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# Enhanced recovery protocols in urological surgery: a systematic review

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**Introduction:** The principles of enhanced recovery after surgery (ERAS) protocols have been developed to optimize care and facilitate recovery after major surgery. The purpose of this systematic review is to present an up-to-date assessment of the perioperative cares in complex urological surgery from the available evidence and ERAS group recommendations.

**Materials and methods:** Systematic searches of PubMed, Embase, Cochrane library and conference abstracts and bibliographies databases.

**Results:** A total of six studies were identified that met the inclusion criteria. Two examined the role of ERAS in radical cystectomy, and the rest examined its role in renal surgery (open, laparoscopic or partial nephrectomy). These studies demonstrated a reduction in duration of inpatient stays with no increase in morbidity in ERAS groups compared with traditional care.

**Conclusions:** ERAS protocols can reduce the length of hospital stay after major urological surgery, without increasing morbidity or mortality.

**Key Words:** enhanced recovery, cystectomy, renal surgery, hospital stay

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## Introduction

Enhanced recovery after surgery (ERAS) or enhanced recovery protocols (ERP) were conceptualized and introduced in the late 1990s in colorectal surgery to optimize the perioperative management of patients undergoing major operations.<sup>1-5</sup> ERPs are designed to address the factors that impede fast recovery following these operations (namely the need for parenteral analgesia, postoperative ileus and reduced mobility secondary to bed rest). On a practical basis, it is usually

implemented as a single structured document in which all those caring for the patient will contribute.

At the outset, ERAS was applied to selected patients who were predicted preoperatively to have a complicated surgical journey. As ERAS has become more established in routine practice however, as it is apparent that the principles are appropriate for the majority of patients undergoing major surgery.

Following the successful application of ERAS in colorectal surgery, other specialties are now implementing ERAS protocols with the aim of achieving similar success.<sup>6-9</sup> Urological surgery, in particular, oncological urology surgery is an ideal area in which ERAS would be beneficial due to the morbid nature and long recovery following such procedures.

ERP are divided into three major elements extending from the preoperative period through the

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TABLE 1. Elements of an enhanced recovery program

**Preoperative**

Pre-admission counseling  
 Fluid and carbohydrate loading  
 Avoidance of prolonged fasting  
 Avoidance of excessive bowel preparation  
 Antibiotic prophylaxis  
 Thromboprophylaxis  
 Avoidance of pre-medications

**Intraoperative**

Use of short acting anesthetic agents  
 Mid-thoracic epidural analgesia  
 Avoidance of drains  
 Avoidance of fluid loading  
 Maintenance of normothermia

**Postoperative**

Avoidance of nasogastric tubes  
 Prevention of nausea and vomiting  
 Early catheter removal  
 Early oral feeding  
 Use of non-opioid analgesia  
 Stimulation of gut motility using adjuncts like chewing gum  
 Audit of compliance and outcome

intraoperative period and covering the postoperative care. These elements<sup>1</sup> are displayed in Table 1.

**Methods**

Systematic searches of the Medline, Embase and PubMed as well as databases from the Cochrane library and conference abstracts were carried out from March 2004 to March 2014. The search strategy used keywords and MeSH terms such as: enhanced recovery, fast track protocols, perioperative care plan, multimodal rehabilitation in combination with cystectomy, nephrectomy and prostatectomy. There was no limit for language applied.

In order to qualify for inclusion, studies had to be case control, cohort or randomized controlled trials. The intervention was defined as a major urological procedure requiring an inpatient stay. Studies had to report use of at least three interventions of an ERP taken from at least two of the three elements of care (pre/intra/postoperative care). Several studies were excluded from the analysis on the basis of the reasons detailed in Table 2. Studies that were included required to report on at least one of the following

outcomes: 1) total hospital stay; 2) complication rate; 3) postoperative ileus; 4) 28-30 day mortality; 5) readmission rate.

**Results**

Six studies were identified that met the inclusion criteria.<sup>10-15</sup> Two of these studies were randomized control trials (RCT) and four were cohort studies (CS). Two of the studies included, looked at the role of ERAS following radical cystectomy and the rest assessed its role in renal surgery. No suitable studies involving prostatectomy were identified. Three of the studies were full journal papers<sup>10-12</sup> and three were only available as conference abstracts but gave sufficient information to meet the criteria for inclusion.<sup>13-15</sup>

The researchers in the cohort studies implemented an ERAS protocol and captured data prospectively. This was subsequently used to compare outcomes with traditional care (TC) pathways that had been the standard of care immediately prior the introduction of the ERP. One CS excluded three patients due to respiratory arrest postoperatively so was unable to analyze data on an intention to treat basis.<sup>11</sup> In the same study two patients withdrew due to lack of consent. In one study, patients undergoing robotic assisted surgery were excluded.<sup>12</sup>

In total, the RCT's recruited 54 patients for TC and 79 patients for ERAS in major urological surgery while the case control trials included 179 patients for TC and 137 for ERAS. Despite the modest sample sizes, statistical significance was achieved in a number of outcomes. The number of ERAS elements incorporated ranged from 3-16 (mean 9.5 and a median 9). Summary of the studies and their findings can be seen in Table 3 and Table 4. The parameters that were assessed with regards the ERAS included the following:

**1. Total hospital stay**

All six studies reported a reduced total hospital stay (THS).<sup>10-15</sup> Karl et al reported reduced THS but did not give numerical data in the conference abstract available.<sup>13</sup> The other five studies reported a statistically significant reduction in total hospital stay following ERAS when compared with TC.<sup>10-12,14,15</sup>

**2. Morbidity**

Postoperative complications ranged from 12%-41% in the TC groups (mean 24.3 %, median 20%) compared to 12%-44% (mean 29.3, median 12) in the ERAS groups. Only one study showed a reduced morbidity following ERAS introduction<sup>10</sup> while the others showed either no change<sup>12</sup> or an increase in morbidity.<sup>11</sup>

TABLE 2. Rejected studies

| Author and procedure                                 | Year | Publication              | Surgery                           | Reason for rejection  |
|--|------|--------------------------|-----------------------------------|---|
| Dutton et al <sup>16</sup>                           | 2012 | Conference abstract only | Radical cystectomy                | Pilot study. Extensive incorporation of ERAS elements in 100 consecutive patients undergoing radical cystectomy. However no control group or comparison group undergoing traditional care (TC) so the authors cannot conclude if ERAS is better than TC despite such a well-designed programme.                           |
| Vasdev et al <sup>17</sup>                           | 2012 | Full text article        | Radical cystectomy                | Description of detailed and specific local ERAS protocol in radical cystectomy but no numerical data measured or control group used.  |
| Dale et al <sup>18</sup>                             | 2011 | Conference abstract only | Radical cystectomy                | Inadequate description of ERAS elements used. No mention of control group despite claims of a reduced hospital stay from 14 days to 8 days.   |
| Mariappan et al <sup>19</sup> (non published poster) | 2007 | Unpublished poster       | Radical cystectomy                | Comparison group used but insufficient information on exact ERAS protocol initiated. Non-published poster found on Google.  |
| Aning et al <sup>20</sup>                            | 2012 | Abstract only            | Radical cystectomy                | No direct comparison between pre-ERAS and post ERAS. Gradual changes to peri-operative care introduced in stepwise manner over a 6-year period. Showed reduced hospital stay, but results may be biased as introduction of robotic assistance.  |
| Azawi et al <sup>21</sup>                            | 2012 | Full article             | Nephrectomy open and laparoscopic | Compares two eras in Denmark 2000-2004 and 2005-2009. Shows that mortality has decreased in nephrectomy, but that length of stay had only decreased 1-2 days following ERAS protocols and was non significant. There is no detail of the exact ERAS protocol used so results cannot be included in the systematic review. |
| Pruthi et al <sup>22</sup>                           | 2009 | Full article             | Radical cystectomy                | Gradual stepwise modifications to fast track program were instituted and investigated over time rather than a pre and post ERAS comparison.   |

## 3. Mortality

Only two studies reported on mortality.<sup>10,11</sup> Both TC and ERAS had equivalent mortality rate of 1.8%.

## 4. Intraoperative blood loss

Intraoperative blood loss was mainly assessed in renal surgery. Firoozfard et al demonstrated a reduction in blood loss in patients who had open nephrectomy when ERAS principles were applied compared to non-ERAS surgery.<sup>11</sup> Chughtai et al however, showed no difference in the median blood loss in patients who had partial nephrectomy between the TC and ERAS groups.<sup>12</sup>

## 5. Postoperative ileus

ERAS have been associated with reduced postoperative ileus as compared to TC (15.7%

versus 22%) but these findings were not statistically significant.<sup>13</sup>

## 6. Readmission rates

Contradiction was observed between studies regarding readmission rates in patients where ERAS was used. Arumainayagam et al reported a reduction in 28-day hospital readmission rates from 8.9% to 5.3% following radical cystectomy in the ERAS group,<sup>10</sup> while Firoozfard et al reported an increase in re-admissions from 2% to 4% following ERAS in open nephrectomy.<sup>11</sup> No statistical p value was reported for either of these studies.

TABLE 3. Included studies. Author, design and reviewed outcomes

| Author and operation  | Design | Preop ERAS elements   | ERAS elements used  |  |
|---|--------|---|---|--|
|   |        |   | Intraoperative  | Postoperative  |
| Arumainayagam <sup>10</sup><br>2007<br>(radical cystectomy)       | Cohort | No bowel prep<br>Stoma therapy counseling<br>Unrestricted clear fluids<br>Assessment of social circumstances  | Epidural anesthesia<br>Pharmacological<br>DVT prevention  | Clear fluids as tolerated in recovery<br>Food chart started day 0<br>Mobilize day 1 with physiotherapist<br>Regular metoclopramide<br>Remove drain early<br>Regular ranitidine (pending < 50 mL per 24 hour)<br>Early oral diet. No NG tube<br>Epidural and catheter out early |
| Firoozfard <sup>11</sup><br>2003<br>(transperitoneal nephrectomy) | Cohort | Counseling of preoperative course<br>Preoperative condition analyzed (activities of daily living, and physical exercise tolerance)  | No pre-med<br>Epidural anesthesia<br>Maintenance of normovolemia<br>Avoidance of hypotension<br>Normothermia via bair-hugger<br>Local anesthesia to wound | Avoid NG tube<br>Early mobilization (day 0-1)<br>Early oral intake (day 0-1) of high protein drinks<br>Oral non opiate analgesia started early day 0<br>Catheter out day 1<br>Epidural out day 2   |
| Chughtai <sup>12</sup><br>2008<br>(open partial nephrectomy)      | Cohort | Patient and family counseling of target goals<br>Medication review<br>Eat and drink lightly day before surgery<br>Minimal bowel prep (3 bisacodyl tablets and 1 bottle magnesium citrate) | Compression pneumatic stockings<br>NG tube out before leaving operating theatre   | Out of bed at least 4 times day 1<br>Regular metoclopramide<br>Oral pain meds day 1<br>Early oral diet<br>Begin liquids day 1<br>Early drain removal<br>Early catheter removal   |
| Karl <sup>13</sup><br>2012<br>(radical cystectomy)                | RCT    | No bowel prep<br>Fluid intake until 2 hours preop<br>Hypercaloric drinks 2 until 2 hours preop  | No use of NG tube   | Avoid NG tube use<br>Hypercaloric drinks < 24 hr postop  |
| Demagnet <sup>14</sup><br>2011<br>(nephrectomy)                   | RCT    | Nil specified   | Front loading of analgesia (non opiate)<br>Wound infiltration of local anesthesia   | Mobilization day 0<br>Feeding day 0<br>Drain out day 1<br>Catheter out day 1   |
| Jacobsohn <sup>15</sup><br>2011<br>(robotic partial nephrectomy)  | Cohort | Preoperative counseling   | Nil specified   | Early oral analgesia<br>Early ambulation   |

TABLE 4. Included studies. Author, design and reviewed outcomes

| Author, year and procedure   | Design | Number of patients |      | THS (median days) |                   | Morbidity (%) |                           | PO ileus symptoms (%) |      | Median intra operative blood loss (mL estimate) |      | Readmission (%) |                           | Mortality (number and %) |                  |
|--|--------|--------------------|------|-------------------|-------------------|---------------|---------------------------|-----------------------|------|---|------|-----------------|---------------------------|--------------------------|------------------|
|  |        | TC                 | ERAS | TC                | ERAS              | TC            | ERAS                      | TC                    | ERAS | TC  | ERAS | TC              | ERAS                      | TC                       | ERAS             |
| Arumain-ayagam <sup>10</sup> 2007<br>(radical cystectomy)                  | Cohort | 56                 | 56   | 17                | 13<br>p < 0.001   | 41            | 32                        | -                     | -    | -   | -    | 8.9             | 5.3                       | n = 1/56<br>1.8%         | n = 1/56<br>1.8% |
| Karl <sup>13</sup> 2012<br>(radical cystectomy)                            | RCT    | 31                 | 57   | *                 | *<br>Less than TC | -             | -                         | 22                    | 15.7 | -   | -    | -               | -                         | -                        | -                |
| Firooz-fard <sup>11</sup> 2003<br>(transperitoneal nephrectomy)            | Cohort | 50                 | 25   | 8                 | 4<br>p < 0.001    | 20            | 44                        | -                     | -    | 1050  | 700  | 2%              | 4%                        | n = 2/50<br>4%           | n = 1/25<br>4%   |
| Chughtai <sup>12</sup> 2008<br>(open partial nephrectomy)                  | Cohort | 25                 | 33   | 4                 | 3<br>p = 0.012    | 12            | 12                        | -                     | -    | 200   | 200  | -               | -                         | -                        | -                |
| Demant <sup>14</sup> 2011<br>(transperitoneal or laparoscopic nephrectomy) | RCT    | 23                 | 22   | 5.8               | 4.2<br>p < 0.05   | -             | **<br>No increase from TC | -                     | -    | -   | -    | -               | -                         | -                        | -                |
| Jacobsohn <sup>15</sup> 2011<br>(robotic partial nephrectomy)              | Cohort | 48                 | 23   | 2.9               | 1.4<br>p < 0.0002 | -             | **<br>No increase from TC | -                     | -    | -   | -    | -               | **<br>No increase from TC | -                        | -                |

\* Data were collected by the authors but no numerical value was reported in the published work

\*\* Was reported as lower in the ERAS group, but no supporting numerical value was published  
TC = traditional care; ERAS = enhanced recovery after surgery

## Discussion

Significant evidence does exist to support the use of ERAS to achieve accelerated recovery following colorectal surgery.<sup>23</sup> Other non-colorectal procedures, such as upper gastrointestinal, bariatric and gynecological surgery have started to adopt ERP's into routine practice.<sup>9,20</sup> Convincing evidence to advocate the use of these protocols in major urological surgery however is currently lacking. Radical cystectomy is still

associated with prolonged hospital stay and significant morbidity<sup>10,24-26</sup> and it is in this group of patients where ERAS may be of the greatest value.

All six studies reviewed in this paper related to major urological surgery and showed reduction in hospital stay and in five the results reached statistical significance.

Studies consistently report that enhanced recovery leads to reduction hospital costs.<sup>29-30</sup> Roulin et al suggested that savings might be explained by the significant reduction in hospital stay.<sup>27</sup> They also concluded that



reduced costs were evident even when the initial setup expense of an ERAS program was taken into account.<sup>27</sup>

Morbidity and mortality rates did not change significantly following the introduction of ERAS protocols and this can support the safety of ERAS protocols.

The effect of ERAS on blood loss was unclear as some studies reported reduction in blood loss while others showed no change. This can reflect the inherent inaccuracy in the estimation of blood loss in different studies.

Postoperative ileus is often one of the major challenges to recovery following radical cystectomy.<sup>22</sup> A randomized controlled trial comparing fast track regime and conservative care in radical cystectomy was undertaken by Karl et al.<sup>13</sup> They investigated amongst other parameters, the rate of postoperative ileus. Eighty-eight patients undergoing radical cystectomy were randomized to either the fast track regime (FT) or the conservative protocol (CP). The FT regime included the use of high calorie drinks, avoidance of NG tubes and bowel prep as well as early postoperative nutrition. The FT group showed a reduced incidence of postoperative ileus symptoms (15.7%) compared to the conservative group (22.5%) and a shorter time to first bowel movement (2.5 days FT versus 3.1 days CP).

Some of the limitations of this systematic review include the lack of well designed RCT or CC trials specifically comparing TC and ERAS in major urological procedures. A number of studies were excluded as a result of lack of control group for comparison, and poor reporting of the exact ERP protocol used. Several studies were only presented as conference abstracts and thus their inclusion was not warranted due to the lack of information regarding study design, numerical data and exact ERP's used. Overall the homogeneity between trials was low, making comparisons limited. Other limitation was the lack of studies addressing the effect of ERAS on patients undergoing radical prostatectomy. This could be explained by the fact that these are already pre-selected patients who are young and fit men who usually undergo laparoscopic or robotic assisted procedures with minimal blood loss. These patients would normally be discharged home on day 1 or 2 post procedure and therefore often only a very limited ERP is used.

## Conclusion

Evidence from published literature supports the use of ERAS in major urological surgery to reduce complication rates and hospital stay. Clinicians have been selective in terms of applying specific elements

of ERAS protocols and most hospitals in the NHS have some form of ERAS protocol for urology. There is however a clear lack of consensus with regards to the ERAS elements to be included and how to organize services to provide this care. Clearly a multidisciplinary team approach is optimal with allocation of a dedicated ERAS team to coordinate and audits the service. Does further work needs to be done in the form of randomized control trials in order to validate, support and encourage the use of ERPs in major urological surgery? Trials of traditional care versus ERAS protocols may no longer be feasible as modern surgical practice already incorporates parts of ERAS. What we really need to know is which elements of ERAS work best for what type of urological surgery. There is likely to be a difference between a minimally invasive prostatectomy with a 1 day stay and an open cystectomy in multiply comorbid elderly patient. □

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