KA Urol 2010	70	8.6%	3%	N/A
Styn NR Urology 2012	150	1%	4%	N/A
Knox ML J Endo Urol 2012	142	8%	7%	N/A
Khan MS Int J Clin Prac 2012	158	10%	0%	4%

Lymph node yield

	N =	Open	Robotic	Lap	
Chade DC J Urol 2010	Literature review 98-2009	10-43 (8135 pts)	16-19 (184 pts)	10-18 (258 pts)	
Abaza R J. Urol 2012	155	36.9	37.5	N/A	P > 0.5
Gondo T Jpn J Clin Onc 2012	26	13.8	20.7	N/A	P = 0.042
Styn NR Urology 2012	150	15.2	14.3	N/A	P=0.56
Knox ML J Endo Urol 2012	142	17.7	21.3	N/A	P=0.06
Khan MS Int JCP 2012	158	11	16	10	P>0.5

ePLND



Completeness of LND

- *MD Andeson Study*
- *11 patients RARC and LND plus a second 'open look'.*
- *Robotic LN yield 43 (19-63), open second look yield 4 (0-8)*
- *93% lymph node yield*

- *Davis JW, Gaston K, Anderson R et al. Robot assisted extended pelvic lymphadenectomy at radical cystectomy: lymph node yield compared with second look open dissection. J Urol 2011; 185: 79–83*

Survival

	Lap	Robotic	Open
RFS	83-85% (1-2 years)	86-95% (1-2 years)	62-68% (5 years)
	60-77% (2-3 years)		
OS	90-100% (1-2 years)	90-96% (1-2 years)	59-66% (5 years)
	50-87% (2-3 years)		

- T3/4 46-56% open vs 19-50% RARC
- T0 0-11% open vs 20-22% RARC

Chade DC J.Urol 2010
Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York

Oncological control

- Equivalent
- Are pts with bulky disease offered open surgery?/Selection bias
- Will there always be a role for open surgery?

Non Cancer related mortality

- 30 day mortality – 2% (27/1359)
- Quek ML, Stein JP, Skinner DG J Urol 2006

Early cancer independent mortality

- Cardiovascular – MI, CVA, arterial thrombosis
- Septic – Post op urine or bowel leak, pneumonia

Early non cancer related mortality in minimally invasive surgery

- Yuh BE, T Wilson (City of Hope National Cancer centre, USA), European Urol Nov 2012

- 196 pt RARC 2003 – 2011

- Mortality 30 days – 2% (4/196)
- Mortality 90 days – 4.1% (8/196)

- Sepsis 2, ARDS 2, MI 1, Unknown 1
- Bca progression 2

- Extracorporeal reconstruction. Robot redocked for the urethra-neobladder anastomosis

The Clavien-Dindo Classification of Surgical Complications

Grade I	Any deviation from the normal postoperative course	
Grade II	Requiring pharmacological treatment. Blood transfusions and total parenteral nutrition	
Grade III	Requiring surgical, endoscopic or radiological intervention	IIIA Interevntion not under GA
		IIIB Intervention under GA
Grade IV	Life-threatening complication	IVA Single organ dysfunction
		IVB Multi organ dysfunction
Grade V	Death	

Complication rates

Series	N=	Clavien 1-2	Clavien 3-4
Haber and Gill LRC BJUI 2007	37	14%	11%
Huang et al LRC Eur Urol 2010	171	26%	13%
Khan et al RARC Urology 2011	50	24%	10%
Guru et al RARC Urology 2007	20	10%	10%
Shabsigh et al ORC Eur Urol 2009	1142 Prospective collection	55%	13%

Direct comparisons

Series	N =	Clavien 3-4/5 LRC	Clavien 3-4/5 ORC	Clavien 3-4/5 RARC
Ng et al Eur Urol 2010	187 (Prospective cohort study)	N/A	31%	17%
Styn et al Urology 2012	150 (Matched pair analysis)	N/A	21.3%	28.1%
Sung et al J Endo Urol 2012	139 (Retrospective comparison)	N/A	23.1%	8.6%
Knox et al J Endo Urol 2012	142 (retrospective review)	N/A	22.6%	25.8%
Khan et al Int J Clin Pract 2012	158 (prospective cohort comparison)	39.6%	30.8%	16.7%

Direct Comparisons – Prospective RCT

- Nix J, Smith A, Pruthi RS (Uni North Carolina, USA) European Urol Feb 2010

- 21 Robotic vs 20 Open
- Robotic – longer op times, decreased bld loss, decreased time to flatus/bowel movement

- No difference in complication rate or hospital stay

Complications

- Reflection of the physical characteristics of the patients?

- Will those treated by minimally invasive technique be more able to tolerate the inevitable complications?

CPEX testing in major surgery

Table 1 - Mortality data: AT above and below 11 ml/min/kg*

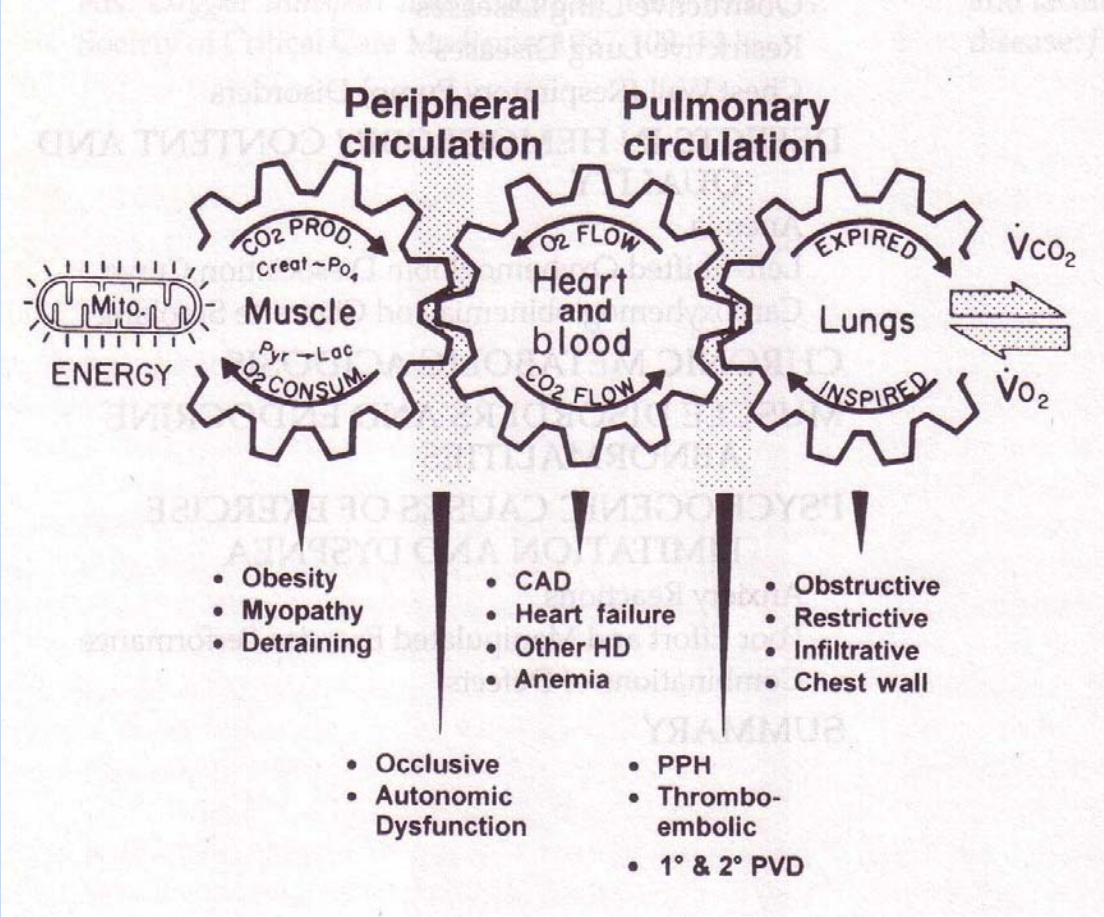
AT ml/min/kg	Number	CVS deaths	Percentage mortality
<11	55	10	18
>/=11	132	1	0.8
Totals	187	11	(p<0.001)

Co-existing cardiac ischaemia and AT<11 = 42% mortality
(AT = anaerobic threshold; CVS = cardiovascular)

Older (1993)Chest 104:701-04

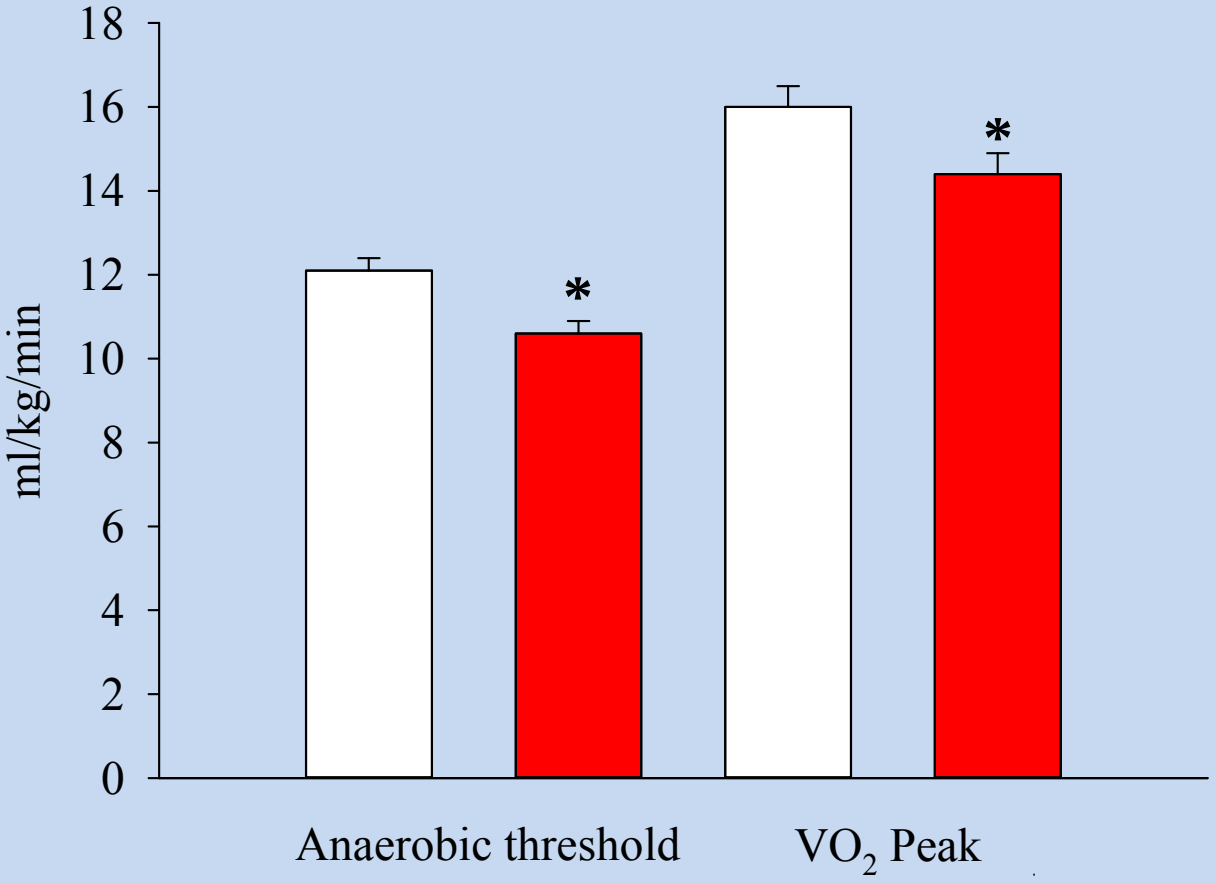
Cardiopulmonary Exercise Testing

Physiological Basis



Wasserman, 2005

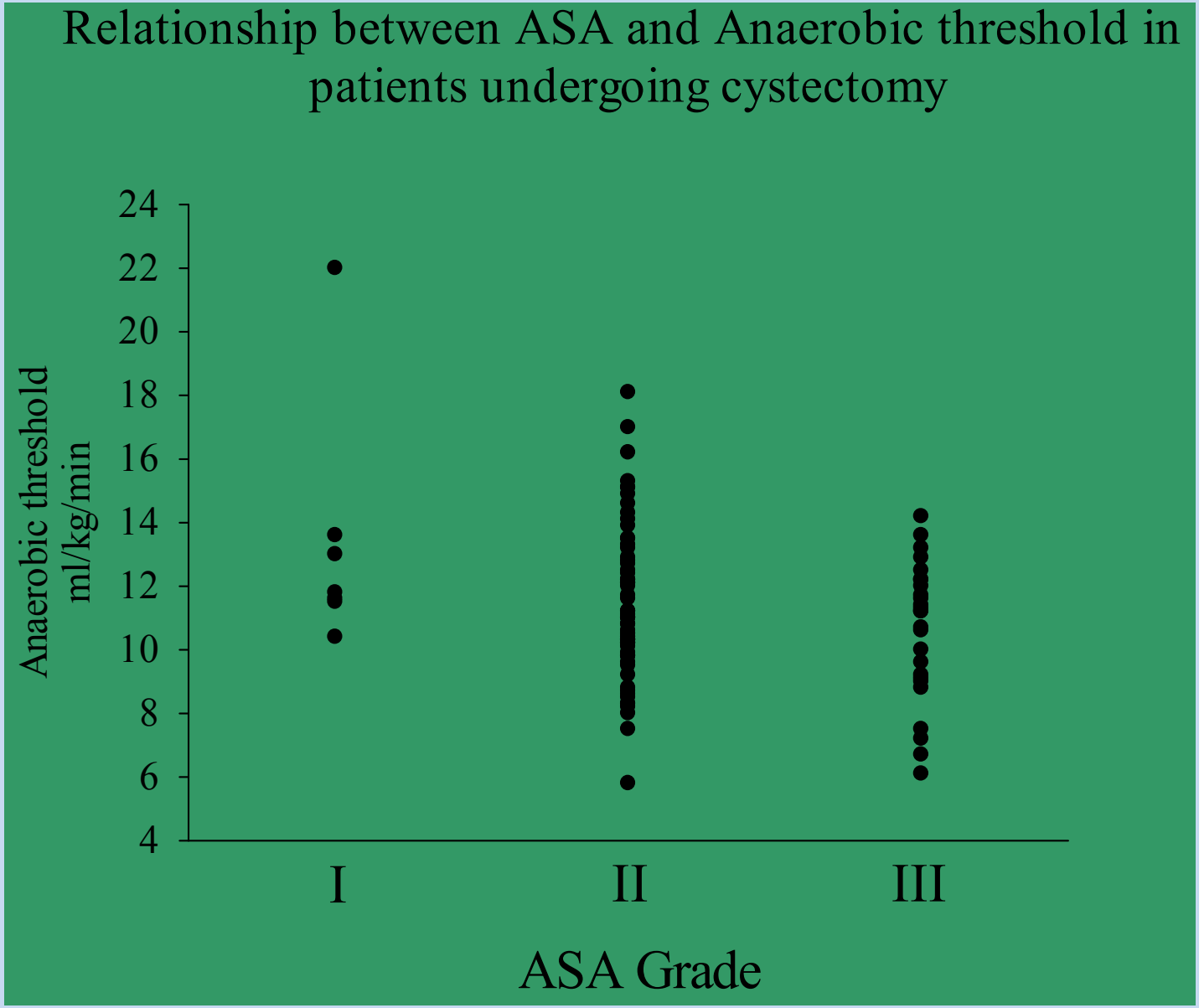
Patients who suffer complications following cystectomy attain a lower pre-operative AT and VO_2 peak



Can we identify cystectomy patients who will have complications?

N = 103	Complication	No Complications
AT > 11, VE/VCO_2<32 (Low risk on CPET)	1 (3%)	32
AT < 11 ± VE/VCO_2>32 (High Risk on CPET)	33 (47%)	37

- *If threshold set at 11 ml/kg/min with Ve/VCO_2 <32 then <5% of patients designated low risk will suffer complications*
- *Complications included: Sepsis (9), Pneumonia (8) MI (6), Dehiscence (5), Death (6),SBO (2),*
- *ARF (1)*


Relationship between ASA and Anaerobic threshold in patients undergoing cystectomy
Anaerobic threshold ml/kg/min
24
22
20
18
16
14
12
10
8
6
4
I
II
III
ASA Grade

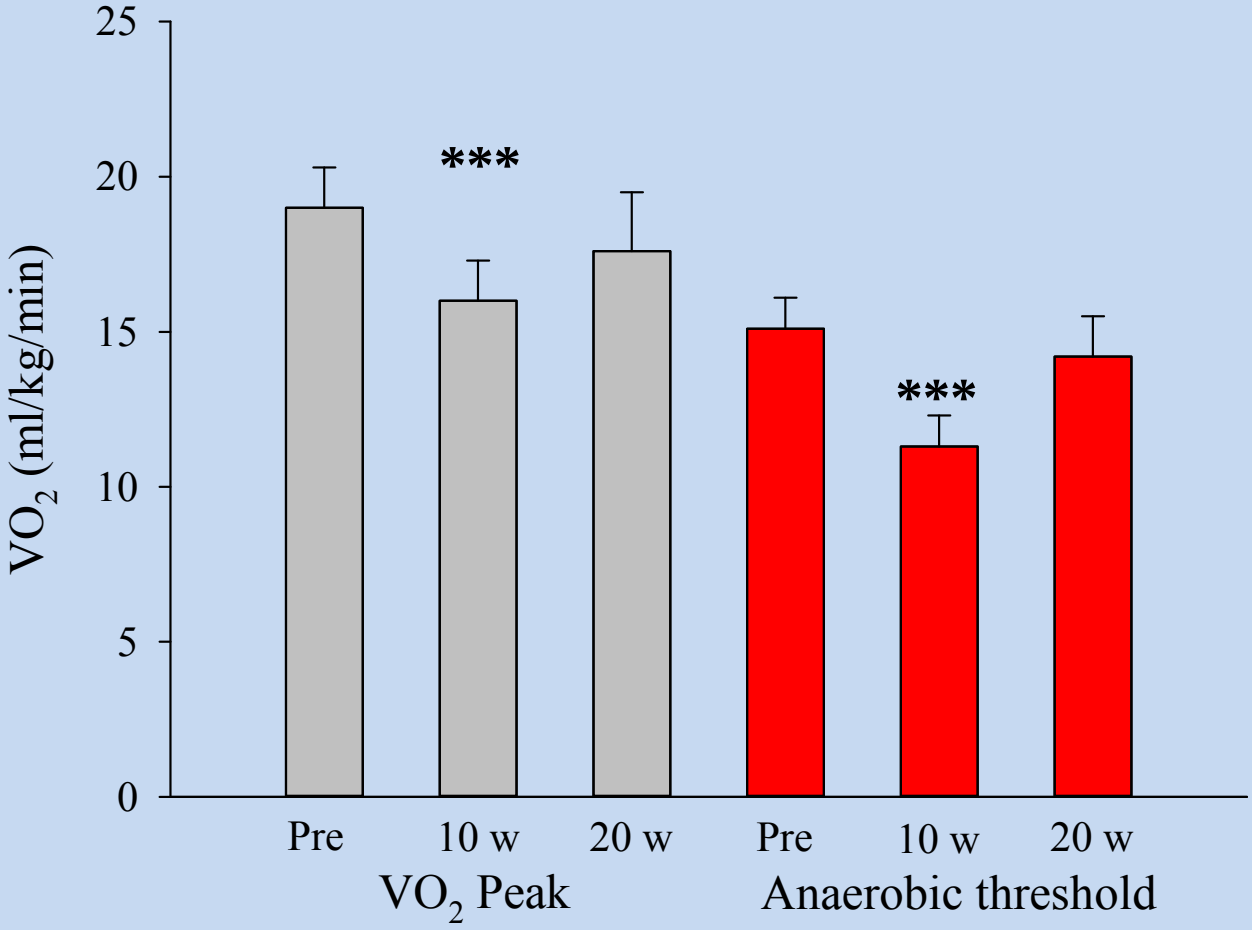
Can we identify cystectomy patients who will have an MI or Die?

N = 103	MI / Death	No MI/ Death
AT > 11, VE/VCO_2<32 (Low risk on CPET)	0	31
AT < 11 ± VE/VCO_2>32 (High Risk on CPET)	11 (18%)	61

•*If threshold set at 11 ml/kg/min with Ve/VCO_2 <34 then no MI or death in any patient designated low risk. Deaths; Sepsis (3), Respiratory failure/ARDS (2) MI (1).*

What happens to the AT post cystectomy?

Changes in Anaerobic threshold and VO_2 peak following cystectomy



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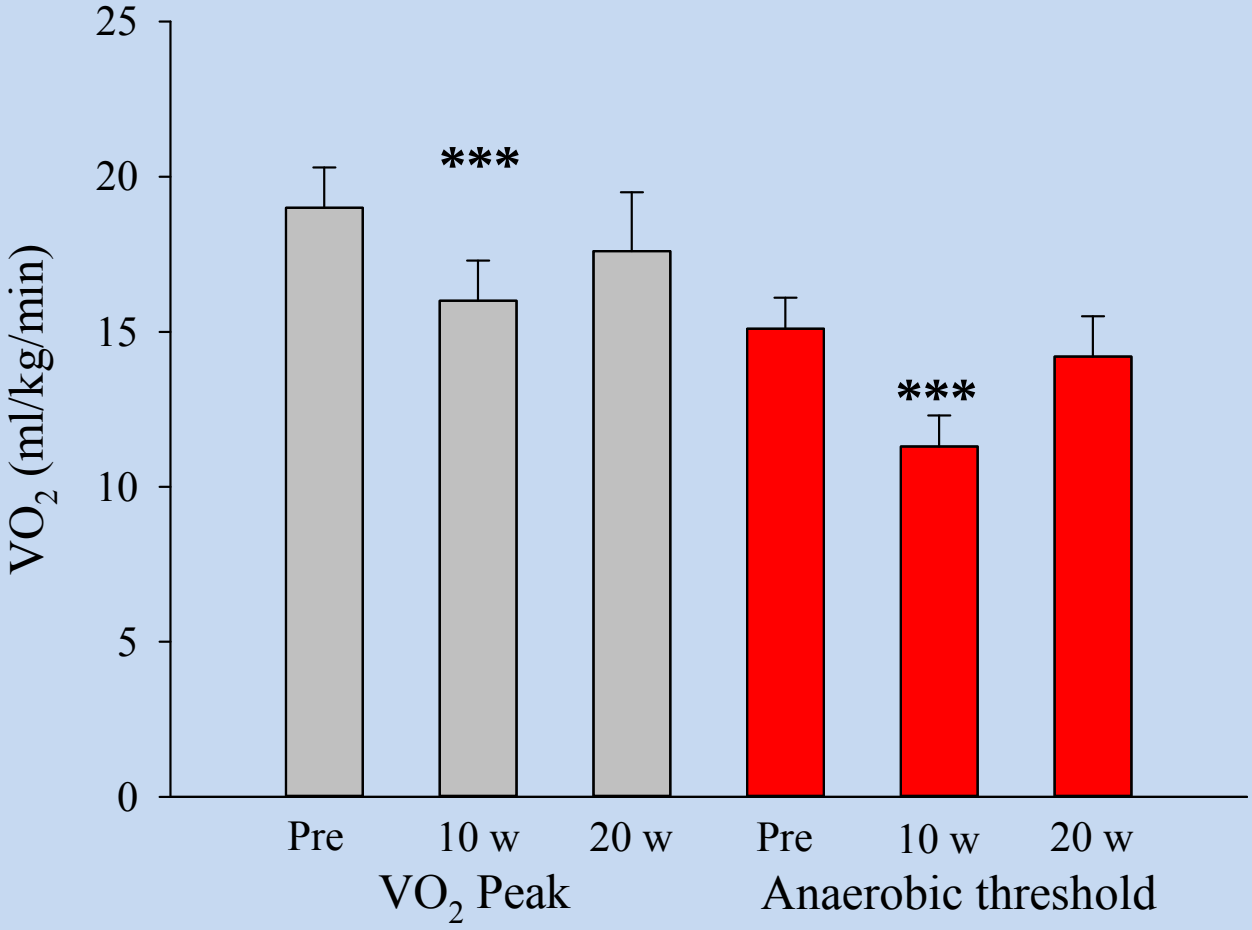

90 day mortality

	n	Open	Robotic	Lap
Styn NR, Urol 2012 ,Ann Arbor Matched pair analysis	150	3% (3/100)	0% (0/50)	N/A
Knox ML, J Endo Urol 2012 Single institution, Alabama, USA	142	2.4% (2/84)	1.7% (1/58)	N/A
Yu HL, European Urol 2012 Observational cohort study Harvard, USA	1668	2.5%(36/1444)	0%(0/224)	N/A
Khan MS Cohort comparison, Int J C Pract 2012	158	2%(1/52)	0%(0/48)	3%(2/58)

Questions

- Can we limit the reduction in AT with minimally invasive surgery?
- Are patients better able to cope with complications after MIS?

- Are more patients able to tolerate adjuvant chemotherapy after MIS (Donat SM et al European Urology 2008)?

Conclusion

- Cancer
  - Margin +ve rate
  - Lymph node yield
- Non cancer related mortality
- BOLERO

- Thank you

Conclusions

- Cancer control – equivalent?
- Complications – Similar
- 1 year survival – enhanced??

- BOLERO

- Elderly sick population
- Patient fitness matters

- Can we reduce the insult to the patient through MIS

Older study

CPEX Bike

Comparison of complication rates

- Khan MS, Challacombe B, Rimmington P, Dasgupta P Int J Clin Pract 2012
- Cohort comparison of 158 patients (52 open, 58 Lap, 48 RARC)

- Transfusion rates >ORC>LRC>RARC
- Complication rates >ORC>LRC>RARC
- LOS >ORC>LRC>RARC

Diagram

90 day mortality

	n	Open	Robotic	Lap
Styn NR, Urol 2012 ,Ann Arbor Matched pair analysis	150	3% (3/100)	0% (0/50)	N/A
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- Knox et al fewer comps in elderly RARC than younger ORC
- Khan challacombe paper less transfusion/shorter hosp stay

- Similar complications but perhaps lower mortality??????????????

Is the patient's physical condition more important

- CPEX

Survival post cystectomy

- 30 day 3.2%
- 90 day 5.2%
- Hautmann RE Eur Urol May 2012

- In hospital deaths USA 1.47% (range 0.54 – 2.70%) 6,728 pts 2002-2005
- Barbieri CE J Urol 2007

- Hes data 6308pts - in hospital death rate 5.53%
- McCabe JE Postgrad Med J Aug 2007

Southmead Cystectomy Population

- Median age 70 years
- 51% 0f patients are > 70 years old
- 55% have hypertension
- 23% have had prior MI or IHD
- 20% smokers
- 21% B-blockade
- 14% have diabetes
- Mean AT 11.2 ml/kg/min, 50% have AT≤11
- *No correlation between PMH and AT*

Post-operative care and complications

N = 103	Complications	No Complications
ICU Days: Mean **Median**	7 3 ***	1 1
Total LOS Days: Mean **Median**	30 22 ***	9 9

*** P<0.001 Mann Whitney U-test

Slide 1: Self explanatory

Slide 2; slide shows that patients develop complications attain a lower Anaerobic threshold and VO_2 peak in **pre-operative** Cardiopulmonary exercise testing. ie.. Relationship between fitness and the development of complications

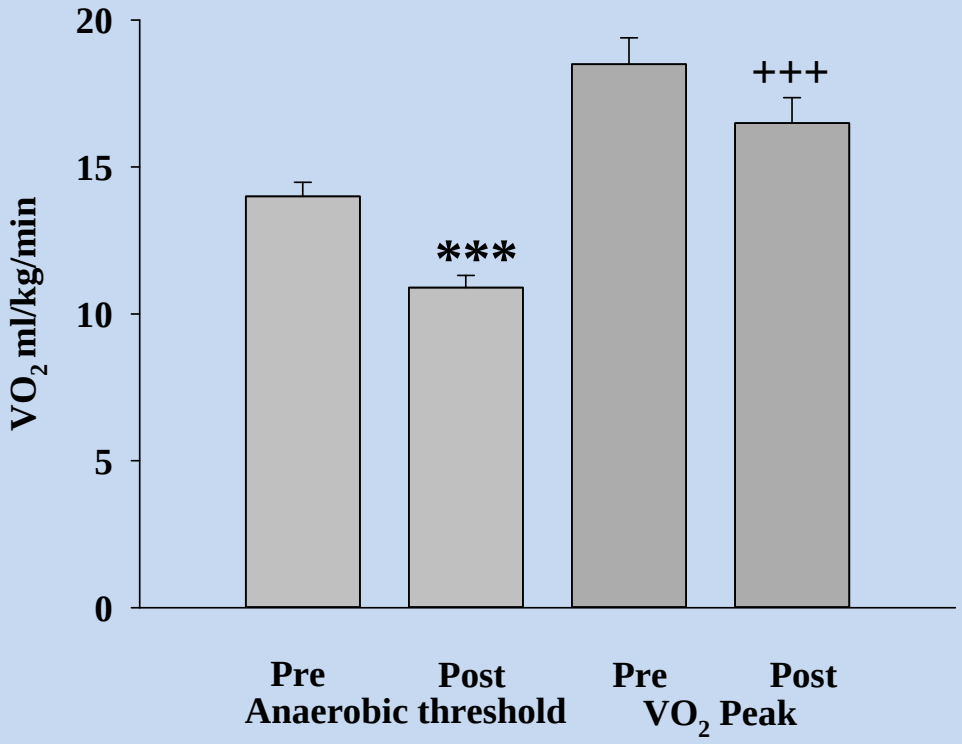
Slide 3; These patients (unfit ones) will stay significantly longer in critical care and on the ward ie relationship between fitness and LOS/ cost of care

Slide 5; we can stratify patients based on

CPET parameters into high and low risk. In so doing we can predict those who have complications.

Slide 6; and we can predict who will have MI or die. Importantly we can tell people who will have, in all likelihood have no problems.

Changes in Anaerobic threshold and Peak VO_2 following major surgery



Data distribution tested using Shapiro Wilk Test: * Paired T-Test, +++ Wilcoxon Signed Rank Test**

Finally; These are about defining recovery from surgery

Slide 8 (n=52) (radical nephrectomy, AAA and cystectomy patients)
Here we have asked whether there is a physiological impact to surgery
And show that at 10 weeks post-op patients have a significantly lower AT
and VO2 peak.

Slide 9 (n=9) patients following cystectomy showing the same post-op fall
In AT and VO2 peak at 10 weeks that is returning to normal by 20 weeks

Message:
1. Using CPET we can define recovery from major surgery
2. If we define risk by CPET parameters: Patients are at higher risk post
Major surgery for up to 20 weeks following cystectomy. This has implications
for patients who have complications or who are returning for follow-up surgeries

Post op anaerobic threshold – Open vs Robotic

Cystectomy margins

- Robotic vs Open 1 vs 3 26 pts
- Jpn J Clin Oncol. 2012 Jul;42(7):625-31. Epub 2012 May 11