

Research Article

Impact of inflammatory bowel disease on radical prostatectomy outcomes and costs of care



Ilana P. Goldberg^a, Steven L. Chang^b, Shilajit D. Kundu^c, Benjamin I. Chung^d,
Eric A. Singer^{e,*}

^a Tufts University School of Medicine, USA

^b Division of Urology, Brigham and Women's Hospital, Boston, MA, USA

^c Department of Urology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

^d Department of Urology, Stanford University Medical Center, Stanford, CA, USA

^e Section of Urologic Oncology, Rutgers Cancer Institute of New Jersey and Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, USA

ARTICLE INFO

Article history:

Received 8 August 2020

Received in revised form

13 August 2020

Accepted 20 August 2020

Available online 3 September 2020

Keywords:

Crohn's disease

Inflammatory bowel disease

Prostate cancer

Radical prostatectomy

Ulcerative colitis

ABSTRACT

Background: Recent studies suggest an association between prostate cancer and inflammatory bowel disease (IBD). Our objectives were to investigate clinical and financial impacts of IBD on radical prostatectomy (RP) and to determine the impact of surgical approach on our findings.

Methods: The Premier Hospital Database was queried for patients who underwent RP from 2003 to 2017. Multivariable logistic regression models were used to determine the independent impact of IBD on complications and readmission rates. We determined 90-day readmissions and examined 90-day hospital costs adjusted to 2019 US dollars with multivariable quantile regression models.

Results: Our study population included 262,189 men with prostate cancer, including 3,408 (1.3%) with IBD. There were higher odds for any complication for IBD patients compared with non-IBD controls for RP (15.64% vs. 10.66%). Patients with IBD had overall complication rates of 14.1% ($P < 0.05$) for open surgery and 17.2% for minimally invasive surgery (MIS) ($P < 0.01$). Between 2013 and 2017, the IBD cohort had significantly more complications (odds ratios (ORs): 2; 95% confidence interval (CI): 1.5 to 2.67; $P < 0.0001$), was more likely to have surgical costs in the top quartile (OR: 1.6; 95% CI: 1.23 to 2.1; $P < 0.01$), and had higher readmission rates (OR: 1.51; 95% CI: 1.1 to 2.06; $P = 0.01$).

Conclusions: The IBD cohort who underwent MIS had the highest complication rates. Hospital readmissions and surgical costs were significantly higher for the IBD cohort who underwent RP between 2013 and 2017, when a minimally invasive approach was more prevalent than an open approach. These findings may be important when deciding which surgical approach to take when performing RP on men with IBD.

© 2020 Asian Pacific Prostate Society. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Inflammatory bowel disease (IBD), which is comprised of Crohn's disease and ulcerative colitis, is estimated to affect 1.3% of US adults [1, 2]. This percentage has steadily increased in industrialized countries and is projected to increase further [3]. As these are chronic conditions, it is reasonable to expect that patients with IBD will undergo surgery for other health problems within their

lifetimes. However, there is a significant knowledge gap regarding the impact of IBD on surgical outcomes and the cost of care.

Prostate cancer has the highest incidence amongst all cancers in men, with one in eight men predicted to develop it in the course of their lives [4]. Therefore, it is reasonable to assume that many men with IBD will also develop prostate cancer. In fact, Burns et al [5] recently demonstrated an increased risk of prostate cancer in men with a history of IBD using a retrospective, matched-cohort study model. They postulated this to be a result of the heightened inflammatory state in people with IBD leading to inflammation of the prostate with subsequent development of carcinoma. Ge et al [6] performed a meta-analysis of nine studies and also demonstrated an elevated risk of prostate cancer in patients with ulcerative

* Corresponding author. Section of Urologic Oncology, Rutgers Cancer Institute of New Jersey, 195 Little Albany Street, New Brunswick, NJ, 08903, USA
E-mail address: eric.singer@rutgers.edu (E.A. Singer).

colitis. Given this link, our study aimed to quantify the risk of complications in the perioperative period for patients with IBD with prostate cancer undergoing radical prostatectomy (RP). This is especially important because patients with IBD are generally steered away from radiotherapy when diagnosed with prostate cancer, thus making surgery the favored treatment modality [7, 8].

Urologists have transitioned from an open retro-pubic approach to minimally invasive surgery (MIS) for RP in recent years. The minimally invasive approach consists of laparoscopic surgery, both with and without robotic assistance, although the intraoperative approach is similar [9]. Studies have found comparable effectiveness and postoperative complications between these different modalities in a normal cohort [10, 11]. However, to the best of our knowledge, the impact of this transition on patients with IBD undergoing RP has never been investigated. Our study is therefore the first to do so.

We hypothesized that patients with IBD would have higher rates of perioperative complications, readmissions, and higher operative costs than a non-IBD cohort for RP because of the chronic inflammation associated with IBD. Specifically, we hypothesized that a minimally invasive approach would be associated with worse outcomes because of intra-abdominal entry versus an extraperitoneal open approach.

2. Materials and Methods

2.1. Data source

Data were extracted from the Premier Hospital Database (Premier Inc., Charlotte, NC), a nationally representative hospital-based dataset. It contains data from approximately 1000 nonfederal academic and nonteaching hospitals, representing approximately 25% of annual inpatients in the United States. There is a unique patient identifier that allows for longitudinal tracking of patients. Thus, length of stay, cost information, and readmission data are collected over a 90-day period. Because patients are deidentified, our study was institutional review board-exempt [12].

2.2. Study cohort

We included all patients who underwent RP from January 1, 2003 to December 31, 2017, with International Classification of Disease, Ninth Revision (ICD9 60.5, 60.62, 60.69) and Tenth Revision (ICD10 OVO0ZZ, OV04ZZ, OV07ZZ, OV08ZZ). We included patients who had an associated diagnosis of prostate cancer (ICD9 185, ICD10 C61). To control for potential confounds, we examined patient characteristics including age, race, marital status, insurance status (Medicare, Medicaid, managed care, commercial, or other), hospital characteristics including type (teaching vs. nonteaching), location (urban vs. rural), and surgical approach (open vs. minimally invasive). To account for baseline health status, we calculated the Charlson Comorbidity Index based on administrative codes [13].

2.3. Outcomes

The primary outcome was 90-day postoperative complications, which was assessed based on Clavien-Dindo classification [14] and organ systems [15]. Minor complications were considered Clavien-Dindo Grades I and II, and major complications were considered Clavien-Dindo Grades III, IV, and V. Secondly, we also calculated 90-day direct hospital costs adjusted to 2019 US dollars and determined 90-day readmissions. For costs, we identified patients who had a high cost hospitalization, defined as the top quartile of cost.

2.4. Statistical analysis

Descriptive statistics were used to evaluate the clinical, demographic, surgical, and hospital characteristics for the study cohort. Pearson's chi-square test was used for categorical variables. The cohort was divided into time periods (2003-2007, 2008-2012, and 2013-2017) to reflect the changing surgical approach during the study period, and we performed trend analysis using Pearson's correlation. Multivariable logistic regression models were used to determine the independent impact of IBD on complication and readmission rates, adjusting for the variables listed in Table 1. Hospital costs were examined with multivariable quantile regression models. We adjusted for hospital clustering and applied sampling weights to achieve a nationally representative analysis as previously described [16]. Statistical significance was determined with an alpha level of less than 0.05 being statistically significant. All data analysis was performed with Stata 15.1 (College Station, TX).

3. Results

3.1. Study cohort

The weighted study population consisted of 262,189 patients, of which 3,408 (1.3%) patients had a history of IBD. Hospital and surgical characteristics are also presented in Table 1. An open surgical approach accounted for 46.9% of RP among patients with IBD and 35% for patients without IBD.

Table 1
Patient, hospital, and surgical characteristics.

	Radical prostatectomy		p
	No IBD n = 258781 (98.7%)	IBD n = 3408 (1.3%)	
Patient characteristics			
Age (years)			0.26
<45	1%	0.4%	
≥45 to 55	15.1%	16.9%	
≥55 to 65	45%	43.8%	
≥65 to 75	36%	34.6%	
≥75	2.9%	3.8%	
Race (%)			<0.001
White	73.8%	81.5%	
Nonwhite	26.2%	18.5%	
Marriage (%)			0.93
Married	28.9%	28.5%	
Not married	71.1%	71.5%	
Charlson Comorbidity Index (%)			0.005
0 to 1	84.4%	79.2%	
2 to 3	12.6%	16.9%	
≥4	3%	4%	
Insurance status (%)			0.08
Medicare	33.8%	36.2%	
Medicaid	1.7%	1.6%	
Managed care	51.4%	46.9%	
Commercial	8.7%	11.5%	
Other	4.4%	3.5%	
Hospital characteristics			
Teaching Hospital (%)			0.35
No	38.9%	43.8%	
Yes	61.1%	56.2%	
Urban (%)			<0.001
No	2.5%	6.7%	
Yes	97.5%	93.1%	
Surgical characteristics			
Surgical approach (%)			<0.001
Open	35%	46.9%	
Minimally invasive	65%	53.1%	

IBD, inflammatory bowel disease.

3.2. Trends in Surgical Approach and Outcomes

Fig. 1 presents trends in surgical approaches for patients with IBD. MIS accounted for 27% of RP in 2013 and 72% by 2017 (Fig. 1). Table 2 presents the odds for the outcomes of 90-day postoperative complications, high cost surgery, and readmission among patients with IBD and patients without IBD who underwent prostate surgery between 2003 and 2017. In the earliest time period (2003 to 2007), there were no statistically significant differences between the non-IBD and the IBD cohorts in complication rates, the odds of high cost surgery, and readmissions. From 2008 to 2012, there was a trend for greater minor complications among patients with IBD (odds ratio [OR]: 1.43; 95% confidence interval [CI]: 0.95 to 2.14; $P = 0.08$), whereas there was no difference for major complications, high cost surgery or readmissions between the two groups. In the most recent time period (2013 to 2017), patients with IBD were consistently more likely to experience a postoperative complication, which was true for minor complications (OR: 1.73; 95% CI: 1.24 to 2.41; $P < 0.01$) and major complications (OR: 2.56; 95% CI: 1.63 to 4.03; $P < 0.01$). Corresponding to the increased complication rate, patients with IBD had significantly higher odds for high cost surgery (OR: 1.6; 95% CI: 1.23 to 2.1; $P < 0.01$) and readmission (OR: 1.51; 95% CI: 1.1 to 2.06; $P = 0.01$).

3.3. Interaction of IBD and surgical approach for complications

Fig. 2A depicts the interaction between IBD status and surgical approach with respect to postoperative complications in our study cohort based on predicted probabilities from our multivariable model. In general, the IBD cohort consistently had higher rates of overall complications, minor complications, and major complications than the non-IBD cohort irrespective of the surgical approach. Although patients without IBD had comparable overall complications rates for both surgical approaches, which were approximately 10% ($P = 0.73$), patients with IBD had overall complication rates of 14.1% ($P < 0.05$) for open surgery and 17.2% for MIS ($P < 0.01$). When specifically examining minor and major complications, the same pattern was observed though the only group achieving a statistically significant difference was the IBD cohort undergoing MIS.

3.4. Complications by system

Fig. 2B shows postoperative complications for patients who underwent a major surgery for urologic cancer. Compared with patients without IBD, patients with IBD who underwent RP had significantly more hematologic (0.8% vs 0.1%; $P < 0.0001$), gastrointestinal (3.4% vs 1.7%; $P < 0.01$), infectious (1.4% vs 0.6%; $P = 0.01$), pulmonary (3.0% vs 1.2%; $P < 0.01$), renal (3.3% vs 1.9%; $P = 0.02$), and venous thromboembolic (VTE) (1.0% vs 0.1%; $P < 0.0001$). Although not significant, neurologic (0.7% vs 0.3%; $P = 0.06$) and

surgical (1.2% vs 0.6%; $P = 0.07$) complications also trended toward higher complication rates in the IBD cohort (Fig. 2B).

4. Discussion

This nationally representative contemporary study of RP in the United States reveals that men with IBD experience more surgical complications, higher cost surgery, and more frequent readmissions compared with patients without IBD (Table 2). Our analysis suggests this discrepancy in surgical outcomes was mostly attributed to the use of MIS approach, which supports our hypothesis that transperitoneal surgery places patients with IBD at a unique risk resulting in worse outcomes. Not only did patients with IBD experience more bowel complications but also had increased complications across multiple systems including pulmonary, renal, infectious, and vascular.

When analyzing the trends for outcomes across time periods, we discovered that outcomes for patients with IBD worsened compared with patients without IBD in parallel to the widespread adoption of MIS for RP. MIS, both with and without robotic assistance, was introduced in 2000 in the United States [17]. The use of robotic-assisted MIS drastically increased from 1% in 2001 to 40% in 2006 [18]. The robotic-assisted approach made up about 75% of RP by 2017 [19]. We found that the proportion of IBD patients with prostate cancer undergoing MIS directly corresponded to national trends (Fig. 1), and as MIS became the predominant approach for RP, we observed progressively worse outcomes for patients with IBD (Table 2).

This contemporary transition for prostate cancer surgery was associated with a shift from an extraperitoneal surgery to a transperitoneal surgery. Although this change is unlikely to dramatically impact most men with prostate cancer, patients with IBD have underlying chronic inflammation of the digestive system. Therefore, it is plausible that this inflammatory process can be aggravated by pneumoperitoneum, manipulation of the bowel, or contact with surgical instruments. Prior gastrointestinal surgery for patients with IBD resulting in scar tissue is another possible explanation.

After stratifying by organ system, patients with IBD suffered more infectious complications (1.4% vs 0.6%; $P = 0.01$). Other studies have shown that infection is one of the most common reasons that patients with IBD are readmitted to the hospital, with infections estimated to make up about 10.8 to 27.8% of readmissions [20, 21]. The high infection rate has often been attributed to the immunosuppression caused by corticosteroid and antitumor factor treatments, previous surgeries, as well as malnutrition, which is common for patients with IBD [22]. However, a study by Navaneethan et al. [23] adjusted for these factors and still found patients with Crohn's disease to have significantly higher rates of postoperative complications after undergoing cholecystectomy, predominantly infection. Our study also found increased hematologic (0.8% vs 0.1%; $P < 0.0001$) and VTE (1.0% vs 0.1%; $P < 0.0001$) complications in patients with IBD compared with patients without IBD who underwent RP. This is consistent with reported data that the risk of VTE is three times higher for people with IBD [24]. Finally, we observed increased rates of gastrointestinal (3.4% vs 1.7%; $P = 0.0029$), pulmonary (3.0% vs 1.2%; $P = 0.0002$), and renal (3.3% vs 1.9%; $P = 0.02$) complications with neurologic and surgical complications also trending toward higher complication rates in the IBD cohort (Fig. 2B). Future studies should investigate these associations.

Our finding is in accordance with studies of patients with IBD in the orthopedic and bariatric literature [25, 26]. Hospital admissions for patients with IBD currently present a significant cost burden to the US health-care system. In fact, in a study using the National Inpatient Sample, the annual inpatient cost was estimated to be \$945 million for patients with ulcerative colitis and \$1.3 billion for

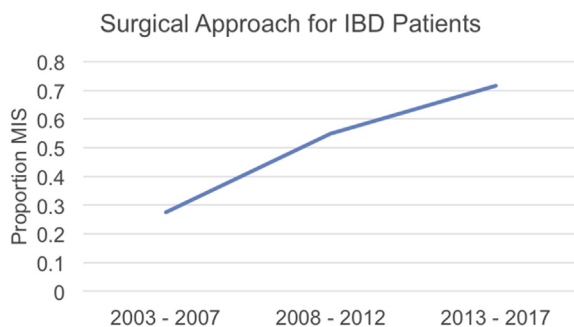


Fig. 1. Surgical approach for patients with IBD. IBD, inflammatory bowel disease.

Table 2

Ninety-day outcomes among patients who underwent prostate surgery between 2003 and 2017. The variables listed in Table 1 were adjusted for using multivariable regression models.

	2003 - 2007		2008 - 2012		2013 - 2017	
	n = 61,119		n = 110,255		n = 90,816	
	IBD vs no IBD aOR (95% CI)	p	IBD vs no IBD aOR (95% CI)	p	IBD vs no IBD aOR (95% CI)	p
Overall complications	1.02 (0.38 to 2.74)	0.97	1.41 (0.97 to 2.05)	0.07	2 (1.5 to 2.67)	<0.0001
Minor complications	0.86 (0.29 to 2.57)	0.79	1.43 (0.95 to 2.14)	0.08	1.73 (1.24 to 2.41)	0.001
Major complications	2.4 (0.31 to 18.61)	0.4	1.15 (0.43 to 3.06)	0.78	2.56 (1.63 to 4.03)	<0.0001
High cost surgery						
Top quartile	1.38 (0.77 to 2.47)	0.27	1.19 (0.88 to 1.6)	0.26	1.6 (1.23 to 2.1)	0.001
Readmissions	1.29 (0.5 to 3.33)	0.6	1.08 (0.49 to 2.38)	0.85	1.51 (1.1 to 2.06)	0.01

aOR = adjusted odds ratios; IBD, inflammatory bowel disease.

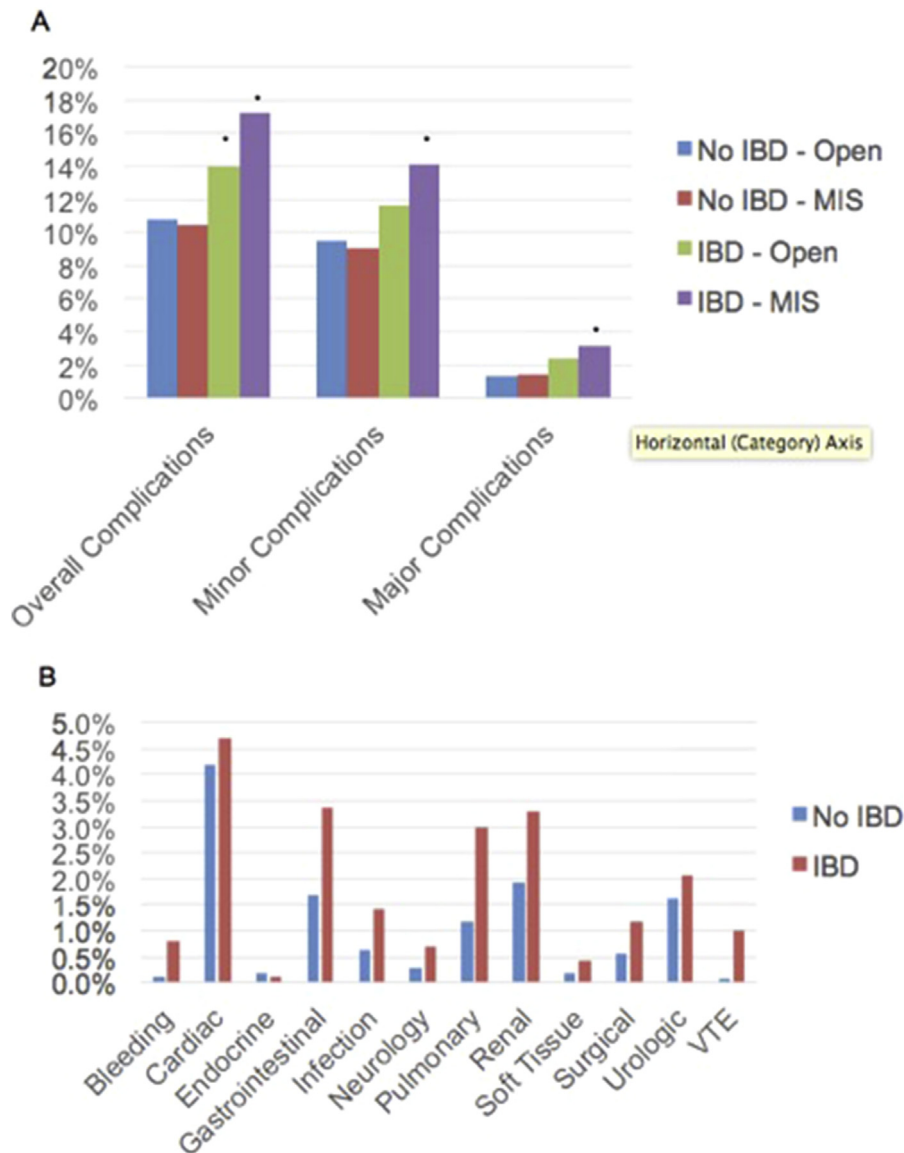


Fig. 2. Surgical complications. (A) Minor complications were considered Clavien-Dindo Grades I and II. Major complications were considered Clavien–Dindo Grades III, IV, and V. (B) Complications by system. * denotes significance with respect to the No IBD – open cohort. IBD, inflammatory bowel disease.

patients with Crohn's disease [27]. This is an important consideration for patients with IBD with urologic malignancies.

The links between IBD and urologic cancers are just beginning to be elucidated. In general, IBD is associated with higher risks of

extra-intestinal malignancies [28, 29]. The previously mentioned study by Burns *et al.* [5] found that men with IBD were at a four to five times higher risk of acquiring clinically significant prostate cancer compared with matched controls. Given the positive

associations of IBD with urologic malignancies and the increasing incidence and prevalence of IBD in the United States, the potential increased morbidity and cost associated with surgical intervention is paramount in perioperative counseling. When deciding which surgical approach to take for men with IBD undergoing RP, it is important for surgeons and patients to consider potentially higher complication rates, costs, and readmissions associated with MIS compared with an open approach. The results of our study suggest that open surgery or an extraperitoneal MIS approach may be preferred options for patients with IBD.

This study has several limitations. First, we were not able to adjust for immune suppression or malnutrition in our study. Thus, future studies could control for these factors by recording medications, inflammatory markers such as C-reactive protein, and prealbumin levels. In addition, we did not have access to patient surgical histories. However, a 2010 study by Ginzburg et al. [30] compared men with and without a history of previous abdominal surgery who underwent robotic-assisted laparoscopic RP and found no significant differences in surgical time or complication rates. Similarly, a 2015 study by Ball et al. [31] compared men with and without a history of previous abdominopelvic or inguinal surgery who underwent minimally invasive RP and found no significant differences in overall, major, or abdominal complications. Thus, we do not expect prior surgical history to impact our results. Moreover, despite using such a large dataset, there were a small number of IBD patients, which could be a result of coding inaccuracies, although coding issues would be expected to be similar between the IBD and non-IBD cohorts. Another limitation is that the Premier Hospital Database only captures inpatient perioperative events although it is likely that only minor complications are managed in the out-patient setting. In addition, we did not have access to prostate cancer stage or grade data, which will could affect postoperative outcomes. However, recent studies have shown similar perioperative complication rates in men with metastatic prostate cancer undergoing cytoreductive RP compared with men who underwent RP for localized disease, making stage and grade less likely contributors to the differences seen [32]. In addition, although our study shows a clear link between surgical approach and complication rates, we are not able to determine causality due to the retrospective nature of our study. Finally, we were unable to control for intraperitoneal vs. extraperitoneal MIS surgery using the Premier Hospital Database. Nevertheless, a vast majority is performed via a transperitoneal approach.

In conclusion, our study shows that men with IBD are at increased risks for various postoperative complications after RP compared with their non-IBD counterparts, largely attributed to a shift in surgical treatment from an open extraperitoneal approach to a transperitoneal MIS approach. This was not the case for the non-IBD cohort, in which the type of surgical approach did not significantly affect complication rates. The IBD cohort also had higher surgical and readmission rates between 2013 and 2017, paralleling the increased proportion of MIS used in more recent years. Patients with IBD presenting with prostate cancer should be counseled about the risks and costs associated with MIS RP.

Funding

This work is supported by a grant from the National Cancer Institute (P30CA072720).

Conflicts of interest

E. A. S. receives clinical trial research support from Astellas/Medivation.

References

- Kappelman MD, Rifas-Shiman SL, Kleinman K, Ollendorf D, Bousvaros A, Grand RJ, et al. The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. *Clin Gastroenterol Hepatol* 2007;5(12):1424–9.
- Dahlhamer JM. *Prevalence of inflammatory bowel disease among adults aged ≥ 18 years—United States, 2015*. *MMWR. Morbidity and mortality weekly report* 2016; 65.
- Kaplan GG, Bernstein CN, Coward S, Bitton A, Murthy SK, Nguyen GC, et al. The Impact of Inflammatory Bowel Disease in Canada 2018: Epidemiology. *J Can Assoc Gastroenterol* 2019;2(Suppl 1):S6–16.
- American Cancer Society. *Cancer facts and figures 2017*. American Cancer Society; 2017;14, 500817.
- Burns JA, Weiner AB, Catalona WJ, Li EV, Schaeffer EM, Hanauer SB, et al. Inflammatory Bowel Disease and the Risk of Prostate Cancer. *Eur Urol* 2019;75(5):846–52.
- Ge Y, Shi Q, Yao W, Cheng Y, Ma G. The association between inflammatory bowel disease and prostate cancer risk: a meta-analysis. *Prostate Cancer Prostatic Diseases* 2019.
- Kirk PS, Govani S, Borza T, Hollenbeck BK, Davis J, Shumway D, et al. Implications of Prostate Cancer Treatment in Men With Inflammatory Bowel Disease. *Urology* 2017;104:131–6.
- Murphy CT, Heller S, Ruth K, Buyyounouski MK, Weinberg D, Uzzo RG, et al. Evaluating toxicity from definitive radiation therapy for prostate cancer in men with inflammatory bowel disease: Patient selection and dosimetric parameters with modern treatment techniques. *Practical Radiation Oncology* 2015;5(3): e215–22.
- Hu JC, Nelson RA, Wilson TG, Kawachi MH, Ramin SA, Lau C, et al. Perioperative complications of laparoscopic and robotic assisted laparoscopic radical prostatectomy. *J Urol* 2006;175(2):541–6. discussion 546.
- Coughlin GD, Yaxley JW, Chambers SK, Ochipinti S, Samarasinghe H, Zajdlewicz L, et al. Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: 24-month outcomes from a randomised controlled study. *Lancet Oncol* 2018;19(8):1051–60.
- Ilic D, Evans SM, Allan CA, Jung JH, Murphy D, Frydenberg M. Laparoscopic and robotic-assisted versus open radical prostatectomy for the treatment of localised prostate cancer. *Cochrane Database Syst Rev* 2017;9. CD009625.
- Premier Healthcare Database White Paper: Data that informs and performs, in Premier Applied Sciences®. Premiere July 29, 2018.
- D'Hoore W, Bouckaert A, Tilquin C. Practical considerations on the use of the Charlson comorbidity index with administrative data bases. *Journal of Clinical Epidemiology* 1996;49(12):1429–33.
- Leow JJ, Reese SW, Jiang W, Lipsitz SR, Bellmunt J, Trinh QD, et al. Propensity-matched comparison of morbidity and costs of open and robot-assisted radical cystectomies: a contemporary population-based analysis in the United States. *Eur Urol* 2014;66(3):569–76.
- Mossanen M, Krasnow RE, Zlatev DV, Tan WS, Preston MA, Trinh QD, et al. Examining the relationship between complications and perioperative mortality following radical cystectomy: a population-based analysis. *BJU Int* 2019;124(1):40–6.
- Pfeffermann D. The use of sampling weights for survey data analysis. *Stat Methods Med Res* 1996;5(3):239–61.
- Hu JC, Gandaglia G, Karakiewicz PI, Nguyen PL, Trinh Q-D, Shih Y-CT, et al. Comparative Effectiveness of Robot-Assisted Versus Open Radical Prostatectomy Cancer Control. *Eur Urol* 2014;66(4):666–72.
- Hu JC, Gu X, Lipsitz SR, Barry MJ, D'Amico AV, Weinberg AC, et al. Comparative Effectiveness of Minimally Invasive vs Open Radical Prostatectomy. *J Am Med Assoc* 2009;302(14):1557–64.
- Wagner C, Srougi V, Sanchez-Salas R. Getting ready for the first robotic prostatectomy, from basics to real practice. *Curr Opin Urol* 2017;27(4):323–9.
- Schmidt T, Feagins LA. How Can We Improve to Keep Our Patients Out of the Hospital? *Inflamm Bowel Dis* 2019;25(6):980–6.
- Mudireddy P, Scott F, Feathers A, Lichtenstein GR. Inflammatory Bowel Disease: Predictors and Causes of Early and Late Hospital Readmissions. *Inflamm Bowel Dis* 2017;23(10):1832–9.
- Biancone L, Onali S, Petruzzello C, Calabrese E, Pallone F. Cancer and immunomodulators in inflammatory bowel diseases. *Inflamm Bowel Dis* 2015;21(3): 674–98.
- Navaneethan U, Parasa S, Venkatesh PG, Ganapathi TT, Kiran RP, Shen B. Impact of inflammatory bowel disease on post-cholecystectomy complications and hospitalization costs: a Nationwide Inpatient Sample study. *J Crohns Colitis* 2013;7(5). p. e164-70.
- Koenigs KP, McPhedran P, Spiro HM. Thrombosis in inflammatory bowel disease. *J Clin Gastroenterol* 1987;9(6):627–31.
- Ehrenpreis ED, Zhou Y. Hospital costs, length of stay and prevalence of hip and knee arthroplasty in patients with inflammatory bowel disease. *World J Gastroenterol* 2017;23(26):4752–8.
- Bazerbachi F, Sawas T, Vargas EJ, Haffar S, Deepak P, Kisiel JB, et al. Bariatric Surgery Is Acceptably Safe in Obese Inflammatory Bowel Disease Patients: Analysis of the Nationwide Inpatient Sample. *Obes Surg* 2018;28(4):1007–14.
- Nguyen GC, Tuskey A, Dassopoulos T, Harris ML, Brant SR. Rising hospitalization rates for inflammatory bowel disease in the United States between 1998 and 2004. *Inflamm Bowel Dis* 2007;13(12):1529–35.

28. Pedersen N, Duricova D, Elkjaer M, Gamborg M, Munkholm P, Jess T. Risk of extra-intestinal cancer in inflammatory bowel disease: meta-analysis of population-based cohort studies. *Am J Gastroenterol* 2010;105(7):1480–7.
29. Yadav S, Singh S, Harmsen WS, Edakkanambeth Varayil J, Tremaine WJ, Loftus Jr EV. Effect of Medications on Risk of Cancer in Patients With Inflammatory Bowel Diseases: A Population-Based Cohort Study from Olmsted County, Minnesota. *Mayo Clin Proc* 2015;90(6):738–46.
30. Ginzburg S, Hu F, Staff I, Tortora J, Champagne A, Salner A, et al. Does Prior Abdominal Surgery Influence Outcomes or Complications of Robotic-assisted Laparoscopic Radical Prostatectomy?(Report). *Urology* 2010;76(5):1125.
31. Ball MW, Reese AC, Mettee LZ, Pavlovich CP. Safety of Minimally Invasive Radical Prostatectomy in Patients with Prior Abdominopelvic or Inguinal Surgery. *J Endourol* 2015;29(2):192–7.
32. Yuh BE, Kwon YS, Shinder BM, Singer EA, Jang TL, Kim S, et al. Results of Phase 1 study on cytoreductive radical prostatectomy in men with newly diagnosed metastatic prostate cancer. *Prostate Int* 2019;7(3):102–7.