The evidence-based pathway for peri-operative management of open and robotically assisted laparoscopic radical prostatectomy


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OBJECTIVE

To assess reports supporting the novel and comprehensive evidence-based pathway for radical prostatectomy (RP), as collaborative-care pathways have helped to optimize management of patients treated with RP and such clinical pathways provide an ideal framework for constructing an original evidence-based pathway for the complete peri-operative care of these patients.

PATIENTS AND METHODS

We searched for articles on Medline via PubMed to identify reports describing consensus opinions on appropriate aspects of the peri-operative management of patients treated with RP, specifically seeking to discern information on preoperative antibiotic regimen, peri-operative laboratory testing, use of β-blockers for those at cardiac risk, pulmonary treatment, deep venous thrombosis prophylaxis, diet advancement, pain management, anti-emetic use, bowel regimen, and catheter removal after RP.

RESULTS

Available reports were used to substantiate each variable of our collaborative-care pathway for RP. When available, meta-analyses were used to provide a broad review of the recognized clinical research. Otherwise, many controlled studies and retrospective reviews were relied upon to provide evidence to construct a framework for clinical decision-making.

CONCLUSIONS

This is the first pathway for the peri-operative management of major urological procedure that is well integrated into current literature. The critical aspects of clinical decision-making in the patient treated with RP were validated by the available research.

KEYWORDS

prostatectomy, evidence-based medicine, clinical pathway, collaborative care, laparoscopic, robotic

INTRODUCTION

Collaborative-care pathways are used for the peri-operative management of many major urological surgical procedures, most notably...
for radical prostatectomy (RP) [1–3]. These pathways allow the integration and optimization of medical and nursing decision-making, and are cost-efficient, improve patient satisfaction, and successfully used with no increase in patient morbidity.

The critical analysis of clinical decision-making has been revolutionized by the use of evidence-based medicine [4]. Consensus opinions and clinical practice guidelines are appropriately determined by vigilant review of available medical publications. Numerous guidelines are readily accessible for managing various chronic medical conditions, and it has been recognized that the ultimate benefit of implementing these guidelines will be achieved with a customized approach tailored to each patient [5]. Our streamlined collaborative-care pathway is ideally suited to each patient [5]. Our streamlined approach to each patient [5]. Our streamlined approach to each patient [5]. Our streamlined approach to each patient [5]. Our streamlined approach to each patient [5]. Our streamlined approach to each patient [5]. Our streamlined approach to each patient [5]. Our streamlined approach to each patient [5].

**PATIENTS AND METHODS**

We used a focused review of published reports in Medline via PubMed and salient articles were identified and included after review by at least two authors. Reports were selected primarily based on the level of evidence provided as recently outlined by Dahm et al. [4]. Systematic reviews with meta-analysis of randomized controlled trials were preferentially chosen when available (Level 1a). In the absence of appropriate Level 1 studies addressing the pathway variables, many studies designated as outcomes research or case series were used. Queries included the keywords ‘prostatectomy’ or ‘prostate’ or ‘surgery’ combined with ‘antibiotic prophylaxis’, ‘blood loss’, ‘thromboembolism’, ‘beta blocker’, ‘incentive spirometry’ (IS), ‘diet’, ‘pain’ management’, ‘anti-emetic’, ‘bowel regimen’, and ‘catheter removal’. In addition to Medline, the Clinical Pathway Constructor (provided by ZynxHealth through the Eskind Biomedical Library of Vanderbilt Medical Center) was used to obtain additional references for selected aspects of the RP pathway.

**RESULTS**

**PERI-OPERATIVE ANTIBIOTICS**

An advisory statement from the National Surgical Infection Prevention Project outlines the use of peri-operative antibiotics for preventing surgical-site infections [6]. The working group endorsed infusion of the first antimicrobial dose within 60 min of incision, and suggested that antibiotic prophylaxis be discontinued within 24 h after surgery. Although the committee did not specifically address RP or urological surgery, cephalosporins were included in the recommendations for general abdominal, colon, cardiac, orthopaedic, gynaecological, and vascular surgery. In concurrence with the suggested dosing outlined by the committee, we use one preoperative dose of cefazolin 1 g i.v. administered within an hour of incision. For patients with β-lactam allergies, we administer preoperative doses of vancomycin 1 g i.v. in conjunction with clindamycin 600-900 mg i.v.

**LABORATORY EVALUATION**

The most well recognized complication during RP is blood loss [7]; although transfusion rates are acceptably low for open RP and extremely low for laparoscopic RP, routine peri-operative monitoring of haematocrit is generally accepted as a reasonable use of resources [8]. Evidence suggests that evaluating the haematocrit before RP might predict transfusion requirement, although preoperative autologous blood donation is not routinely recommended [9,10]. Indeed, with transfusion of either allogeneic or autologous blood occurring at a rate of <3%, the vast majority of preoperatively donated blood would not be used. There is a correlation between transfusion rates and increasing body mass index, indicating that patients with an elevated body mass index might be an appropriate group for peri-operative autologous blood donation [10]. It is also valuable to recognize that the level of haematocrit sufficiently low to merit transfusion remains at the discretion of the individual surgeon. Preoperative administration of recombinant erythropoietin is used by some groups for patients deemed at high risk of transfusion after RP [11]. Selective use of peri-operative erythropoietin might be useful in patients who decline to receive either allogeneic or autologous blood transfusions. Additional laboratory evaluation is rarely indicated unless there are known pre-existing conditions that would merit such assessments [12,13].

**β-BLOCKADE**

RP is rated as an intermediate-risk procedure for cardiac complications, according to the American College of Cardiology (ACC) guidelines [14]. For patients having RP and with a history of cardiac disease, or those currently managed with β-blockade, a recommendation for continuing the drugs before RP is straightforward [15]. More controversial is whether β-blockers should be used routinely in patients having RP and with no history of known cardiac events. Reviews of published reports have been used to stratify cardiac risk in surgical patients to major, intermediate and minor [16]. Notably, for those having RP, an intermediate risk is assigned to all patients aged >70 years. Examples of minor risk factors include smoking, hypercholesterolaemia, and a family history of coronary artery disease. Using a treatment algorithm based on the ACC guidelines, our decision to begin β-blockade depends on the individual’s preoperative risk factors, and often involves collaboration with anaesthesia and cardiology colleagues. Evidence suggested that patients in the intermediate-risk categories have a lower incidence of cardiac events after RP with the appropriate administration of β-blockers [17]. A recent meta-analysis confirmed that the use of β-blockers in other than cardiac surgical procedures decreases peri-operative cardiac morbidity [18]. However, data also indicate that peri-operative β-blocker therapy is associated with a decrease in in-hospital death only among those at high risk, as calculated by a Revised Cardiac Risk Index score [19,20].

**PULMONARY CARE**

A large meta-analysis reported that there is no conclusive evidence to support the use of IS in patients after surgery [21]. Although substantiation for the use of IS is limited and controversial, we routinely provide a device for IS to provide feedback to the patient and thus promote deep breathing and pulmonary care after general anesthesia. The cost associated with the device for our institution is only US $3.31 and is provided with no additional charges from the Department of Respiratory Therapy. We consider the performance feedback of IS induces patients
to take an active role in their recovery, and merits the nominal cost of the disposable device.

**THROMBOEMBOLIC PROPHYLAXIS**

In a recent consensus statement on preventing venous thromboembolism, the American College of Chest Physicians (ACCP) comprehensively reviewed available medical reports to define evidence-based guidelines for deep vein thrombosis (DVT) prophylaxis, with specific recommendations for major urological surgery [22]. These recommendations are also underscored by the higher incidence of DVT in patients with cancer [23]. Specific recommendations for urological surgery were outlined based on the ACCP guidelines [24,25] (Table 1).

The grade of data and recommendations for DVT prophylaxis as outlined in the ACCP review are presented here. Data deemed Grade 1A indicate that the magnitude of benefits, risks, burdens and costs are certain; randomized controlled trials generated consistent results. The Grade 1A data were used to recommend, for patients undergoing major urological surgery, the routine use of thromboprophylaxis, using low-dose unfractionated heparin (LDUH) two or three times daily.

Grade 1C+ data indicate that the magnitude of benefits, risks, burdens and costs was certain, and observational studies showing large effects or results from related randomized controlled trials can be extrapolated. This grade of data was used to recommend that, for patients undergoing major urological surgery, thromboprophylaxis using a low molecular weight heparin (LMWH) is an acceptable alternative to the use of LDUH two or three times daily. In patients undergoing urological surgery who are actively bleeding or who are at very high risk of bleeding, the use of graduated compression stockings (GCS) and/or intermittent pneumatic compression (IPC), until the bleeding risk decreases, is recommended. In patients undergoing urological surgery who have several risk factors for venous thromboembolism, the combination of LDUH or LMWH plus GCS and/or IPC is recommended.

For laparoscopic procedures, no routine thromboprophylaxis is recommended, other than aggressive mobilization. For those patients with additional thromboembolic risk factors, the use of one or more of LDUH, LMWH, IPC or GCS is recommended. Additional data recently reported and specifically addressing urological laparoscopy found increased haemorrhagic complications associated with use of fractionated heparin with no reduction of thrombotic complications vs sequential compression devices [26]. For our patients having robotically assisted laparoscopic prostatectomy (RALP) we routinely use IPC and GCS, with early and aggressive mobilization.

For DVT prophylaxis in our patients having open retroperitoneal RP (RPP) we use IPC with GCS and subcutaneous enoxaparin 40 mg, giving one dose before surgery and a daily dose thereafter while the patient is hospitalized. Studies show that anticoagulation with pelvic surgery increases the risk of prolonged lymphatic drainage and lymphocele formation [27,28]. However, other prospective studies of men undergoing RP with pelvic lymphadenectomy failed to detect an association between heparin administration and lymphoceles or transfusion [29].

There is controversy as to the optimum duration of thromboembolic therapy when administered for DVT prophylaxis [22]. Continuing anticoagulant therapy after hospital discharge is determined for the individual patient, with special consideration to patient history, age and mobility [30].

**DIET**

Early oral feeding was advocated by many in the general surgery community, even for complex colorectal procedures [31]. Multimodal strategies to decrease the length of stay after surgery often involve early advancement of diet [32,33]. For both open and laparoscopic RP, we adopted a policy of early diet advancement and patients are not required to have bowel activity or tolerate solid food before hospital discharge. We routinely advance patients after RP to a full liquid diet on the first morning after RP. After tolerating two full liquid meals, patients are considered suitable for hospital discharge from a dietary standpoint.

**PAIN MANAGEMENT**

Pain after RP can be well controlled without patient-controlled analgesia. A large, randomized trial of patients undergoing various surgical procedures indicated that the use of ketorolac supplemented with adjuvant narcotics provides better analgesia than either method alone [34]. Specific studies addressing patients after RP also support the use of ketorolac with no other contraindications [35,36]. Our current protocol includes no patient-controlled analgesia, ketorolac 30 mg i.v. in the post-anesthesia care unit and 15 mg every 6 h for 36 h after RP, supplemented with intermittent oral narcotic as needed [3]. Ketorolac is withheld in patients with previous evidence of renal dysfunction. The mean pain perception scores were quite low for both surgical methods. On a 1–10 scale, the Likert pain perception score was measured at 1.76 for RALP and 1.73 for RRP on the first day after RP [37].
TABLE 2 The RRP and RALP pathways

<table>
<thead>
<tr>
<th>Procedure</th>
<th>RRP</th>
<th>RALP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel preparation</td>
<td>Clear liquid diet, bisacodyl</td>
<td>Clear liquid diet, magnesium citrate, neomycin and metronidazole</td>
</tr>
<tr>
<td>Preoperative</td>
<td>Enoxaparin 40 mg s.c., cefazolin 1 g i.v.</td>
<td>Same as RRP except no enoxaparin</td>
</tr>
<tr>
<td>Care reminders and treatments</td>
<td>15 mg 6-hourly i.m.; esomeprazole 40 mg daily; enoxaparin 40 mg s.c.</td>
<td>Same as RRP except no enoxaparin</td>
</tr>
<tr>
<td>Diet</td>
<td>Nil by mouth: No ice chips</td>
<td>Same as RRP</td>
</tr>
<tr>
<td></td>
<td>+ full liquid diet at breakfast first day after RRP</td>
<td>Same as RRP</td>
</tr>
<tr>
<td></td>
<td>+/- regular diet at lunch first day after RRP</td>
<td>Same as RRP</td>
</tr>
<tr>
<td>Laboratory</td>
<td>Haematocrit morning of first day after RRP</td>
<td>Same as RRP</td>
</tr>
<tr>
<td>Catheter removal</td>
<td>7–10 days after RP</td>
<td>Same as RRP</td>
</tr>
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Data are conspicuously sparse on the interaction between ketorolac and anticoagulation with LMWH in patients after surgery. Animal models indicate that ketorolac does not augment bleeding after treatment with LMWH [38]. A large prospective trial evaluating adverse outcomes related to giving ketorolac after surgery specifically included urological surgery, and determined that the risk of surgical-site bleeding was 3.05 times higher with the combined use of ketorolac and anticoagulants [39]. Therefore, the possibility of haemorrhagic complications from this combination of medication merits close monitoring in patients having RP.

PRO-MOTILITY AGENTS AND STRESS ULCER PROPHYLAXIS

There is no substantial evidence from controlled trials to support the use of metoclopramide as an adjunct to prevent postoperative nausea and vomiting by promoting intestinal motility [40]. We do not routinely use pro-motility agents in our pathway for the care of patients after RP. These patients are treated with oral esomeprazole to decrease gastric pH and facilitate prevention of clinically significant gastric bleeding [41]. Esomeprazole therapy is also beneficial for alleviating symptoms from postoperative reflux associated with a brief paralytic ileus. Our use of oral esomeprazole has also been cost-efficient; the patient charge per dose of 40 mg oral esomeprazole is $18.23, if administered daily and the pharmacy cost is $0.23. In comparison, a dose of 20 mg oral famotidine is $18.07 (pharmacy cost $0.07) administered twice daily, for a total daily charge of $36.14, and 20 mg i.v. famotidine is $75.36 (pharmacy cost $0.36), also administered twice daily for a daily charge of $150.72.

BOWEL REGIMEN

Rectal injury is a recognized complication associated with RP, with a reported incidence of 0.3–9% [42,43]. Bowel preparation is thus necessary before either open or laparoscopic RP in the event that there is a rectal injury, and primary closure or a temporary diverting colostomy is required. There is no consensus of opinion on the appropriate bowel preparation [42]. Regimens range from the use of an enema only to the use of both mechanical and antibacterial bowel preparation. We routinely prepare our patients for open RP with a clear liquid diet combined with mechanical cleansing, using two doses of the laxative bisacodyl on the day before RP. Because RALP is intraperitoneal, a more robust bowel preparation is used, with a clear liquid diet and a magnesium citrate solution combined with a modified Nichol’s antibiotic preparation with neomycin and metronidazole [44–46].

CATHETER REMOVAL

Early catheter removal has been advocated in studies where patients have a cystogram taken to evaluate extravasation before catheter removal [47]. In one study, 97% of patients had their catheter removed 7 days after RP. However, 15% of these patients developed acute urinary retention (AUR) requiring catheter reinsertion. There were no episodes of AUR in men who had their catheters removed at 14 days after RP. Some groups reported a low incidence of AUR of 1.3% in patients with the catheter removed at 6–14 days with no use of cystography, with most catheters discontinued at 6–8 days [48]. The 8–9 day period after RP with success for catheter removal is reinforced by additional studies showing 2% rates of AUR [49]. Some authors advocated catheter removal as early as 4 days after RP, with a low rate of AUR or long-term complications [50,51]. However, other studies show high rates of AUR with catheter removal at 4 days [52,53]. Data from our institution for removal of the catheter at 7–10 days after RP show a rate of AUR of 2.2% [3]. Thus, our current pathway supports removing the urinary catheter at ≥7 days after RP.

DISCUSSION

In the current climate of medical practice, optimization of resources has become an increasingly recognized goal. Collaborative-care pathways provide a framework to streamline the peri-operative management of many patients undergoing even complex surgical procedures such as RP (Table 2). These pathways optimize the use of both time and financial resources, while providing state-of-the-art medical care. Historically, a significant proportion of peri-operative care has relied upon anecdotal information that represents an amalgam of any individual surgeon’s collective influences and experience. This is partly due to a paucity of published data and guidelines that specifically address comprehensive care of the urology patient [54]. In this review, we show that our
clinical pathway for RP is evidence-based, as determined by the integration of current reports into our peri-operative management strategy.

As with any preferential group of clinical practices, treatment biases can influence the selection of publications. We tried to incorporate as many large scale meta-analyses and randomized trials as possible in creating guidelines to support our management strategies. Indeed, our practice has been modified during the development of the present study to accommodate robust reports supporting selected aspects of the RP pathway.

These evidence-based systems also present an ideal means to integrate immediate feedback into patient care activities. To track adherence to our outlined care pathways and determine if these pathways change patient outcome, we are implementing a set of clinical goals, e.g. length of stay and use of pain medication, that can be tracked through our inpatient order system and combined with a patient questionnaire and outpatient follow-up. We also provide, within our computerised ordering system, links to the relevant reports for each section of the peri-operative pathway, for use by the care provider at the point of service when critical clinical decisions must be completed.

CONFLICT OF INTEREST

None declared.

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Abbreviations: (R)RP, (retropubic) radical prostatectomy; IS, incentive spirometry; RALP, robotically assisted laparoscopic prostatectomy; ACC, American College of Cardiology; GCS, graduated compression stockings; IPC, intermittent pneumatic compression; ACCP, American College of Chest Physicians; DVT, deep vein thrombosis; LDUH, low-dose unfractionated heparin; LMWH, low molecular weight heparin; AUR, acute urinary retention.