Comparison of Outpatient Narcotic Prescribing Patterns After Minimally Invasive Versus Retropubic and Perineal Radical Prostatectomy

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Purpose: Studies comparing pain after minimally invasive vs retropubic and perineal radical prostatectomy are conflicting. We characterized population based outpatient narcotic prescribing patterns after minimally invasive, retropubic and perineal radical prostatectomy.

Materials and Methods: We evaluated outpatient prescription data after minimally invasive, retropubic and perineal radical prostatectomy from 2003 to 2006 using MarketScan®. Baseline and postoperative narcotic prescriptions were identified using the National Drug Code. Total prescribed narcotic strength in morphine sulfate equivalents, the number of prescriptions filled and costs were compared. We performed multivariate analysis adjusted for surgical approach, age, comorbidity, baseline narcotic use, health plan and geographic region.

Results: We identified 2,206 minimally invasive, 8,037 retropubic and 463 perineal radical prostatectomies with no differences in baseline narcotic prescription use. Perineal and retropubic operations were associated with greater total morphine sulfate equivalent use than the minimally invasive operation. Perineal prostatectomy was associated with more narcotic refills than minimally invasive and retropubic prostatectomy (42.3% vs 20.2% and 28.9%, respectively, $p < 0.001$). Median narcotic costs were lower for minimally invasive than for perineal and retropubic prostatectomy. On adjusted analysis perineal radical prostatectomy, younger age, baseline narcotic use and preferred provider organization health plan were associated with greater morphine sulfate equivalents and narcotic refills while minimally invasive surgery was associated with fewer refills and lower costs but not with total morphine sulfate equivalents. There was significant geographic variation in narcotic use and costs.

Conclusions: Postoperatively minimally invasive radical prostatectomy required fewer narcotic refills and had lower narcotic costs while perineal radical prostatectomy required the greatest amount of narcotics. However, minimally invasive vs retropubic radical prostatectomy morphine sulfate equivalent requirements did not differ on adjusted analysis. While our findings support the purported advantage of minimally invasive radical prostatectomy of less postoperative pain, confirmatory prospective studies with objective outcomes are needed.

Key Words: prostate; prostatectomy; pain, postoperative; narcotics; robotics

Abbreviations and Acronyms

HMO = health maintenance organization
LRP = laparoscopic RP
MIRP = minimally invasive RP
MSe = morphine sulfate equivalent
POS = point of service
PPO = preferred provider organization
PRP = perineal RP
RALP = robot-assisted RP
RP = radical prostatectomy
RRP = retropubic RP

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MINIMALLY invasive RP use surged in the United States after the demonstration of reproducible technique in 2000 with an estimated 85% of RPs done with robotic assistance in 2008.[1] MIRP offers smaller incisions, decreased blood loss and shorter length of stay than open RRP.[2] Furthermore, single center series show equivalent oncological and functional outcomes for the laparoscopic, robotic and open approaches.[3,4] However, while other minimally invasive urological procedures confer significantly less postoperative pain,[5,6] the promise of decreased pain and shorter convalescence for MIRP has been debated, particularly by open surgeons using lower midline or Pfannenstiel mini-incisions.[7,8]

Theoretically MIRP is associated with less postoperative pain than RRP and PRP due to smaller incisions and decreased traction on the abdominal wall musculature.[9] However, studies are inconsistent in showing significant amelioration of postoperative pain for MIRP[2,10–13] with variations in measuring and reporting postoperative pain. Also, few groups have compared longer term objective outpatient narcotic requirements after RP and extended postoperative pain may be a societal burden since men may require more time away from work.[14] Using a population based approach we compared outpatient narcotic prescription use for MIRP, RRP and PRP.

MATERIALS AND METHODS

Study Population

We identified 31,729 men diagnosed with prostate cancer during 2003 to 2006 from MarketScan using ICD-9 code 185.0. MarketScan incorporates the health services of approximately 3 million employees, dependents and retirees in the United States with primary or Medicare supplemental coverage through privately insured fee for service, POS or capitated health plans.[15] MarketScan is generally representative of the demographic makeup of the United States, although more subjects reside in the South and Midwest than the general population.[16] Men who underwent decreased RP, RRP or MIRP, ie laparoscopic RP with or without robotic assistance, were identified using the CPT-4 codes 55810, 55812 and 55815 for PRP, 55840, 55842 and 55845 for RRP, and 55866 for MIRP.

Many private payers do not contribute outpatient prescription data. Thus, to ensure that we captured narcotic prescription use specific to post-prostatectomy pain we limited the cohort to men who filled a narcotic prescription within 7 days of discharge home. Men were also censored if they changed health plan coverage within 90 days surgery to capture complete followup. After censoring the final cohort consisted of 10,706 men, including 2,206 with MIRP, 8,037 with RRP and 463 with PRP.

Variables

Dependent. We identified outpatient narcotic prescription use up to 90 days before and after RP using Food and Drug Administration designated national drug codes for oral narcotics, including codeine, hydrocodone, hydromorphone, meperidine, morphine, MS Contin®, oxycodone, OxyContin®, pentazocine, propoxyphene and tramadol. To assess the various strengths, types and amount of postoperative narcotic use the cumulative MSe was derived.[5,6] Since distributions were nonnormal, medians were compared by surgical approach.

Independent. Age at diagnosis (less than 55, 55 to 64, 65 to 74 or greater than 75 years), comorbidities using the Charlson index derived from health care encounters the year before prostatectomy,[17] health plan type (comprehensive, HMO, PPO, POS or other) and geographic region classified according to United States Census Bureau regions (Northeast, Midwest, South or West) were obtained from the enrollment files.

Statistical Analysis

Demographic characteristics and narcotic use patterns, including refills, median narcotic strength in MSe and median narcotic costs, were compared with the Pearson chi-square and Kruskal-Wallis tests. Analgesic costs were derived as total primary health plan expenditures for narcotics within 90 days of surgery, excluding insurance deductibles, copayments and other third party payments from supplemental insurance. Multivariate models were constructed to determine the effect of surgical approach, age, comorbidity, geographic region, health plan type and baseline narcotic use on postoperative outpatient MSe use, refills and costs. Statistical significance was considered at 2-sided $p \leq 0.05$. Statistical analysis was done with SAS® 9.1.3.

RESULTS

Table 1 lists study population demographic characteristics. Men undergoing MIRP were younger ($p = 0.002$) while men undergoing RRP had fewer comorbidities ($p = 0.005$). Men with HMO and PPO coverage were less and more likely to undergo MIRP, respectively ($p < 0.001$). MIRP was more commonly done in the Midwest while RRP and PRP were most commonly done in the South ($p < 0.001$). There were no differences in baseline preoperative narcotic use by surgical approach.

On unadjusted analysis MIRP was associated with lower median total narcotic strength consumption than RRP and PRP (6.7 vs 6.9 and 8.3 MSe, respectively, $p < 0.001$, fig. 1). Similarly fewer additional narcotic refills were associated with MIRP than with RRP and PRP (20.2% vs 28.9% and 42.3%, respectively, $p < 0.001$, table 2). Correspondingly lower median narcotic costs were associated with MIRP vs PRP and RRP ($8 vs $10 and $10, respectively, $p < 0.001$, fig. 2).

On adjusted analysis PRP (RR 1.11, 95% CI 1.03–1.21, referent RRP), younger age (less than 55 years RR 1.22, 95% CI 1.04–1.43 and 55 to 64 years RR 1.17, 95% CI 1.00–1.37, referent greater than 75

Table 1. *Baseline patient demographics*

	No. MIRP (%)	No. PRP (%)	No. RRP (%)	p Value
Preop narcotic use	260 (11.8)	70 (15.1)	1,093 (13.6)	0.146
Age:				
Less than 55	547 (24.8)	105 (22.7)	1,807 (22.5)	0.002
55–64	1,213 (55.0)	247 (53.4)	4,272 (53.2)	
65–74	422 (19.1)	109 (23.5)	1,866 (23.2)	
Greater than 75	24 (1.1)	2 (0.4)	92 (1.1)	
Insurance:				
Comprehensive	622 (28.2)	155 (33.5)	2,095 (26.1)	<0.001
HMO	313 (14.2)	66 (14.3)	1,606 (20.0)	
PPO	962 (43.6)	192 (41.5)	3,325 (41.4)	
POS	277 (12.6)	41 (8.9)	896 (11.2)	
Other	12 (0.5)	1 (0.2)	24 (0.3)	
Unknown	20 (0.9)	8 (1.7)	91 (1.1)	
Charlson comorbidity index:				
0	1,661 (75.3)	336 (72.6)	6,317 (78.6)	0.005
1	330 (15.0)	87 (18.8)	1,304 (16.2)	
2	42 (1.9)	13 (2.8)	169 (2.1)	
3+	28 (1.3)	4 (0.9)	50 (0.6)	
Unknown	145 (6.6)	23 (5.0)	197 (2.5)	
Geography:				
Midwest	914 (41.4)	177 (38.2)	2,565 (31.9)	<0.001
Northeast	203 (9.2)	17 (3.7)	650 (8.1)	
South	730 (33.1)	213 (46.0)	2,829 (35.2)	
West	350 (15.9)	51 (11.0)	1,948 (24.2)	
Unknown	9 (0.4)	5 (1.1)	45 (0.6)	

years) and baseline narcotic use (RR 2.70, 95% CI 2.56–2.84) were associated with greater MSe consumption (table 3). Although MIRP was not associated with differences in MSe consumption vs RRP, MIRP was associated with fewer narcotic refills (OR 0.6, 95% CI 0.54–0.69) and lower narcotic prescription costs (RR 0.94, 95% CI 0.90–0.98). Similar to MSe consumption, younger age (less than 55 years OR 2.22, 95% CI 1.38–3.59 and 55 to 64 years OR

Table 2. *Postoperative narcotic prescription refills by surgical approach*

	No. MIRP (%)	No. PRP (%)	No. RRP (%)	Total No (%)
No. refills after initial postop prescription:*	445 (20.2)	196 (42.3)	2,319 (28.9)	2,960 (27.6)
1	265 (12.0)	114 (24.6)	1,498 (18.6)	1,877 (17.5)
2	89 (4.0)	45 (9.7)	354 (4.4)	488 (4.6)
3 or Greater	91 (4.1)	37 (8.0)	467 (5.8)	595 (5.6)

* p <0.001.

1.66, 95% CI 1.04–2.67) and baseline narcotic use (OR 2.85, 95% CI 2.50–3.25) were associated with additional narcotic refills. Paralleling the determinants of MSe use, PRP (RR 1.16, 95% CI 1.08–1.26), younger age (less than 55 years RR 1.48, 95% CI 1.26–1.73 and 55 to 64 years RR 1.34 95% CI 1.15–1.57) and baseline narcotic use (RR 3.00, 95% CI 2.85–3.15) were associated with higher narcotic prescription costs. Significant geographic variation was observed for MSe consumption, narcotic refills and narcotic prescription costs.

DISCUSSION

Direct to consumer advertising suggests that MIRP offers smaller incisions, less postoperative pain and more rapid return to normal activity.[18] However, direct comparisons of pain after MIRP, RRP and PRP remain sparse and inconsistent. For example, Tewari et al reported improved pain using a visual scale in men undergoing RALP vs RRP[2] but Webster et al found that significant differences in RALP vs RRP postoperative pain did not last beyond the postoperative day 1.[10] Wood et al reached a similar conclusion, finding that RALP vs RRP was associated

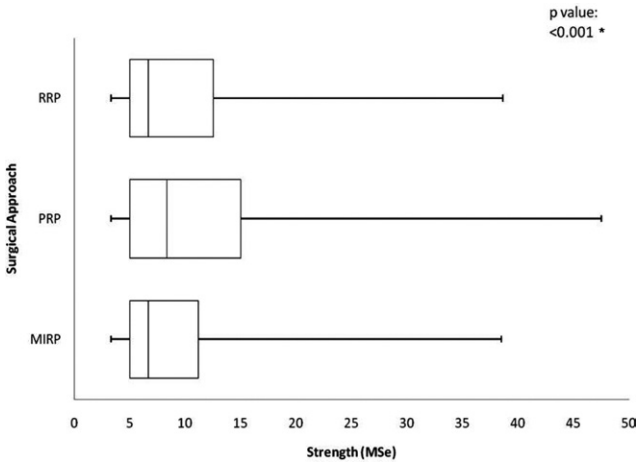

Figure 1. Postoperative narcotic strength in MSe by surgical approach. Asterisk indicates Kruskal-Wallis test.

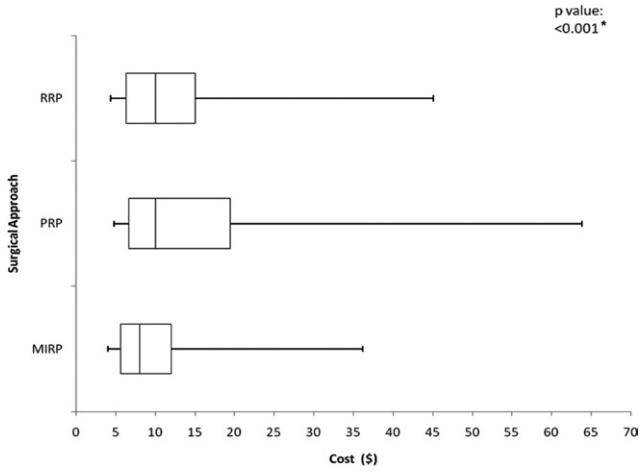

Figure 2. Postoperative narcotic costs by surgical approach. Asterisk indicates Kruskal-Wallis test.

Table 3. *Multivariate model of total postoperative narcotic prescription strength in MSe, narcotic prescription refills needed and total postoperative narcotic cost*

	Total Strength		Additional Refills		Total Cost	
	RR (95% CI)	p Value	OR (95% CI)	p Value	RR (95% CI)	p Value
Surgical approach (vs RRP):						
MIRP	0.97 (0.93–1.01)	0.104	0.61 (0.54–0.69)	<0.001	0.94 (0.90–0.98)	0.003
PRP	1.11 (1.03–1.21)	0.010	1.75 (1.43–2.15)	<0.001	1.16 (1.08–1.26)	<0.001
Age (vs greater than 75):						
Less than 55	1.22 (1.04–1.43)	0.015	2.22 (1.38–3.59)	0.001	1.48 (1.26–1.73)	<0.001
55–64	1.17 (1.01–1.37)	0.045	1.66 (1.04–2.67)	0.035	1.34 (1.15–1.57)	<0.001
65–74	1.13 (0.97–1.32)	0.126	1.27 (0.79–2.05)	0.326	1.17 (1.01–1.37)	0.047
Region (vs West):						
South	1.18 (1.12–1.24)	<0.001	1.07 (0.93–1.22)	0.329	0.91 (0.87–0.95)	<0.001
Midwest	0.84 (0.79–0.91)	<0.001	0.78 (0.64–0.96)	0.016	0.78 (0.73–0.84)	<0.001
Northeast	1.01 (0.96–1.06)	0.674	1.14 (1.00–1.30)	0.050	1.14 (1.09–1.19)	<0.001
Insurance plan (vs HMO):						
Comprehensive	1.02 (0.97–1.08)	0.404	0.94 (0.81–1.10)	0.428	1.01 (0.96–1.07)	0.599
PPO	0.95 (0.91–1.00)	0.045	0.82 (0.72–0.93)	0.002	0.92 (0.88–0.97)	<0.001
POS	0.94 (0.88–1.00)	0.064	0.79 (0.66–0.94)	0.009	1.00 (0.94–1.07)	0.997
Other	0.89 (0.67–1.20)	0.449	0.99 (0.46–2.13)	0.980	0.62 (0.46–0.83)	<0.001
Baseline narcotic use (vs none)	2.70 (2.56–2.84)	<0.001	2.85 (2.50–3.25)	<0.001	3.00 (2.85–3.15)	<0.001
Charlson score (vs 3 or greater):						
0	0.99 (0.82–1.19)	0.904	0.80 (0.49–1.30)	0.370	0.90 (0.75–1.08)	0.246
1	1.18 (0.98–1.42)	0.084	1.06 (0.64–1.75)	0.820	1.09 (0.91–1.31)	0.328
2	1.13 (0.92–1.40)	0.252	0.90 (0.51–1.59)	0.716	0.95 (0.77–1.17)	0.612

with a similar duration of narcotic use.[13] While observational case series are inconsistent, population based comparisons without potential observation biases are lacking. We used a population based approach to determine patterns of postoperative narcotic prescription use among men undergoing MIRP, RRP and PRP.

Our study has several important findings. 1) MIRP was associated with fewer narcotic refills and a lower cost of outpatient narcotics. Similar to our findings, Rassweiler et al found that only 9% of laparoscopic RPs required narcotics on postoperative day 2 vs 55% of RRPs.[4] Also, Bhayani et al found that men undergoing laparoscopic RP postoperatively required fewer narcotics and had shorter time to complete convalescence.[11] More recently Miller et al prospectively compared health related quality of life assessed by a validated questionnaire for RALP vs RRP.[12] RALP was associated with better quality of life 6 weeks after hospital discharge and decreased postoperative pain was a contributing factor. These findings suggest that MIRP confers decreased postoperative pain.

However, despite requiring fewer refills at lower cost MIRP did not differ in MSe requirements compared to RRP on adjusted analysis. While the 8% increment in RRP vs MIRP refills may be statistically significant and contribute to greater narcotic costs since each refill is accompanied by health plan expenses, it did not contribute to significant differences in MSe requirements.

Conversely PRP was associated with more MSe use, narcotic refills and greater costs than MIRP and RRP. This contrasts with the notion that the perineal approach is associated with significantly less postoperative pain. For instance, in a prospective study Namiki et al found less postoperative pain during hospitalization for PRP than for RRP and MIRP.[19] While our findings contrast with those of Namiki et al, the greater PRP outpatient narcotic prescription use may reflect neuropathic pain not captured by inpatient studies. Also, PRP is done with the patient in an exaggerated lithotomy position, which may result in lower extremity neuropraxia in up to 21% of patients.[20]

2) Younger men required more outpatient narcotics at a greater cost. This finding correlates with that of Mattila et al, who noted that age greater than 65 years was a significant predictor of decreased postoperative pain after ambulatory surgery.[21] In a large meta-analysis Ip et al found that younger age was a strong predictor of postoperative pain and analgesia requirement.[22] Suggested influences contributing to lower narcotic requirement in elderly patients may include blunted nociceptive function resulting in increased pain tolerance[23] and an alteration in pharmacokinetics with age that leads to increased narcotic sensitivity.[24,25] Elderly patients are also given fewer narcotic prescriptions due to concern regarding increased postoperative pulmonary and gastrointestinal complications.[26] Finally, younger men may need to return to work and resume daily life activity at a more rapid pace than potentially retired older men, leading to a greater need for narcotics

3) Health plan type was significantly associated with post-prostatectomy narcotic prescription use. The 4 health care plans examined in our study included the most commonly used health plans for insurance coverage in the United States. Comprehensive care coverage is the least restrictive of the health plan types with few barriers in choice of physicians and medications, although at higher cost. HMO plans are capitated with an assigned primary care physician selected from a list of providers that coordinate all patient care. POS and PPO plans have financial incentives to use specific providers in a physician network with the former requiring an assigned primary care physician to coordinate care.[27] After RP men with PPO and POS plans required fewer narcotic refills while PPO was also associated with lower cost and total narcotic prescription strength. Joyce et al found that prescription costs among employer provided health care plans were lower in plans with tiered copayment systems for patients seeking out of network care and nonpreferred medications.[28] Thus, higher copayments in PPO and POS plans may have dissuaded men in our study from seeking additional narcotic refills postoperatively.

4) There was significant geographic variation in narcotic prescribing patterns. Men in the Midwest required fewer narcotic refills, corresponding to lower total narcotic strength and cost. Similarly Webster et al observed that patients in the South were more likely to receive a greater amount of narcotics for lower back pain due to numerous socioeconomic factors.[29] Using a population based approach Curtis et al noted significant geographic variation in narcotic prescription use among states with notably lower rates of narcotic prescription use in states with prescription monitoring programs that prevent narcotic abuse.[30]

Our findings must be interpreted in the context of our study design. 1) We characterized outpatient narcotic prescribing patterns and refills rather than directly measuring pain with validated instruments. We could not assess inpatient analgesic requirements. 2) We could only capture narcotics filled with a prescription and covered by health plans. Thus, we could not assess the use of nonsteroidal anti-inflammatory drugs and acetaminophen purchased over the counter without a prescription. 3) While our study design assessed whether a prescription had been filled, we could not determine whether all prescribed narcotics were consumed. Since our data reflects narcotic prescriptions provided and not necessarily consumed, this may simply be an over reflection of physician practice patterns rather than of patient narcotic need. However, to our knowledge our population based findings are the first to characterize post-prostatectomy outpatient narcotic use in the United States. Most studies of post-prostatectomy pain have not used objective assessment of long-term pain requirements, focusing primarily on immediate postoperative pain with reliance on subjective, nonvalidated pain scales. 4) Our cost analysis likely underestimates post-prostatectomy outpatient narcotic costs and may underestimate cost differences by surgical approach since we could not assess contributions from copayments, deductibles and supplementary insurance.

CONCLUSIONS

While up to 27.6% of men require narcotic refills after RP, those who underwent MIRP vs RRP and PRP required fewer narcotic refills with lower narcotic costs. However, MIRP and RRP MSe requirements did not differ on adjusted analysis. Conversely men who underwent PRP required the greatest amount of narcotics at the highest cost. Our findings are consistent with those of others revealing less postoperative pain for MIRP than for open surgical approaches to RP. However, prospective studies with objective outcomes are required to confirm this finding.

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EDITORIAL COMMENTS

These authors address the controversy surrounding whether MIRP causes less postoperative pain than RRP and brings to mind some thought provoking issues for future study. On multivariate analysis they found that the MSe between MIRP and RRP was equivalent but patients with RRP required more refills, creating higher overall prescription costs. One wonders why this is the case. Perhaps patients undergoing RRP were given more pills per prescription than their MIRP counterparts due to prescribing physician biases that those with RRP would need more medication. Also, patients who did not fill a narcotic prescription within 7 days of hospital discharge were excluded from analysis. It would be interesting to know whether there were any differences between groups in these patients. Lastly and somewhat surprisingly the patients with the highest MSe requirement were the PRP group, possibly due to postoperative neuropathic pain issues, as the authors propose.

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Comparing pain and convalescence after prostate cancer surgery is challenging when considering single surgeon experiences. In that regard population based data despite some inherent limitations provide information that may be more generalizable to all practitioners. This study allows for several observations. To my surprise PRP appears to be significantly more painful than a minimally invasive or retropubic approach. Also, MIRP may cause less pain than RRP, although the jury is still out. Indeed, adjusted analysis revealed no differences in narcotic prescription strength between the 2 modalities, although patients with RRP required more refills (table 3). The latter observation begs the obvious question of the clinical vs the statistical significance of such differences. Finally, while it is beyond the scope of this data set, one wonders whether a difference in pain may be attributable to postoperative ileus when considering intraperitoneal vs extraperitoneal MIRP. Prospective evaluation at a multicenter study may delineate this further.

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