



Enhanced Recovery After Surgery

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Enhanced recovery after surgery

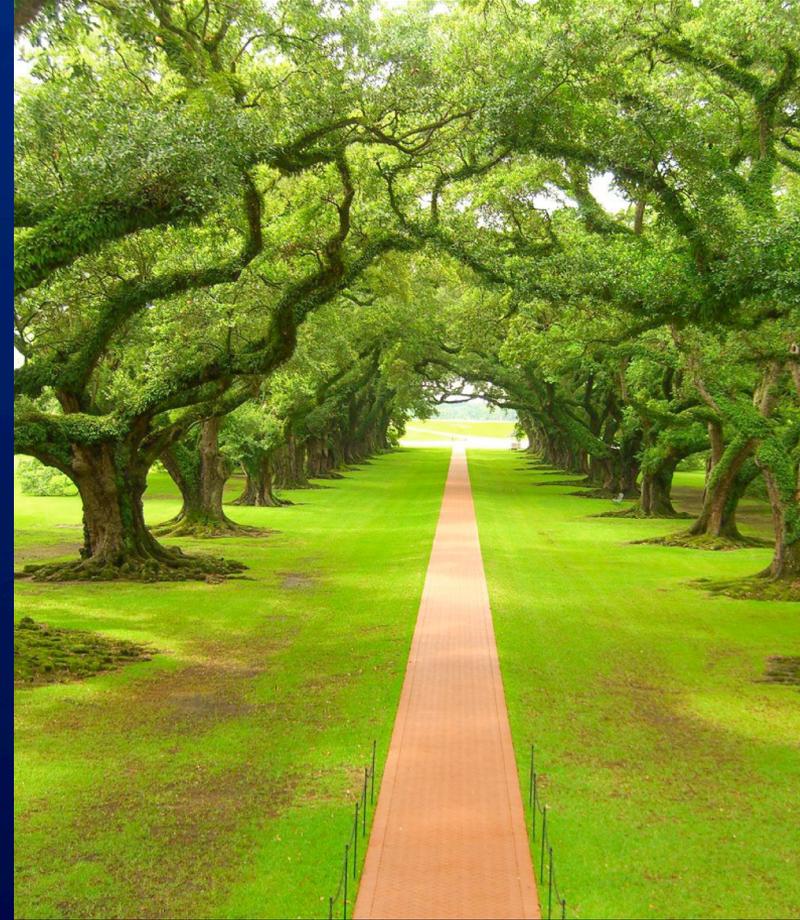
- Goal of modern ERAS:
 - Make a positive impact from diagnosis, through surgery, to return of normal function
 - Not exclusively dependent on one measure
- Full ERAS adoption
 - Reduces complications by up to 50%
 - Decreases length of stay by 30%
 - Decreases readmissions
 - Reduces cost

Collins et al. Eur Urol 2016
Azhar et al. Eur Urol 2016



ERAS is a pathway

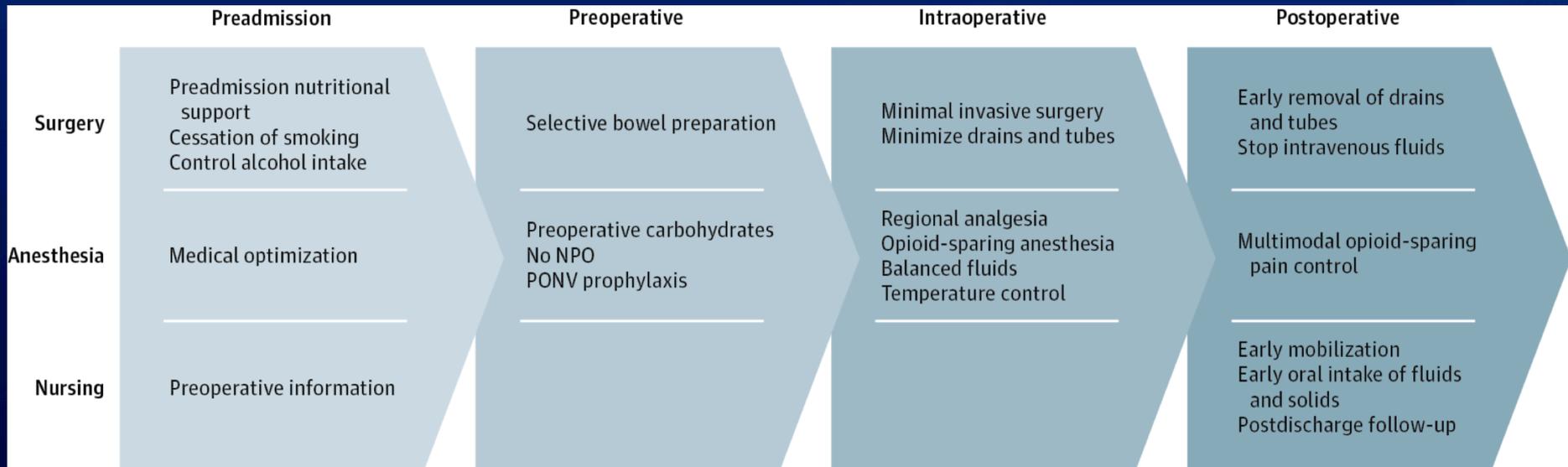
- ***No single intervention is adequate***
- Includes components of
 - Pre-operative
 - Intra-operative
 - Post-operative
 - Post-discharge
- Requires 'buy-in' from patients, surgeons, anesthesiologists, and nursing
- Requires education and monitoring





ERAS is a pathway

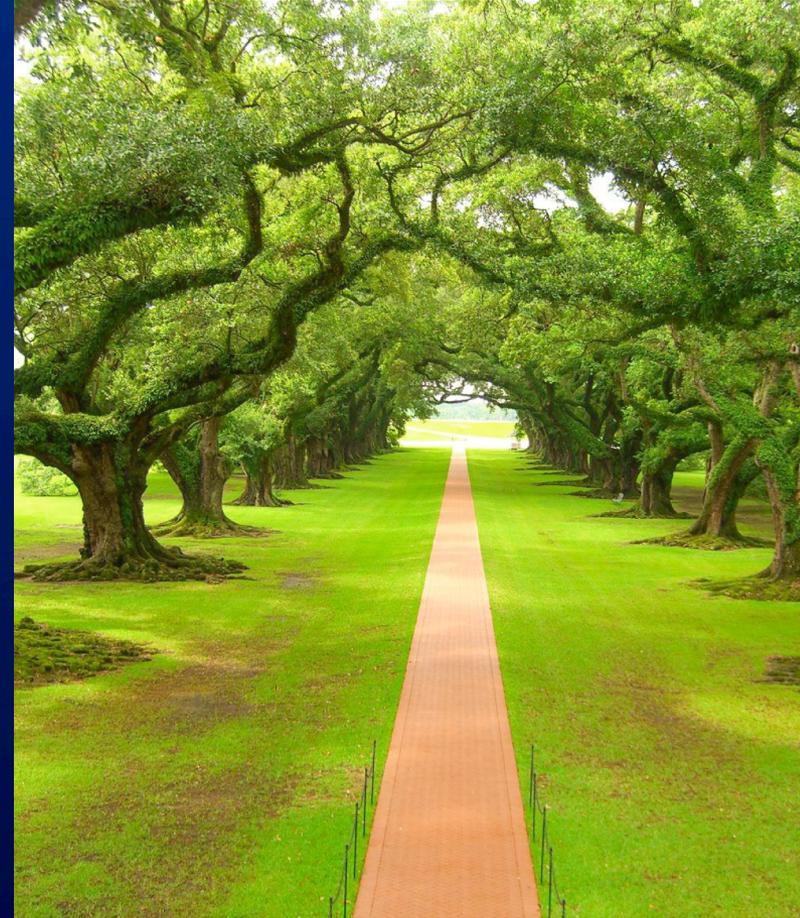
- ERAS as a continuum of care
 - Encourage engagement with stakeholders





ERAS is a not just a pathway but also a process

- Requires analysis and data tracking
- Patient care dashboards
- Continuous improvement

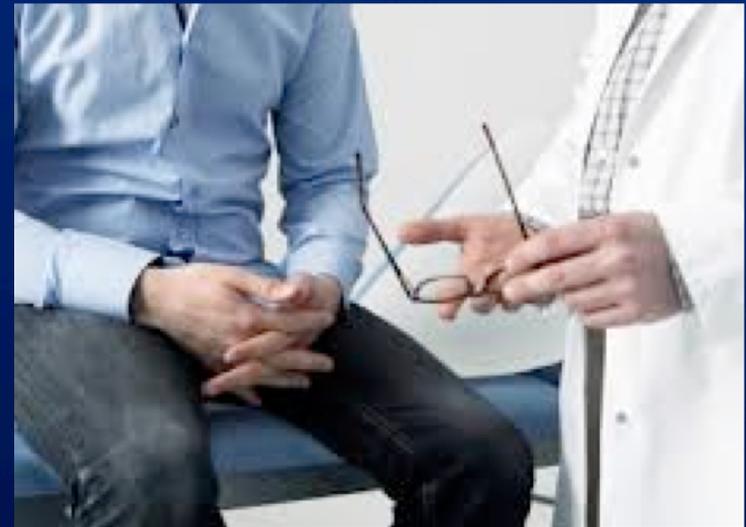




Enhanced recovery after cystectomy

• *Pre-operative*

- Patient counseling, expectations, education
- Preadmission nutritional support
 - Treatment of hypoalbuminemia and anemia
 - SIM (specialized immunonutrition)
 - Improvements in 2 weeks
- Plan for post-discharge care

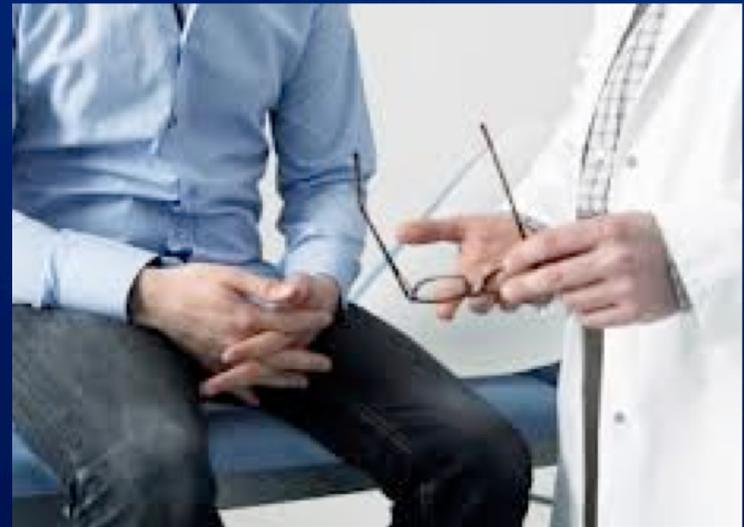




Enhanced recovery after cystectomy

- ***Pre-operative***

- Carbohydrate-rich fluid intake
 - Specialized formulas or sports drinks
- Avoid mechanical and antibiotic bowel preparation
- Smoking cessation
- Exercise





Effect of Preoperative Nutritional Deficiency on Mortality After Radical Cystectomy for Bladder Cancer

Justin R. Gregg, Michael S. Cookson,* Sharon Phillips, Shady Salem, Sam S. Chang,† Peter E. Clark,‡ Rodney Davis, C. J. Stimson, Jr., Monty Aghazadeh, Joseph A. Smith, Jr. and Daniel A. Barocas§,||

- Nutritional deficiency = preoperative albumin < 3.5, BMI < 18.5, weight loss > 5% body weight
- 90-day mortality 16.5% vs 5.1% (p<0.01)

Table 3. Cox proportional hazards models

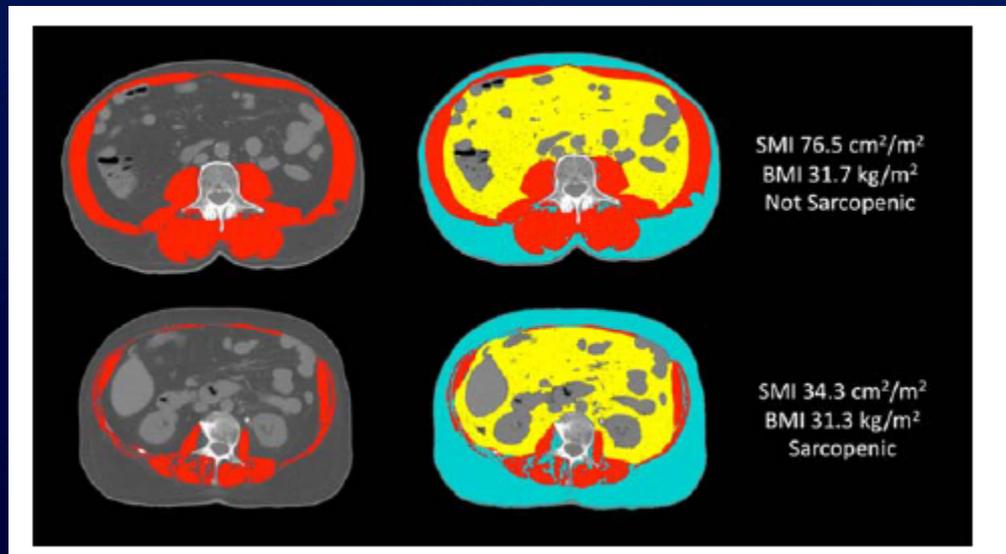
	90-Day Mortality	
	HR (95% CI)	p Value
Nutritionally normal (referent)	1	
Nutritionally deficient	2.91 (1.36–6.23)	<0.01
AA CCI (continuous)	1.12 (0.95–1.31)	0.19
No periop transfusion (referent)	1	
Periop transfusion	2.59 (1.17–5.74)	0.02
No complication present (referent)	1	
1 or More complications	2.81 (1.33–5.94)	0.01
Lymph node density (continuous)	1.56 (0.89–2.75)	0.12
Pathological stage 2b or lower (referent)	1	
Pathological stage 3a or higher	2.28 (1.03–5.06)	0.04

Sarcopenia in Patients With Bladder Cancer Undergoing Radical Cystectomy

Impact on Cancer-Specific and All-Cause Mortality

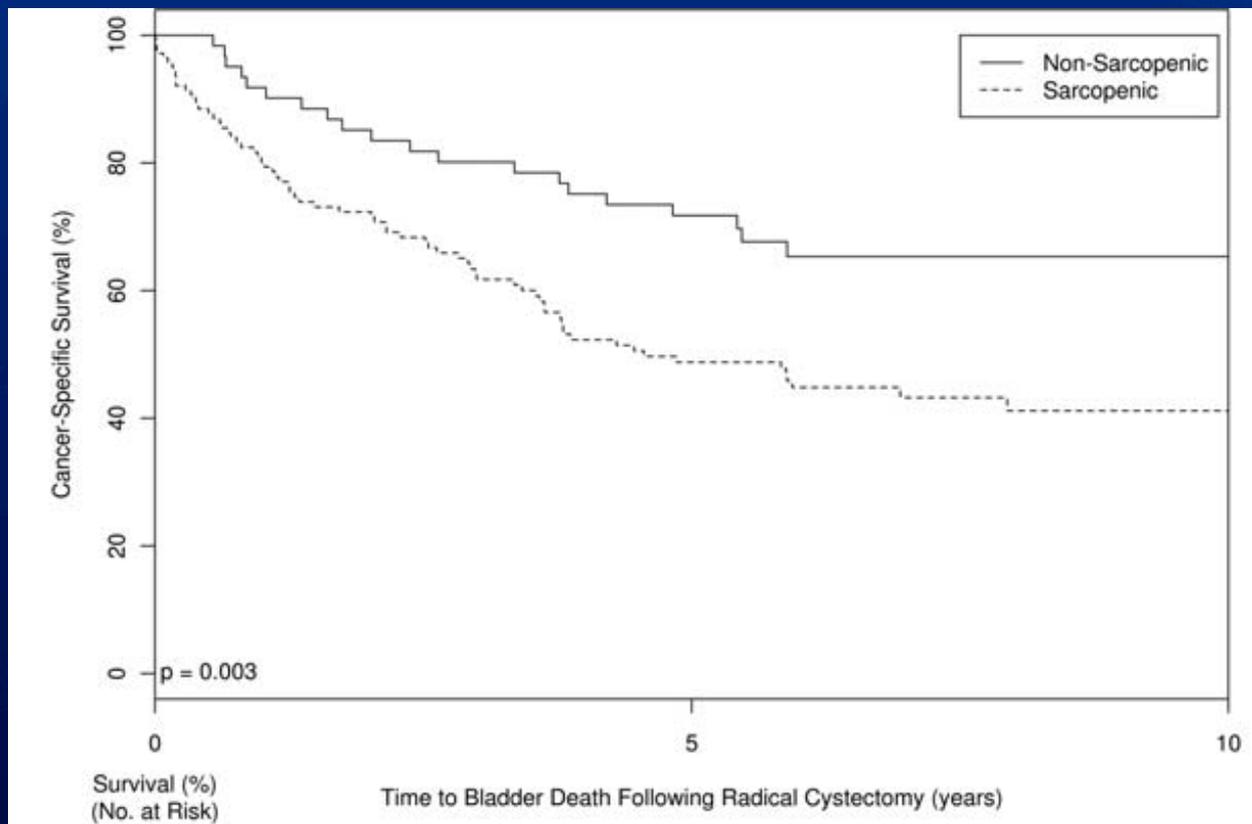
Sarah P. Psutka, MD¹; Alonso Carrasco, MD¹; Grant D. Schmit, MD²; Michael R. Moynagh, MD²; Stephen A. Boorjian, MD¹; Igor Frank, MD¹; Suzanne B. Stewart, MD¹; Prabin Thapa, MS³; Robert F. Tarrell, MS³; John C. Cheville, MD⁴; and Matthew K. Tollefson, MD¹

- Sarcopenia = skeletal muscle wasting
- Assess skeletal muscle index at level of L3
 - Quantify using imaging software from CT scan





SARCOPENIA AND OUTCOMES AFTER RC



- Associated with increased risks of cancer death and all-cause mortality on multivariate analysis
 - Noted as early as 90-day ACM (7.8% vs 1.6%)



WHAT CAN BE DONE PREOPERATIVELY TO “OPTIMIZE” PATIENTS FOR RC? PREHABILITATION

Optimizing a frail elderly patient for radical cystectomy with a prehabilitation program

Francesco Carli, MD, MPhil; Rashami Awasthi, BSc;* Chelsia Gillis, MSc;* Wassim Kassouf, MD, FRCSC†*

- Exercise program prior to surgery

Can Urol Assoc J 2014

Effects of Immunonutrition for Cystectomy on Immune Response and Infection Rates: A Pilot Randomized Controlled Clinical Trial

Jill M. Hamilton-Reeves^{a,b,}, Misty D. Bechtel^a, Lauren K. Hand^a, Amy Schleper^a, Thomas M. Yankee^c, Prabhakar Chalise^d, Eugene K. Lee^b, Moben Mirza^b, Hadley Wyre^b, Joshua Griffin^b, Jeffrey M. Holzbeierlein^b*

- Patients provided with specialized immunonutrition (arginine, fish oil, vit A, and nucleotides) prior to surgery
 - 33% decreased risk of complications
 - 39% decreased risk of infection

Eur Urol 2016



Enhanced recovery after cystectomy

• *Intra-operative*

- Minimization of intraoperative fluids
 - Vasopressors instead
- Minimally invasive approach
 - RARC with intracorporeal diversion
- Limited narcotics for pain control
 - Regional anesthesia
 - Improved local anesthesia
- Efficient operation
 - Target operative time less than 4 hours
 - Reduce need for transfusion



Wuethrich et al. Eur Urol 2014
Parekh et al. AUA 2017



BLOOD TRANSFUSION AT RC

- Given in up to 60% of cases

Shabsigh et al, Eur Urol 2009

Linder et al, Eur Urol 2013

- Costly
 - Each unit \$1500-\$2000 at Mayo
- Risk of transfusion reaction
- Risk of infectious transmission
- Adverse cancer consequences?



The Impact of Perioperative Blood Transfusion on Cancer Recurrence and Survival Following Radical Cystectomy

Brian J. Linder^a, Igor Frank^a, John C. Cheville^b, Matthew K. Tollefson^a, R. Houston Thompson^a, Robert F. Tarrell^c, Prabin Thapa^c, Stephen A. Boorjian^{a,*}

Variable	Tumor recurrence			Death from bladder cancer			All-cause mortality		
	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value
Age at surgery	1.00	0.99–1.01	0.87	1.01	1.00–1.01	0.20	1.03	1.02–1.04	<0.0001
Gender (ref. female)	1.19	0.98–1.45	0.08	1.22	1.01–1.47	0.04	1.33	1.16–1.53	<0.0001
Body mass index	0.96	0.88–1.05	0.34	0.97	0.88–1.06	0.44	1.02	0.95–1.08	0.65
ECOG performance status	1.06	0.93–1.20	0.37	1.28	1.15–1.44	<0.0001	1.40	1.29–1.52	<0.0001
Preoperative hemoglobin level	0.96	0.92–1.01	0.12	0.90	0.86–0.94	<0.0001	0.89	0.87–0.93	<0.0001
Receipt of PBT	1.20	1.01–1.42	0.04	1.31	1.10–1.57	0.003	1.27	1.12–1.45	0.0002
Pathologic tumor stage (pT2–4 compared with ≤pT1)	2.16	1.84–2.54	<0.0001	3.04	2.55–3.62	<0.0001	1.83	1.64–2.05	<0.0001
pN+	1.91	1.54–2.37	<0.0001	1.78	1.45–2.18	<0.0001	1.68	1.42–1.99	<0.0001
Total no. nodes removed	0.98	0.97–0.99	0.0005	0.99	0.98–0.99	0.002	0.99	0.98–1.00	0.0008
Positive radial margin	0.97	0.86–1.08	0.53	1.00	0.98–1.02	0.65	1.00	0.98–1.02	0.80
Receipt of perioperative chemotherapy	1.03	0.82–1.29	0.82	1.31	1.06–1.62	0.01	1.07	0.90–1.27	0.46
Year of cystectomy	1.00	0.99–1.01	0.77	1.00	0.99–1.02	0.59	1.00	0.99–1.01	0.89
Early complication	1.05	0.90–1.23	0.51	1.04	0.88–1.21	0.66	1.09	0.98–1.22	0.13

- Each unit transfused → 7% increased risk of death from bladder cancer



SOLUTIONS TO PROBLEM OF BLOOD TRANSFUSION AT RC?

- More restrictive threshold Hb for transfusion
 - Non-inferior to liberal transfusion strategy among patients undergoing cardiac surgery

Mazer CD et al, N Engl J Med 2018

- Identify at-risk patients/pre-operative iron supplementation
- Robotic cystectomy
- Tranexamic Acid



TRANEXAMIC ACID

- Lysine analog
- Given as IV infusion during surgery
- Prevents clot breakdown
- No demonstrated increased risk of thromboembolic events
- Shown to reduce need for transfusion in cardiac and orthopedic surgeries
 - 21% reduction in transfusion for RRP
- Cost-effective (\$60-80/case at Mayo)

Crescenti et al, BMJ 2011



Efficacy and Safety of Intraoperative Tranexamic Acid Infusion for Reducing Blood Transfusion During Open Radical Cystectomy



Harras B. Zaid, David Y. Yang, Matthew K. Tollefson, Igor Frank, Jeffrey L. Winters, Prabin Thapa, William P. Parker, R. Houston Thompson, R. Jeffrey Karnes, and Stephen A. Boorjian

- N=103 – open RC patient treated with tranexamic acid (TXA) as intraoperative infusion
 - Matched 1:2 to (historic control) patients who did not receive TXA during RC, based on:
 - Age
 - Preoperative Hb
 - Receipt of NAC
 - Pathologic T and N stage



DECREASED RATE OF BLOOD TRANSFUSION WITH TXA

Table 2. Receipt of PBT stratified by preoperative hemoglobin: (A) Overall cohort; (B) Baseline anemia; (C) Normal baseline hemoglobin. Furthermore, timing of PBT for the 115 control and 32 TA-treated patients who received a PBT with RC is depicted in (D)

			P Value
(A) Overall PBT			
	Controls (n = 200)	Received TA (n = 103)	
No PBT	19 (42.5%)	71 (68.9%)	.0001
+PBT	115 (57.5%)	32 (31.1%)	
(B) PBT with preoperative HgB <13.5 mg/dL			
	Controls (n = 92/200)	Received TA (n = 51/103)	
No PBT	19 (20.7%)	26 (51.0%)	.0012
+PBT	73 (79.3%)	25 (49.0%)	
(C) PBT with preoperative HgB ≥13.5			
	Controls (n = 108/200)	Received TA (n = 52/103)	
No PBT	66 (61.1%)	45 (86.5%)	.003
+PBT	42 (38.9%)	7 (13.5%)	

DECREASED TRANSFUSION RISK, REGARDLESS OF PREOPERATIVE Hb



IS TXA SAFE?

- No adverse events attributable to TXA usage
 - In particular:
 - No increased risk of DVT/PE within 30 days of RC ($p=0.52$)
- Caveat = do not use if:
 - Preoperative history of DVT/PE
 - History of cardiac stenting



COMPARATIVE COST ANALYSIS OF TXA

Table 4. Comparative institutional cost data of tranexamic acid and red blood cell transfusion

Resource	Cost [†]
Tranexamic acid*	
Bolus and 5 hour infusion for a 70 kg patient with normal renal function	\$40
Pharmacy handling or overhead	\$227
	\$267
Red blood cell transfusion	
Direct cost of 1 unit	\$270
Overhead cost of 1 unit	\$1034
Compatibility testing	\$125
Administration cost	\$109
	\$1538

* Administered as a 10 mg/kg bolus, then 2 mg/kg/hour maintenance infusion for normal renal function.

† All costs rounded down to nearest dollar.



Enhanced recovery after cystectomy

- ***Post-operative***

- No post-operative nasogastric tube
- Early feeding (gastro-colic reflex)
 - POD 1 – clear liquids
 - POD 2 – general diet
 - Chewing gum/hard candy throughout
- Alvimopan
- Aggressive ambulation
 - 6-8 times daily
- VTE thromboprophylaxis (30 days)



The Question of Alvimopan

Alvimopan Accelerates Gastrointestinal Recovery After Radical Cystectomy: A Multicenter Randomized Placebo-Controlled Trial

Cheryl T. Lee^{a,}, Sam S. Chang^b, Ashish M. Kamat^c, Gilad Amiel^d, Timothy L. Beard^e, Amr Fergany^f, R. Jeffrey Karnes^g, Andrea Kurz^f, Venu Menon^f, Wade J. Sexton^h, Joel W. Slatonⁱ, Robert S. Svatek^j, Shandra S. Wilson^k, Lee Techner^l, Richard Bihrlé^m, Gary D. Steinbergⁿ, Michael Koch^m*

- μ -opioid receptor antagonist
- Among 277 patients randomized to alvimopan vs. placebo
 - Time to GI recovery (5.5 vs. 6.8 days, $p < 0.0001$)
 - Ileus related morbidity (8.4% vs. 29.1%, $p < 0.001$)
 - Length of stay (7.4 vs. 10.1 days, $p = 0.0051$)



Alvimopan Points

- Needs to be started before surgery
 - 12 mg BID
 - Not effective once patients develop ileus
- Should not be used beyond 7 days post-op
- Unclear if there is a cost advantage
 - Bowel-related costs vs. overall costs
- Alone does not equal ERAS
 - Neither 10.1 nor 7.4 day hospitalization is in accord with modern paradigms



Enhanced recovery after cystectomy

- ***Post-discharge***

- Continue VTE prophylaxis 30 days
- Maintain hydration
- Keep in contact
 - Intervene if not progressing
 - Evaluate for readmission rate
 - ET nurse visit
- Audit compliance
 - Understand variance
 - Evaluate new techniques
 - Ensure 'buy-in' from whole team



INSTITUTIONAL PRACTICE CHANGES TO EXTENDED DURATION PROPHYLAXIS

Extended Duration Enoxaparin Decreases the Rate of Venous Thromboembolic Events after Radical Cystectomy Compared to Inpatient Only Subcutaneous Heparin

Joseph J. Pariser,* Shane M. Pearce, Blake B. Anderson, Vignesh T. Packiam, Vivek N. Prachand, Norm D. Smith and Gary D. Steinberg

Extended outpatient chemoprophylaxis reduces venous thromboembolism after radical cystectomy

John Schomburg, M.D., Suprita Krishna, M.B.B.S., Ayman Soubra, M.D., Katherine Cotter, M.D., Yunhua Fan, M.P.H., Graham Brown, M.D., Badrinath Konety, M.D., M.B.A.*

- Extended duration prophylaxis decreased 90-day rate of VTE: 12% → 5% (p=0.024)

- Extended duration prophylaxis decreased 90-day rate of VTE: 17.6 % → 5.06% (p=0.024)
- Multivariable analysis for 90 day DVT: Extended prophylaxis
 - HR 0.22 (95% CI 0.06-0.89) p=0.03

Table 3. Multivariate logistic regression of risk factors for VTE

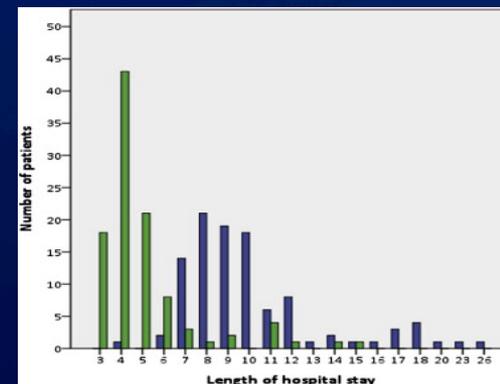
	OR	95% CI	p Value
Enoxaparin (ref: heparin)	0.33	0.14–0.76	0.009
Female (ref: male)	1.10	0.51–2.39	0.802
Neoadjuvant chemotherapy	0.66	0.22–1.97	0.453
CCI (per unit increase)	1.13	0.94–1.37	0.201

- No increase in transfusions
- No increase in hemorrhage



ERAS: Current State

- ERAS is evidenced-based
 - Plethora of data in the literature
 - Within urology, cystectomy is best studied
 - Need for ongoing evaluation, especially of individual features
- Compliance with ERAS associated with:
 - Shorter hospitalization
 - Improved bowel recovery
 - Earlier return to normal activity
 - Similar rate of re-admission
 - Fewer complications
 - Rate of complications inversely associated with compliance with pathway





Barriers to ERAS Implementation

- Majority of RC is performed at low-volume centers
 - Slower adaption of protocols
- Different provider and health care incentives
- Patient perception
 - Not being 'kicked to the curb'
 - Need for ongoing engagement
- Need better evaluation of total costs of care
 - ERAS requires resources
 - Post-discharge requirements beyond readmission



Conclusions

- ERAS represents a continuum of evidence-based care improvements
- Recovery after major surgical procedures can be improved with ERAS pathways
 - Pathways are multifactorial in scope
 - Focus on safe recovery, not just length of stay
 - Require engagement from patients, surgeons, anesthesia and nursing
- Standardized pathways and consistent evaluation of outcomes should be encouraged



Thank you!

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<https://youtu.be/AkX2ipPFipM>

