IMPROVING OUTCOMES IN RADICAL CYSTECTOMY

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Cystectomy: M&M

- 90-day complication rate: 64%- 78%
  - Clavien: 0 (36%), 1-2 (51%), 3-5 (13%)
  - 29% GI, 25% infectious, 15% wound
- 90-day readmission rate: 25-43%
- 90-day mortality rate: 7%-10%

Challenge = Opportunity for Quality Improvement

Shabsigh et al., *Eur Urol* 2009; Stimson et al, *J Urol* 2011

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Improving Outcomes

- Refining Multimodal Therapy
  - Improving utilization of perioperative chemo
  - Development of new agents

- Improving Peri-operative Outcomes
  - Clinical care pathways
  - Refining the role of Robotics
 - Overcoming obstacles to optimal care

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Improving Outcomes

- *Refining Multimodal Therapy*
  - *Improving utilization of perioperative chemo*
  - *Development of new agents*

- Improving Peri-operative Outcomes
  - Clinical care pathways
  - Refining the Role of Robotic Cystectomy
  - Overcoming obstacles to optimal care

Radical Cystectomy

- Cystectomy provides best treatment for localized disease

- Is it possible to improve outcomes with *peri-operative* chemotherapy?

Cystectomy + Chemotherapy

Peri-operative

neoadjuvant

adjuvant

therapeutic
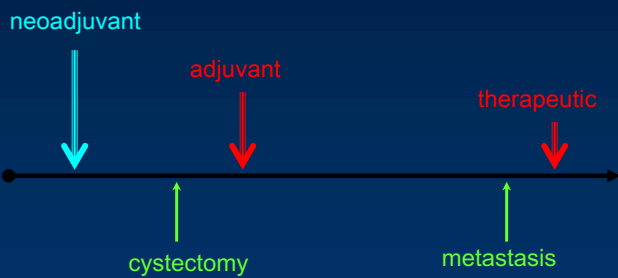
cystectomy

metastasis
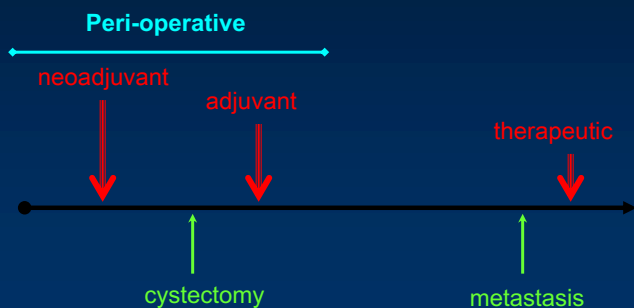
Cystectomy + Chemotherapy

- Rationale for early chemotherapy

  – Early treatment of micrometastatic disease

  – Increased chemosensitivity of small volume tumors

  – Inverse relationship of tumor burden + cure

  – Ascertain chemosensitivity

Cystectomy + Chemotherapy

neoadjuvant

adjuvant

therapeutic

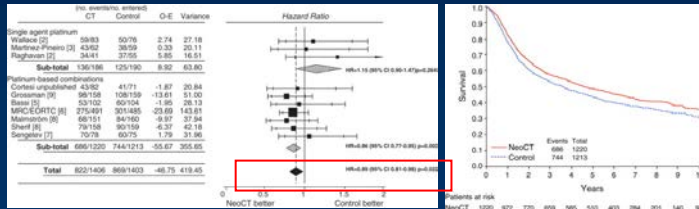cystectomy

metastasis

Neoadjuvant Chemotherapy: Potential Benefits

- Early treatment of occult metastases

- Downstaging primary tumor
  - Pathologic response rates = 60-70%
  - P0 in 25-38% patients
  - *unresectable → resectable*

- Possible to assess response

- Survival benefit

Neoadjuvant Chemotherapy: Meta-analysis

- >3000 pts; 11 RCTs; Cisplatin-based chemo
  - Significant benefit
    - OS (HR 0.86, CI 0.77 - 0.95), p =0.003
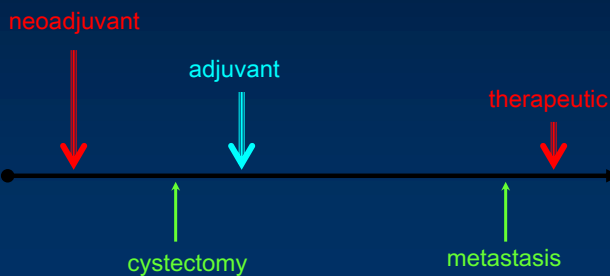   - *5% absolute survival benefit at 5 years*

ABC Collaboration (2005)

Neoadjuvant Chemotherapy

- Platinum-based therapies
  - MVAC, CMV, Gem-cisplat
  - *Carbo is not an effective substitute*

- 3 cycles X 28 days/cycle

- Approx. delay in surgery = 4 months.

Cystectomy + Chemotherapy

neoadjuvant

adjuvant

therapeutic

cystectomy

metastasis

Adjuvant Chemotherapy: Potential Benefits

- Early treatment of occult metastatic disease

- Need for treatment based on pathologic (not clinical) criteria
  - Staging error of cT vs. pT
  - Avoid toxicities in those potentially-cured by surgery

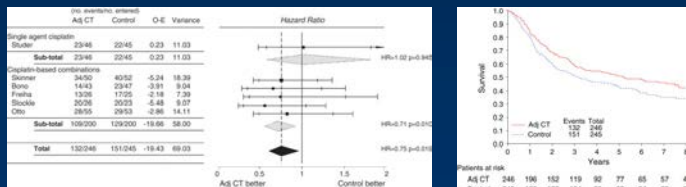- Minimal tumor volume

- ? Survival benefit

Adjuvant Chemotherapy

- Potential Deficits

  - Inability to assess response

  - Enhanced toxicity (after surgery)

  - Delay in receipt of systemic therapy

Adjuvant Chemotherapy: Meta-analysis

- 491 pts; 6 RCTs; Cisplatin-based chemo
  - Significant benefit
    - OS (HR 0.75, CI 0.60 - 0.96), p =0.019
    - *9% absolute survival benefit at 5 years*

ABC Collaboration (2006)

Perioperative Chemotherapy

- Increased use of platinum-based peri-operative chemotherapy
  - 12% (1997-2003) → 30% (2003-2007) per NCDB
  - 2% → 23% in Alberta GU Onc Grp after establishing CPG
- BCAN QoC Survey: n=4541 (Feifer, AUA 2011 #405)
  - 34% (12% NAC, 22% AC); 35% non-Cis-Pt regimens
- Neoadjuvant versus adjuvant – still uncertain
- Need for alternative (less toxic) agents

Radical Cystectomy: 2018

- Refining Multimodal Therapy
  - Improving utilization of perioperative chemo
  - Development of new agents

- *Innovation to improve peri-operative Outcomes*
  - *Clinical care pathways*
  - *Refining the role of Robotics*
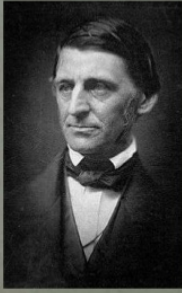 - *Overcoming obstacles to optimal care*

Innovation

- Product innovation
  - e.g. robotics

- Process innovation
  - Care pathways
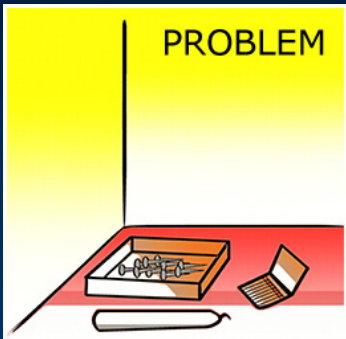 - Telecare, outpatient management, task transfer

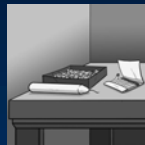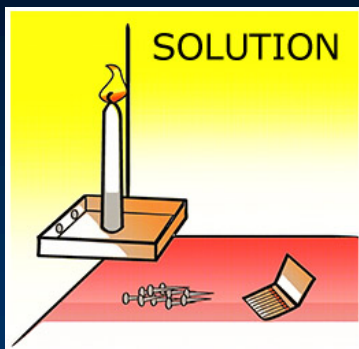"People only see what they are prepared to see..."
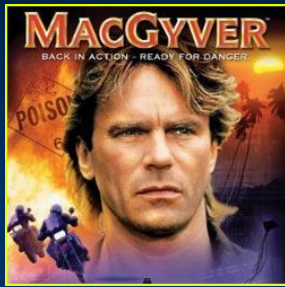*Ralph Waldo Emerson*

The Candle Problem

PROBLEM

Karl Duncker (1945)

SOLUTION

Overcoming Functional Fixedness

Innovation

- Process innovation
  - *Care pathways*
  - Telecare, outpatient management, task transfer

- Product innovation
  - e.g. robotics

Care Pathways

Potential for Clinical Pathways

- Cost reduction
- Improve quality of care / error reduction
- Transparency of treatment
- Staff satisfaction
- Training/education

- *Standardization*

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Cost Reduction

- Most important for decision-makers / administrators
- Focus of much research on CP
- Cost reduction seen for all surgeries
  - Colorectal, hepatic, pancreatic, cardiac, ortho, transplant, bariatric, thoracic, hernia, obstetric, and urologic

Ruchlin (2001)
Chang (2005)
Ronellenfitsch (2008)
Melbert (2005)
Joh (2003)
Rouse (1998)
Jacavone (1999)

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Cost Reduction

- Length of Stay
- OR time
- Parallelization of processes
- Diagnostic tests
- Materials
  - Surgical equipment, meds
- Avoid duplication

Ruchlin (2001)
Chang (2005)
Ronellenfitsch (2008)

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Quality of Care

- Morbidity
  - Decrease pneumonia, nausea, wound infections, overall complications (error reduction)
  - Early NGT removal and feeding
  - Mortality

Lemmens (2008)
Pruthi (2004)
Chang (2001)
Ronellenfitsch (2008)
Pitt (1999)

Transparency of Treatment

- Structure and organization
- Steps in a well-defined continuum
  - Available
  - Documented
  - Evidenced-based
- Physicians, staff, patients

Parker (1999)
Holzbeierlein (2000)
Ronellenfitsch (2008)

Staff Training / Satisfaction

- Education - implementation of structured, evidenced-based approaches
  - Move away from "guild" system
  - Mode of translating scientific evidence to clinical practice in multidisciplinary setting

- CP lead to increased staff satisfaction
- Increased quality of care --> increased staff satisfaction

Goede (1995)
Holzbeierlein (2000)
Ronellenfitsch (2008)

Which cases make sense?

- High volume
- Relatively complex
- Resource intensive
- Potential for variation
- High morbidity

★ *Radical Cystectomy*

Ruchlin (2001)
Ronellenfitsch (2008)
Melbert (2005)

University of North Carolina Clinical Care Pathway for Radical Cystectomy

- Pre-op counseling

  - Probably the most important step
  - Inform about clinical pathway and what to expect
  - Provide pre-op literature regarding peri-operative course
  - Expected hospital stay should be 4 days
    - If you tell them a week they will stay a week

Pruthi (2003)

General Concepts

- Antibiotics
  - 24 hrs peri-operative
  - Start within 1 hr before incision
  - Ertapenem or Ancef/Flagyl

- Cardiovascular
  - Anti-coagulation / anti-platelet therapy
  - Development institutional policy w/ cards and anesthesia

General Concepts

- DVT/PE prophylaxis
  - Early and frequent ambulation
  - TED / SCD
  - SQ Heparin or Lovenox

- Pulmonary
  - IS -- little data to support use, but inexpensive (< $5)

- Multi-modal use of non-narcotic analgesics

Pre-op

- Bowel prep
  - Regular diet all day before; NPO after MN
  - Fleets® enema morning of surgery
  - (no po antibiotics)
- No pre-op admission
- Antibiotics
  - 24 hrs peri-operative - Start within 1 hr before incision
  - Ertapenem or Ancef/Flagyl
  - Pregabalin (Lyrica) 150 mg po
- Alvimopan po
- VTE prophylaxis begun pre-op in holding area
  - Heparin SQ 5000 units

Day of Surgery

- OG removed at end of case
- Use of Exparel 20 mg SQ -- ? Better than bupivicaine ?
- Post-op labs
- DVT/PE - Ambulation; TED/SCD
- Pulmonary - IS
- Pain
  - IV Ketorolac 30mg IV then 15mg IV q 6h X 48h (if renal function OK)
  - (and/or IV Acetaminophen)
  - Pregabalin (Lyrica) 75mg bid
  - IV narcotics (MSO4) prn
- GI
  - PPI until D/C
  - Alvimopan
  - Pro-motility agents - metoclopramide (less N/V)
- Diet -- NPO
- Catheter / drain management

POD #1

- AM labs
- Antibiotics -- peri-op X 24h
- DVT/PE - Ambulation; TED/SCD; *start lovenox or heparin SQ*
- Pulmonary - IS
- Pain
  - Ketorolac
  - Pregabalin (Lyrica) 75mg bid
  - (and/or IV Acetaminophen)
  - IV narcotics (MSO4) prn
- GI -- PPI; metoclopramide; alvimopan; *chewing gum*
- Diet – *clears (irrespective of bowel function)*
- Catheter / stoma / drain management and teaching
- *Discharge planning*

POD #2

- (AM labs prn)
- DVT/PE - Ambulation; TED/SCD (LMWH)
- Pulmonary - IS
- Pain
  - *Convert to po meds (oxycodone/acetaminophen; celecoxib, lyrica)*
  - IV narcotics (MSO4) prn
- GI -- PPI; metoclopramide; stool softener; alvimopan; chewing gum
- Diet -- *clears (irrespective of bowel function)*
- Catheter / stoma / drain management and teaching
- Discharge planning

POD #3

- AM labs
- DVT/PE - Ambulation; TED/SCD (LMWH)
- Pulmonary - IS
- Pain
  - po meds (oxycodone/acetaminophen; celecoxib, lyrica)
  - IV narcotics (MSO4) prn
- GI -- PPI; stool softener; chewing gum
- Diet – *regular diet (irrespective of bowel function)*
- Catheter / stoma / drain management and teaching
- Discharge planning

POD #4

- (AM labs prn)
- DVT/PE - Ambulation; TED/SCD (LMWH)
- Pulmonary - IS
- Pain
  - po meds (oxycodone/acetaminophen; celecoxib, lyrica)
- GI -- PPI; stool softener; chewing gum
- Diet -- regular diet
- Catheter / stoma / drain management and teaching
- Discharge planning
- *? Discharge*

Discharge

- Remove drain (unless leak)
- Meds
  - *Pain meds (e.g. oxycodone/acetaminophen) = #15*
  - *(median use = 10 (+/- 4))*
  - *Pregabalin (Lyrica) 75mg bid X 2 weeks*
  - *Celecoxib 200mg bid X 2 weeks*
  - Stool softener
  - Resume ASA
- *VTE prophylaxis - Lovenox 40 mq SQ X 4 weeks*
- Catheter / stoma teaching
- Home health coordination
- RTC POD #7-10 for stent removal
- (RTC 2-3 wks for cystogram + catheter removal for neobladder)

UNC Experience

	2004-2005	1999-2000	1996-1997
ICU stay (days)	0.0	0.8	1.8
Time (days) to clears	2.0	5.3	6.9
Time (days) to reg diet	3.9	7.9	8.3
Time (days) to D/C	5.1	10.0	11.2
Day of Discharge (%)			
-POD 4-5	79%	0%	0%
-POD 6-7	17%	23%	13%
-POD > 8	4%	77%	87%
Hospital costs	$4290	$10375	$13155
OR costs	$3480	$5069	$6257
Total costs	$7770	$15444	$19412

Evans (2005)

UNC Experience

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Total costs	$7770	$15444	$19412

Summary Points: Clinical Pathways

- Positive effects on:
  - Quality of care
  - Health care costs
  - Education
  - Staff satisfaction
  - Patient expectations
  - Translating scientific evidence to clinical practice

- Encourage more widespread use in urologic surgery
 - Multidisciplinary fashion led by surgeon

Improving Outcomes in Radical Cystectomy

- *Clinical care pathways*
  - *Method to improve outcomes and reduce costs*

- *Role of robotics/minimally-invasive surgery*

Robotic Cystectomy

- Has emerged from growing experience with robotic assisted prostatectomy

- May offer viable alternative to open radical cystectomy in select patients

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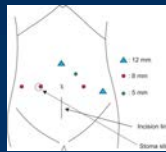## Benefits of Minimally-invasive Surgery
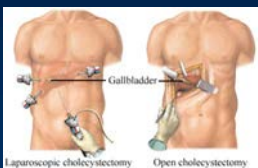
choleycystectomy

nephrectomy

Radical Cystectomy

ORC

RARC

Minimally-invasive Surgery:
Robotic Radical Cystectomy

- Potential benefits
  - Reduced ebl
  - Decreased incision / pain
  - Less fluid imbalances
  - Decreased bowel manipulation

- Potential Concerns
  - Maintain oncological principles
    - Margins, bladder entry, tumor seeding, LN's
  - Prolonged OR times
  - Costs
  - Learning curve

Menon (2004)
Pruthi and Wallen (2006)

UNC Contributions to
Robotic Cystectomy Literature

INTUITIVE

da Vinci®
Radical Cystectomy

Raj S. Pruthi, M.D.
and
Eric M. Wallen, M.D.

University of North Carolina at Chapel Hill

Erik P. Castle · Raj S. Pruthi
Editors

Robotic Surgery
of the Bladder

Springer

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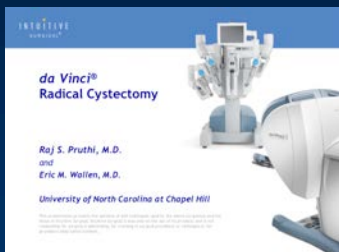
Robotic vs. Open

- **Comparable**
  - Survival – RFS and OS   -- Costs
  - Surgical margin status   -- Long-term QOL
  - Lymph node yield
  -
- **Potential Benefits**
  - EBL   -- Complications
  - Pain   -- LOS
  - Recovery of bowel function

- **Potential Negatives**
  - OR time

Value

$$\uparrow \text{Value} \quad = \quad \frac{\text{EBL/Transfusion, Pain, LOS, Complications}}{\text{OR Time}}$$

No difference for oncologic outcomes, survival, costs, or QOL

Porter (2010)

Summary: Robotic Cystectomy

- Improves patient outcomes – EBL, transfusions, pain, LOS, and complications
- Provides thorough extirpative procedure – preserves oncologic integrity
- Increases in OR time

Adds value to care of patients undergoing radical cystectomy

Future Directions

- Increased worldwide experience
- Long-term oncologic assessment
- Multi-institutional RCT

- *Intracorporeal urinary diversion*

Robotic-assisted Laparoscopic Intracorporeal Urinary Diversion

Pruthi (Eur Urol) (2010)
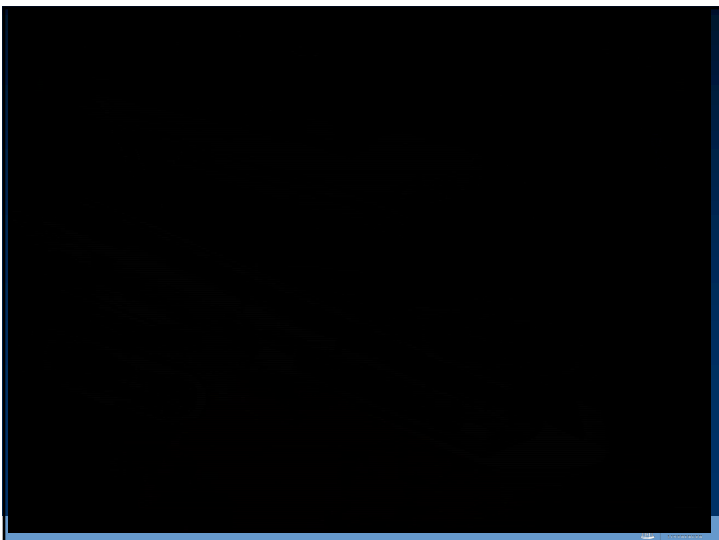
UNC Initial Experience

	IC Diversion (n=40)	EC Diversion (n=40)	p value
Mean EBL (range)	223 (50-400)	266 (50-900)	0.304
Mean OR Time (range)	5.3 hrs (3.9 – 7.3 hrs)	4.2 hrs (3.8 – 4.8 hrs)	< 0.001
Post-op			
-- Mean time to flatus	2.2 d	2.4 d	0.427
-- Mean time to BM	3.1 d	3.3 d	0.762
-- Mean time to DC	4.5 d	5.2 d	0.209
Inpatient narc use (MSO4 eq)	57.6	93.2	0.034
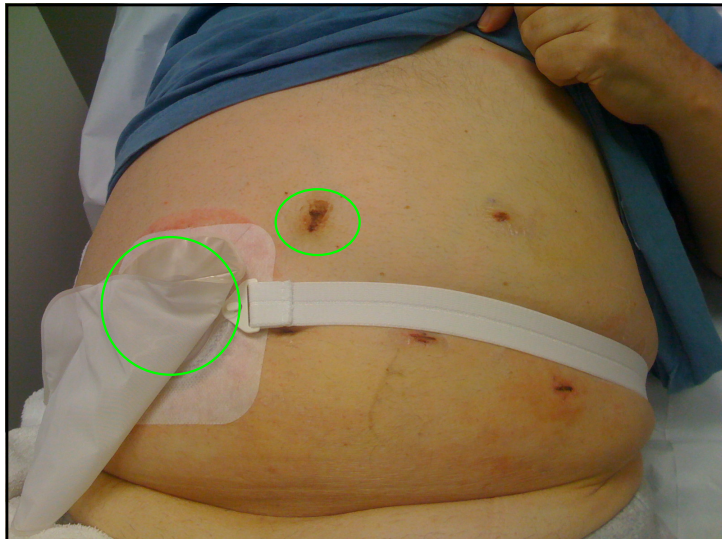
Transvaginal extraction
Via posterior vaginal incision

Improving Outcomes in Radical Cystectomy

- *Clinical care pathways*
  - *Method to improve outcomes and reduce costs*

- *Role of robotics/minimally-invasive surgery*

- *Overcoming obstacles to optimal care*
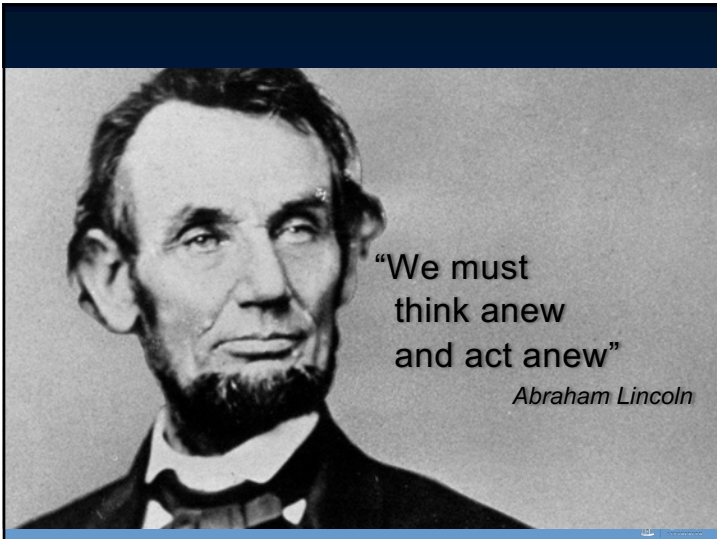
"We must
think anew
and act anew"

Abraham Lincoln

Obstacles to optimal healthcare delivery in bladder cancer

- Travel Distance
- Financial Toxicity
- Nutrition

Obstacles to optimal healthcare delivery in bladder cancer

- *Travel Distance*
- Financial Toxicity
- Nutrition

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Travel Distance

- National trend toward regionalization of health care and major surgery such as cystectomy
- Recent studies indicate an association between high-volume centers & improved post-op outcomes for major surgery
- Spurred interest in association of patient travel distance on cystectomy care and outcomes.

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Background

- 90-day complication rate = 64 - 78%
- Population-based estimates of readmissions following cystectomy range from 25-43%

Readmission rates by disease site
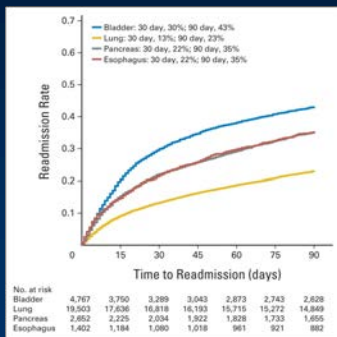
Stitzenberg et al. JCO 2015;33:455-464

K-M estimates of survival by readmission group for (A) bladder cancer, (B) lung cancer, (C) pancreas cancer, and (D) esophagus cancer.
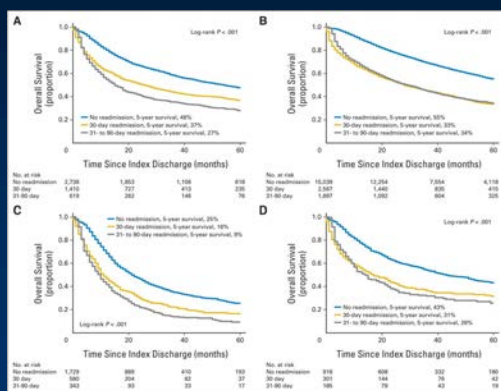
Stitzenberg et al. JCO 2015;33:455-464

Background

- 30% of bladder cancer re-admissions are to a different hospital
  - More likely later, lower socioeconomic status, through the ED, and for medical DRGs
  - Decreased survival (HR 1.35)
  - Only 8% transferred – majority to index hospital

- The relationship between distanced traveled for surgery and risk of readmission and complications remains unclear

Question

How does distance traveled for surgery affects risk of readmissions and other outcomes following radical cystectomy for bladder cancer.

Methods

- Using linked data resource combining North Carolina Cancer Registry with administrative claims data from Medicare, Medicaid, and private insurance
  - Integrated Cancer Information and Surveillance System (ICISS)
- Included adult patients diagnosed with bladder cancer from 2003−2010 who received RC.
- Complications coded and grouped based on previously published standards*
- Travel distances calculated using straight-line distance between patient zip code & cystectomy provider

* Konety et al., Birkmeyer et al., Hollenbeck et al.

Results

- 735 cystectomy patients for bladder ca.
  - n = 171 (23%) readmitted within 30 days
  - n = 156 (21%) readmitted between 31-90 days

- Mean age higher among readmitted, but not statistically significant

- No significant differences in readmission
  - race, gender, pathology stage, neoadjuvant chemotherapy, discharge to SNF comorbidity status, or complication type.

Results

Distance & 30-day readmission at different hospital

| Characteristic		30-day Readmission into different Hospital		P-Value
	Total (N = 171)	No (N = 107)	Yes (N = 64)	
Distance <= 30 miles	75 (44%)	56 (52%)	19 (30%)	0.004
Distance > 30 miles	95 (56%)	51 (48%)	45 (70%)	

Distance & 31-90-day readmission at different hospital

Characteristic		31-90-day Readmission into different Hospital		P-Value
	Total (N = 156)	No (N = 80)	Yes (N = 76)	
Distance <= 30 miles	77 (49%)	53 (66%)	24 (32%)	<0.001
Distance > 30 miles	79 (51%)	27 (34%)	52 (68%)	

Multivariable Analysis:
Predictors of 30-day readmission

Variable		Odds Ratio	95% CI	p-value
Distance between residence & cystectomy provider (Ref <=30mi)	>30 miles	1.27	1.05, 1.54	0.014
Gender (Ref = Male)	Female	0.96	0.76, 1.20	0.707
Race (Ref = Non-white)	White	1.17	0.81, 1.67	0.402
Age (Ref = 65-74)	19-64	1.05	0.72, 1.54	0.798
	75+	1.06	0.78, 1.43	0.706
Pathologic Stage (Ref = T0-T2)	Ta-Tis-Tx	0.88	0.62, 1.25	0.480
	T3-T4	0.98	0.70, 1.37	0.892
	Missing	1.02	0.62, 1.68	0.931
Major complication	Yes	0.89	0.73, 1.08	0.245
Distance to SNF	Yes	0.74	0.50, 1.08	0.116
Imaging during Initial Hospitalization	Yes	1.05	0.77, 1.42	0.769
Neoadjuvant chemotherapy	Yes	1.35	0.93, 1.97	0.114
Length of stay < = 7 days	Yes	0.91	0.73, 1.13	0.394
Comorbidity (Ref = 0)	1	1.16	0.94, 1.43	0.180
	>=2	0.98	0.68, 1.41	0.924
Insurance type (Ref = Medicare)	Private	0.97	0.68, 1.39	0.870
	Medicaid	1.06	0.69, 1.64	0.788

Results

Survival Curve By Readmission Into Different Hospital
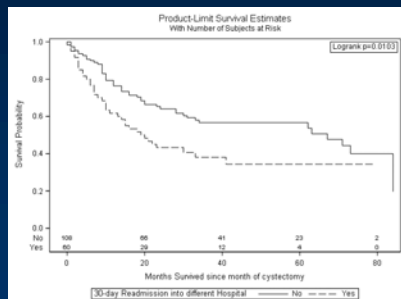
< 30d re-admission to a different hospital has lower survival probability

Conclusions

- Longer travel distance to a cystectomy provider is associated with higher 30-d readmission rates, readmission to a different hospital (closer to home), and worse survival

- Travel distance may indeed be a barrier to high quality care

Conclusions

- Patients with longer travel distance may benefit from shorter and more frequent follow-up via phone, virtual post-op check, and PCP visits.

- Highlights need for better care coordination between index hospital and surrounding hospitals

Future Directions

- Identify and compare early and late post-operative complications.

- Explore reasons for underlying disparities between outside versus index hospitals – which can be managed by outside and which should be transferred

Obstacles to optimal healthcare delivery in bladder cancer

- Travel Distance
- *Financial Toxicity*
- Nutrition

The burden of cancer isn't just cancer

By Carolyn Y. Johnson April 8

(Rachel Orr/The Washington Post)

Introduction

- Financial Toxicity - "an adverse financial condition as a consequence of medical treatment"

- Cancer patients are 2.7X more likely to declare bankruptcy than those without cancer (even higher for younger cancer patients).

Ramsey et al, Health Affairs (2013)

Financial Toxicity

- 13 percent of non-elderly patients with cancer spend at least a fifth of their income on treatment.

- Medicare cancer patients spent an average of $4,727 of their own money on health care -- about $1,000 more than people without cancer.

Davidoff et al, Cancer (2013)   Bernard et al, JCO (2011)

Financial Toxicity

- Of the 20 million cancer survivors evaluated, 29 percent reported financial burden of some kind
  – Bankruptcy to borrowing money to not being able to pay for medical visits.

- Among those reporting FT, 86% _**had**_ health insurance

Hrishikesh et al, Cancer (2014)

Financial Toxicity

- *Is FT a health issue - does it affect QOL? Survival? Were people skipping doctor's visits, drugs or other treatments?*

- A copay of $50 a month kept nearly a fifth of patients from continuing to fill prescriptions for TKI therapy for CML.

- For oral TKIs, patients more likely to stop or delay drug therapy as the portion they paid increased.
  – 13-20% increase stopping/delaying use per $10 increase in OOP costs

Dusetzina JCO (2014)   Kaisaeng et al, JMCP (2014)

Financial Toxicity

- Half of insured cancer patients cut spending on food and clothing or dipped into savings to pay for their treatment.
  - Majority cut back on leisure activities
  - Three-quarters received financial assistance with their drug copayments.

Zafar et al, The Oncologist (2013)

Financial Toxicity

- Cancer patients who declared bankruptcy are 1.8X likely to die (any cause) (HR = 1.79) than cancer patients who didn't declare

  - Highest for colorectal (HR= 2.47) and prostate (HR=2.07)
  - More likely to be younger, female, and non-white, to have local- or regional- (v distant-) stage disease at diagnosis
  - Mean age was 53.0 years, men (54%), mean income $49,000, and white (86%), married (60%), and urban (91%) and had local- or regional-stage disease at diagnosis (84%)

Ramsey et al, JCO (2016)

Financial Toxicity and Bladder Cancer

- GU malignancies require expensive treatments and long-term surveillance

- Bladder cancer is estimated to be the most expensive cancer from diagnosis to death

- The effect of Financial Toxicity on GU malignancies has not been well defined

Methodology

- UNC Health Registry/Cancer Survivorship Cohort

- 144 bladder cancer patients enrolled; 138 completed baseline questionnaire

- Patients surveyed via phone within 2 weeks of enrollment

Methodology

- Financial Toxicity (FT) defined as agreement with the statement "you have to pay more for medical care than you can afford" via PSQ - 18

- HR-QOL measured using FACT-G, FACT-BI and PROMIS questionnaires

Patient Demographic Characteristics

		N = 138 (%)
Age (years)	<56	22 (15.9%)
	56-72	68 (49.3%)
	>72	48 (34.8%)
Gender	Female	34 (24.6%)
	Male	104 (75.4%)
Race	Black	14 (10.1%)
	Hispanic	1 (0.7%)
	White	123 (89.1%)
Bladder Cancer Clinical T Stage	Non-invasive (Tis, Ta, T1)	69 (51.1%)
	Invasive (T2-T4)	66 (48.9%)
Financial Toxicity	Yes	33 (24%)
	No	105 (76%)

Patient Characteristics and Financial Toxicity

		Overall N= (%)	Financial toxicity N= (%)	No Financial toxicity N= (%)	p-value
Age (yrs)	<56	22 (15.9%)	10 (45.5%)	12 (54.5%)	<.0001
	56-72	68 (49.3%)	21 (30.9%)	47 (69.1%)	
	>72	48 (34.8%)	2 (4.2%)	46 (95.8%)	
Gender	Female	34 (24.6%)	8 (23.5%)	26 (76.5%)	1.000
	Male	104 (75.4%)	25 (24.0%)	79 (76.0%)	
Race	Black	14 (10.1%)	8 (57.1%)	6 (42.9%)	0.005
	Hispanic	1 (0.7%)	0 (0.0%)	1 (100.0%)	
	White	123 (89.1%)	25 (20.3%)	98 (79.7%)	
BMI (kg/m^2)	<18.5	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.554
	18.5-24.9	41 (29.7%)	8 (19.5%)	33 (80.5%)	
	25-29.9	52 (37.7%)	11 (21.2%)	41 (78.8%)	
	30-34.9	24 (17.4%)	8 (33.3%)	16 (66.7%)	
	>35	21 (15.2%)	6 (28.6%)	15 (71.4%)	

Patient Characteristics and Financial Toxicity

		Overall	Financial toxicity	No Financial toxicity	p-value
Marital Status	Single	14 (10.2%)	3 (21.4%)	11 (78.6%)	0.949
	Married/Living with partner	95 (69.3%)	22 (23.2%)	73 (76.8%)	
	Divorced/Separated/Widowed	28 (20.4%)	7 (25.0%)	21 (75.0%)	
Education	Eighth grade or less	4 (2.9%)	1 (25.0%)	3 (75.0%)	0.014
	Some high school	9 (6.5%)	4 (44.4%)	5 (55.6%)	
	High school degree/GED	45 (32.6%)	13 (28.9%)	32 (71.1%)	
	Some college or Technical school	33 (23.9%)	11 (33.3%)	22 (66.7%)	
	Some graduate/masters	28 (20.3%)	4 (14.3%)	24 (85.7%)	
	Completed postgraduate/Professional	19 (13.8%)	0 (0.0%)	19 (100.0%)	
Bladder Cancer Clinical T Stage	Non-invasive (Tis, Ta, T1)	69 (51.1%)	48 (69.6%)	21 (30.4%)	0.042
	Invasive (T2-T4)	66 (48.9%)	56 (84.8%)	10 (15.2%)	

Patient Quality of Life and Financial Toxicity

	Overall Mean (SD)	Financial toxicity, Mean (SD)	No Financial toxicity, Mean (SD)	p-value
FACT-GP[1], Total score	79.4 (18.3)	72.2 (21.4)	81.5 (16.7)	0.01
FACT-GP[1], Physical well being	22.3 (5.3)	20.3 (5.7)	23.0 (5.0)	0.01
FACT-GP[1], Social/family well being	20.6 (5.8)	19.2 (6.6)	21.1 (5.5)	0.11
FACT-GP[1], Emotional well being	19.2 (5.0)	18.3 (5.3)	19.5 (4.9)	0.21
FACT-GP[1], Functional well being	17.1 (8.0)	14.6 (9.2)	17.8 (7.5)	0.05
FACT-BL[2], Bladder cancer specific	33.3 (6.6)	32.4 (7.5)	33.5 (6.3)	0.41
PROMIS[3] Global Physical Health T-Score	46.4 (9.8)	43.2 (11.2)	47.4 (9.2)	0.03
PROMIS[3] Global Mental Health T-Score	49.9 (9.7)	45.5 (10.0)	51.3 (9.3)	<0.01

[1]FACT-GP: Functional Assessment of Cancer Therapy- General Population
[2]FACT-BL: Functional Assessment of Cancer Therapy- Bladder Cancer
[3]Patient-Reported Outcomes Measurement Information System

Observations

- 24% of bladder cancer patients endorsed FT

- Younger patients more likely to experience FT; may be related to Medicare Eligibility

- Increased prevalence of FT among
  - African Americans
  - those with less education

Observations

- Higher rates of FT among patients with non-invasive disease
  - Frequency and length of surveillance
  - Expensive surveillance procedures

- FT negatively associated with physical, functional and mental health-related QoL

Next Steps

- Does FT effect healthcare adherence?
- Does FT have an effect of mortality?
- When and how does FT develop?
- What is the prevalence of FT in other GU malignances?
- What strategies can be put in place to limit the development of FT?

What are the obstacles to optimal healthcare delivery in bladder cancer?

- Travel Distance
- Financial Toxicity
- *Nutrition*

Nutritional Deficiency

- Inadequacy of nutrients in tissues; result of inadequate dietary intake or impairment of digestion, absorption, transport, or metabolism.

Nutritional Deficiency

- Elderly at increased risk for nutritional deficiency
  - Mean age of bladder cancer patient = 73 years

- 40-80% of cancer patients are Nutritionally Deficient

- *Elderly cancer patient are at particularly high risk*

Anecdotal Case

- 70 year-old male presented with bladder cancer
- Complaints of "bad taste" and weight loss in preceding months before surgery (cystectomy)
- Postoperative course was complicated wound problems, readmission, prolonged stay, and need for IV nutrition (TPN)

Could this have been prevented by a preoperative evaluation and intervention?

Nutrition & Surgery

- Nutritional deficiency is a well-known risk factor for complications in surgery patients
  - Infections
  - Poor wound healing
  - Mortality
  - Decreased overall survival

- Several studies have demonstrated correlation between malnutrition and high clinical and economic effect
  - Increased morbidity
  - Prolonged hospital stay
  - Substantial increased cost of healthcare
  - Increased mortality

Urology & Nutrition

- Urologic surgery represents an exceptional position in surgery

- Many patients who undergo a major procedure are ≥ 70 years

- Using NRS-2002 tool, patients ≥70 who undergo major surgery will have a score ≥3 (at risk of malnutrition), independent of other factors.

- Malignancy is another risk factor

Terry & Bueschen, 1986

- Retrospective review of 69 radical cystectomies
- Preop nutritional status assessed by WBC & serum albumin
- 75% with severe nutritional depletion had severe complications

COMPLICATIONS OF RADICAL CYSTECTOMY AND
CORRELATION WITH NUTRITIONAL ASSESSMENT

WILLIAM J. TERRY, M.D.
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Recent Studies

- 2011 (Gregg et al)
  – 103 of 538 (19%) met criteria for ND
  – 90-day mortality 16% ND vs. 5% non-ND
  – Overall survival at 3 years was 44% for ND vs. 68% for non-ND

- 2013 (Johnson et al)
  – Analysis of 1092 cystectomy patients in NSQIP
  – Low albumin was strongest predictor of complications

- 2014 (Smith et al)
  – Sarcopenia (muscle wasting) measured on CT scan
  – Predictor of complications and trend towards 2-yr survival

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Assessment of Nutritional Status

- Not straightforward
- No standardized definition of nutritional depletion
- Traditional markers of nutritional status
  – Weight
  – Serum albumin
  – Pre-albumin
  – CRP
  – Immune competence
  – Appetite, GI symptoms, energy level, loss of SQ fat, muscle wasting, edema, ascites
  – Hand-grip strength
  – Nutritional Indices

Nutrition Markers

- Ideally should consider multiple factors:
  - Patient's physiologic requirements
  - Nutritional intake
  - Functional Status
  - Body composition

- Ideal nutritional marker:
  - Sensitive enough to identify alterations in early stage
  - Specific enough to modify only due nutritional imbalances
  - A nutritional intervention would correct its alteration
  - Correction of its levels would result in a better outcome

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Albumin

- Albumin
  - Hepatic protein, 60% of plasma proteins
  - 20-day half-life – marker of chronic malnourishment
  - Negative acute phase reactant

- Hypoalbuminemia – non-specific
  - Liver disease, nephrotic syndrome, burns, protein-losing enteropathy, malignancy, malnutrition
  - May be better surrogate of disease state

Nutritional Indices

- Absence of a single gold standard objective measure has led to nutritional indices

  - Nutritional Risk Index & Maastricht Index
  - Mini Nutritional Assessment
  - Malnutrition Universal Screening Tool
  - Nutritional Risk Index-2002
  - Patient-Generated Subjective Global Assessment (PG-SGA)

Malnutrition Universal Screening Tool

- http://www.bapen.org/uk/pdfs/must/must_full.pdf

Interventions:
Role of Patient and Referring MD

- Arguably play the most important role in nutrition

- Provides the largest window between diagnosis and surgical therapy

- Nutrition optimization needs to begin at time of diagnosis to provide the most impact

UNC

Nutrition Supplementation

- Encourage nutrition supplementation
  - Boost
  - Ensure
- Daily multivitamin
- Referral to dietitian/nutritionist
- Exercise program

UNC

A quick word about other preoperative factors…

- Smoking cessation
- Weight loss in obese patients
- Exercise/Prehab

Prehab FOR PHYSICAL OPTIMIZATION

UNC

UNC Cystectomy Nutrition Protocol

Visit 1 – at initial consultation in MDC (+ FU at time of pre-op if NAC)
- All patients seen by RD in adjoining clinic
- Patient-Generated Subjective Global Assessment (PG-SGA)
- Labs (at visit and repeat at pre-op)
  – *Prealbumin*
  – *CRP*
  – *Albumin*

UNC Cystectomy Nutrition Protocol

Visit 1 (cont'd)
- Preoperative diet optimization & possible carb loading
  – e.g.
    - Prealbumin <18mg/dL → check nitrogen balance preop, increase protein to >1.5 gm/kg/d
    - If prealbumin is <18mg/dL with negative nitrogen balance, increase protein to 1.8-2gm/kg/d
    - Recheck in 2-3 weeks
- Receive nutrition packet with individual protein recommendations, meal plans, protein lists, protein loading,

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UNC Cystectomy Nutrition Protocol

Visit 2 – In-patient after cystectomy
  – RD consult on POD #3
  – Reiterate home recommendations & decide on improvements for nutrition
  – Multivitamin use (i.e. zinc deficiency relates to possible taste alterations?)

Visit 3 - Post-operative Visit (2-3 weeks postop)
  – Further review of recommendations and improvements

UNC Cystectomy Nutrition Protocol

Visit 4 – Post-operative FU (3 months) (optional)
- Repeat ND assessment
- Further review of recommendations and improvements
- Labs
  - _Prealbumin_
  - _CRP_
  - _Albumin_

Conclusion

- Malnutrition is an important risk factor for all patients undergoing urologic surgery

- Multiple nutrition assessment indices exist
  - PG-SGA

- Further nutrition studies are needed identify malnutrition and best source of nutrition

- Need to identify and intervene early
  - Diet, exercise, other health-related behaviors

Radical Cystectomy: 2019

- Refining Multimodal Therapy
  - Improving utilization of perioperative chemo
  - Development of new agents

- _Innovation to improve peri-operative Outcomes_
  - _Clinical care pathways_
  - _Refining the role of Robotics_
  - _Overcoming obstacles to optimal care_

Improving Outcomes

- Increasing number of patients with invasive / advanced disease
  - Aging population = more bladder cancer
  - Referral practices: ad hoc regionalization
  - Reimbursement environment: QI

- *Need for Innovation in the treatment of bladder cancer patients to improve outcomes*

Future Directions

- Optimizing patient
  - Nutrition
  - Pre-hab
- Better care coordination (role of travel distance)
- Financial toxicity
- mHealth

At home PROs

- Structured patient phone calls by APP
  - question categories: symptoms, emotional/social, functional assessment.
  - Weekly < 30 days; bi-weekly 30-90 days

- Reduced ER visits and re-admissions
- High patient satisfaction
- *Improved communication*

Smith et al (2017)

mHealth

- Address preventable complications / re-admissions Use of HIT – e.g. mobile health (mHealth)
- Tracks PROs and allows real-time feedback via internet-enabled devices

mHealth

- Patient-centered care
- Increase quality
- Timely intervention of complications (UTIs, dehydration, fevers)
- High patient satisfaction
- Reduce morbidity, healthcare utilization (costs/penalties), death

Improving Outcomes

- Increasing number of patients with invasive / advanced disease
  - Aging population = more bladder cancer
  - Referral practices: ad hoc regionalization
  - Reimbursement environment: QI

- *Need for Innovation in the treatment of bladder cancer patients to improve outcomes*

"*The fundamental problem with the quality of American medicine is that we've failed to view delivery of health care as a science.*"

- Peter Pronovost MD