Robotic-assisted Surgery in Partial Nephrectomy and Cystectomy: A Systematic Review

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program is comprised of four ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program and Cochrane Collaboration. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, and interface with stakeholders. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee comprised of health system leadership and researchers. The program solicits nominations for review topics several times a year via the program website.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, Deputy Director, ESP Coordinating Center at Nicole.Floyd@va.gov.

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This topic was developed in response to a nomination by William Gunnar, MD, for the purpose of understanding the potential benefits and costs or robot-assisted surgery. The scope was further developed with input from the topic nominators (*ie*, Operational Partners), the ESP Coordinating Center, the review team, and the technical expert panel (TEP).

In designing the study questions and methodology at the outset of this report, the ESP consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

The authors gratefully acknowledge Roberta Shanman, Jon Bergman, and the following individuals for their contributions to this project:

Operational Partners

Operational partners are system-level stakeholders who have requested the report to inform decision-making. They recommend Technical Expert Panel (TEP) participants; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on draft report; and provide consultation on strategies for dissemination of the report to field and relevant groups.

Mark Wilson, MD
National Director of Surgery (10NC2)
Department of Veterans Affairs

William Gunnar, MD
Former National Director of Surgery (10NC2)
Department of Veterans Affairs

Technical Expert Panel (TEP)

To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members are listed below:

John Gore, MD
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Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center and the ESP Center work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

EXECUTIVE SUMMARY

INTRODUCTION

The adoption of robotic surgery continues to increase, although there remain questions concerning the utility of the robotic approach as compared to both laparoscopic and open surgery. One question that remains is whether the technical advantages of this approach translate into better clinical outcomes for patients – or at least similar. Recent studies have raised concerns that for some operations the oncologic outcomes may be worse. Further complicating the debate is the economics of the robotic platform and whether or not the benefits balance the tradeoff of increased costs.

The robotic approach is widely used across urology, with over 125,000 procedures performed in 2017.[1,2] In light of recent evidence questioning the utility of the robotic platform, it is important to re-visit the evidence surrounding the use of the robotic platform in urologic surgery, especially for long-term clinical and oncologic outcomes. And while the robotic approach has become the standard approach to prostatectomy, there are other urologic procedures – namely partial nephrectomy and cystectomy – where the introduction of the robotic approach is occurring, and an evidence synthesis is warranted.

To help clinicians, patients, and policymakers decide between robotic and other surgical approaches in patients undergoing partial nephrectomy and cystectomy, we were asked to conduct a systematic review of the literature.

METHODS

This topic was developed in response to a nomination by Dr. Mark Wilson, National Director of Surgery (10NC2), and Dr. William Gunnar, former National Director of Surgery (10NC2). Key questions were then developed with input from the topic nominator, the ESP coordinating center, the review team, and the technical expert panel (TEP).

The Key Questions were:

KQ1A: What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy?

KQ1B: What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy?

KQ2A: What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

KQ2B: What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

Data Sources and Searches

We conducted searches in PubMed from 1/1/2010-6/29/2019 and Cochrane (all databases) from 1/1/2010-6/29/2019.

Study Selection

Studies were included if they were randomized control trials or observational studies comparing robotic surgery with either laparoscopic or open surgical approaches for either of the included surgical procedures. We also included publications of cost-effectiveness models that compared robotic surgery with laparoscopic or open surgical approaches. We included all RCTs regardless of outcomes and sample size. To be included, observational studies had to report long-term oncologic outcomes and include at least 80 robotic operations.

Data Abstraction and Quality Assessment

We abstracted data on the following: study design, patient characteristics, sample size, tumor characteristics, intraoperative outcomes, postoperative outcomes (early), long-term functional outcomes (including kidney function) and cancer outcomes, and duration of follow-up. Randomized controlled trials were assessed for quality (risk of bias) with the Cochrane Risk of Bias tool. We used the Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I) for observational studies.

Data Synthesis and Analysis

Because the randomized control trials were too heterogeneous, we did not conduct a meta-analysis of trials. The observational studies were too clinically heterogeneous to support meta-analysis; hence, our synthesis is narrative. We used the criteria of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group to assess the certainty of evidence across studies.

RESULTS

Results of Literature Search

We identified 3,877 potentially relevant citations, of which 556 were included at the abstract screening. From these, a total of 305 abstracts were excluded. A total of 42 publications were identified at full-text review as meeting initial inclusion criteria: cost-effectiveness analyses (n=4), cost-only studies (n=4), publications describing 5 cystectomy RCTs (n=16), cystectomy observational studies (n=11), and nephrectomy observational studies (n=7). See Figure 1 for literature flow.

Summary of Results for Key Questions

Key Question 1A – What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for Cystectomy?

In general, estimated blood loss was less and operating room (OR) time was longer in patients treated with robot-assisted cystectomy compared to open cystectomy. The evidence about lymph node sampling shows that in most studies, but not all, there is no difference between procedures. The few studies comparing robot-assisted cystectomy to laparoscopic cystectomy found no

difference in intraoperative outcomes. RCTs and observational studies support a conclusion that there are not significant differences between robot-assisted and open cystectomy in major complications, genitourinary complications, or length of stay (LOS). Data are too imprecise to draw any conclusions about differences or lack thereof between robot-assisted cystectomy and laparoscopic cystectomy.

Key Question 1B – What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for Cystectomy?

The 2 primary limitations are the underlying data behind the models and the short time horizon (which is similar to partial nephrectomy, which will be discussed to follow). The first study in cystectomy used a propensity matched internal data set and did not incorporate randomized data, despite its existence. The second does appear to have included some randomized data, but the method of pooling this data was not well-described and included both randomized and observational data. As a result, they found wide variation in their estimates on sensitivity analysis. They also did not include the latest, largest, RCT (RAZOR). While the cost analysis of one study was relatively granular and robust,[3] the generalizability of their operative time and LOS measures to contemporary US practice is questionable. Further, the time horizon for both studies was 90 days – which is better than for either of the partial nephrectomy studies (discussed later), but still is too short to capture any meaningful oncologic outcomes.

Key Question 2A – What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

The data comparing robot-assisted partial nephrectomy to other approaches are sparse and have underlying methodologic limitations. With this caveat, there is a consistent finding of lower estimated blood loss in patients treated with robot-assisted partial nephrectomy compared to laparoscopic and open approaches. There is also a signal that length of stay is shorter and major complications are fewer with robot-assisted partial nephrectomy, but the evidence falls short of being conclusive.

Key Question 2B – What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

The 2 primary limitations of these studies are (1) the data that inform their underlying model assumptions come from observational, often out-of-date, studies and (2) the very limited time horizon of their analysis (in hospital only). Without randomized data, treatment effect estimates are prone to bias from underlying patient or time differences, and these biased treatment effects are often amplified when included in a modeling study. The fact that in one of the above studies the authors assumed no difference in complications, and in the other, the authors assumed large differences, illustrates the uncertainty. For costs, one study excluded the purchase and maintenance of the robot – despite it being the primary determinant of higher costs in the other study – and both studies only looked at in-hospital costs. The time horizon for therapy dedicated to oncology treatment should at least include readmissions and subsequent care dedicated to cancer management. Small differences in readmissions, reoperations, or oncologic recurrences would like lead to large differences in the average cost of a treatment approach, none of which was considered in these studies.

DISCUSSION

Key Findings and Strength of Evidence

Robot-assisted surgery probably results in less blood loss than open or laparoscopic approaches, for both cystectomy and partial nephrectomy procedures. Most other differences in outcomes probably are small or nonexistent (complications, lymph node sampling, warm ischemia time, *etc*); however, the certainty of evidence is low or very low. There is a signal that length of stay may be shorter and major complications may be fewer for robot-assisted cases of partial nephrectomy, but again the certainty of evidence is low. Operating room time in cystectomy was judged to have moderate certainty that robot-assisted procedures take more time. On the crucial issues of long-term functional or oncologic outcomes, data are too sparse and imprecise to reach any conclusions. Cost effectiveness, likewise, has not been estimated with high certainty of evidence.

Applicability

No studies were specific to VA populations. The applicability of these results to VA populations may depend on both the similarity of the patients studied to VA patients and the experience of the surgical teams using the robot to VA surgical team experience. However, the benefits for robotic approach may still be realized despite patient-level differences (VA patient population has greater burden of comorbidities than the general population), which will need to be confirmed in future studies. Urology as a surgical field has widely adopted robotic surgery, so the experience will likely translate well into the VA setting.

Research Gaps/Future Research

Two research gaps are apparent. The first is randomized data for patients undergoing partial nephrectomy, in terms of short-term outcomes. The second is high-quality evidence with adequate long-term follow-up and sufficient statistical power to assess cancer outcomes between the operative approaches for either cystectomy or partial nephrectomy. Only 40 patients have been enrolled in RCTs with 5-year follow-up for either of these 2 procedures.

Conclusions

Robotic-assisted surgery for cystectomy and partial nephrectomy has a few documented short-term benefits over open or laparoscopic approaches, but the cost effectiveness is unknown, and long-term oncologic outcomes are inadequately studied.

ABBREVIATIONS TABLE

ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CFS	Cancer-Free Survival
CKD	Chronic Kidney Disease
CSS	Cancer-Specific Survival
EBL	Estimated Blood Loss
FACT	Functional Assessment of Cancer Therapy
FDA	Food and Drug Administration
GFR	Glomerular Filtration Rate
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GU	Genitourinary
LNS	Lymph Node Sampling
LOS	Length of Stay
LPN	Laparoscopic Partial Nephrectomy
LR	Local Recurrences
LRC	Laparoscopic Radical Cystectomy
NACT	Neoadjuvant Chemotherapy
NIS	National Inpatient Samples
NMI	Non-Muscle Invasive
OR	Operating Room
OPN	Open Partial Nephrectomy
ORC	Open Radical Cystectomy
OS	Overall survival
PSM	Positive Surgical Margin
QALY	Quality-adjusted life year
QOL	Quality of Life
RAPN	Robot-Assisted Partial Nephrectomy
RARC	Robot-Assisted Radical Cystectomy
RCT	Randomized Controlled Trial
ROBINS-I	Risk of Bias in Non-Randomized Studies- of Interventions
TR	Total Recurrences
WIT	Warm Ischemia Time