Robotic-assisted Surgery in Partial Nephrectomy and Cystectomy

Presenters: Paul Shekelle, MD, PhD and Mark Girgis, MD

Co-authors: Margherita Lamaina, MD; Christopher P. Childers, MD, PhD; Qiao Ruan, BS; Selene S. Mak, MPH, PhD; Meron Begashaw, MPH; Marika S. Booth, MS; and Amber Tang, BS, and Melinda Maggard-Gibbons, MD
VA Evidence Synthesis Program overview

• Established in 2007

• Provides tailored, timely, and accurate evidence syntheses of VA-relevant, Veteran-focused healthcare topics. These reports help:
  • Develop clinical policies informed by evidence;
  • Implement effective services and support VA clinical practice guidelines and performance measures; and
  • Set the direction for future research to address gaps in clinical knowledge.

• Four ESP Centers across the US:
  • Directors are VA clinicians, recognized leaders in the field of evidence synthesis, and have close ties to the AHRQ Evidence-based Practice Center Program and Cochrane Collaboration

• ESP Coordinating Center in Portland:
  • Manages national program operations and interfaces with stakeholders
  • Produces rapid products to inform more urgent policy and program decisions

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.
ESP Center locations

Coordinating Center
Portland, OR

ESP Center
Portland, OR

ESP Center
Minneapolis, MN

HSR&D/QUERI, VACO
Washington, DC

ESP Center
Durham, NC

ESP Center
Los Angeles, CA
Acknowledgements

Operational Partners

Mark Wilson, MD
National Director of Surgery
Department of Veterans Affairs

William Gunnar, MD
Former National Director of Surgery
Department of Veterans Affairs

Technical Expert Panel (TEP)

John Gore, MD
University of Washington
Seattle, WA

Jim C. Hu, MD
Weill Cornell Medicine
New York City, NY

Mark Jordan, MD
Long Beach Department of Veterans Affairs
Long Beach, CA

John Leppert, MD
Stanford University and Palo Alto
Department of Veterans Affairs
Palo Alto, CA

Joe Liao, MD
Stanford University
Department of Veterans Affairs
Palo Alto, CA

Matthew Rettig, MD
David Geffen School of Medicine at UCLA
Los Angeles, CA

Kevin Win, MD
Department of Veterans Affairs
West Los Angeles
Los Angeles, CA
This report is based on research conducted by the Evidence Synthesis Program (ESP) Center located at the **West Los Angeles VA Medical Center, Los Angeles, CA**, funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.
Robotic-assisted Surgery in Partial Nephrectomy and Cystectomy

February 2020

Full-length report available on ESP website:
http://www.hsrdr.research.va.gov/publications/esp/reports.cfm
Background

• Over 750,000 robotic procedures are performed annually in the US, 125,000 in urology.

• While its use for prostatectomy has become fairly standard (better outcomes), it is unclear if these clinical benefits are realized for other operations and specialties.
Caution When Using Robotically-Assisted Surgical Devices in Women's Health including Mastectomy and Other Cancer-Related Surgeries: FDA Safety Communication

- Benefits and risks are not established and long-term clinical and oncologic outcomes are questioned.

- Robotic platform requires economic investment and unclear whether improvements in outcomes outweigh costs (cost-effectiveness questions remain).
Key questions

• Partial Nephrectomy
  1A) What is the clinical effectiveness of robotic-assisted surgery compared to open or laparoscopic surgery for partial nephrectomy?

  1B) What is the cost-effectiveness of robotic-assisted surgery compared to open or laparoscopic surgery for partial nephrectomy?

• Cystectomy
  2A) What is the clinical effectiveness of robotic-assisted surgery compared to open or laparoscopic surgery for cystectomy?

  2B) What is the cost-effectiveness of robotic-assisted surgery compared to open or laparoscopic surgery for cystectomy?
Selection of Studies

556 References

- 251 Publications
  - 305 References
    - Background/other: 17
    - Comparison group: 129
    - Systematic review: 58
    - Procedure: 40
    - Outcome: 15
    - Review/editorial: 46
  - 209 Publications
    - Sample size <80: 84
    - Intervention: 3
    - Comparison: 4
    - Procedure: 3
    - Follow up <1yr bladder: 22
    - Follow up <3yr kidney: 63
    - No clinical data: 7
    - Other: 1
    - Review/editorial: 16
    - Duplicate: 4
    - Unavailable: 2

34 includes

- 18 observational studies
- 5 trials (15 publications)

- 4 cost-effective analyses
- 4 cost only studies

References Publications
Partial Nephrectomy: Included Studies

1A) What is the **clinical effectiveness** of robotic-assisted surgery compared to open or laparoscopic surgery for partial nephrectomy?

- 7 observational studies
- No RCTs

1B) What is the **cost-effectiveness** of robotic-assisted surgery compared to open or laparoscopic surgery for partial nephrectomy?

- 2 cost-effectiveness analyses
- 2 cost studies
Partial Nephrectomy: Intraoperative Outcomes

Point estimates with 95% CI for difference between complications and EBL between robotic partial nephrectomy and open or laparoscopic.

Robot vs. open
- Robot had lower mean EBL
- No difference in intraoperative complications

Robot vs. laparoscopic
- Robot had lower mean EBL
- No difference in intraoperative complications
Partial Nephrectomy: Intraoperative Outcomes

Point estimates with 95% CI for difference between complications and EBL between robotic partial nephrectomy and open or laparoscopic.

Robot vs. open
• No differences in WIT or OR time

Robot vs. laparoscopic
• No differences in WIT
• Robot had shorter OR time
Partial Nephrectomy: Postoperative Outcomes

Point estimates with 95% CI for difference between LOS between robotic partial nephrectomy and open or laparoscopic.

Robot vs. open
- Robot had lower LOS

Robot vs. laparoscopic
- Robot had lower LOS
Partial Nephrectomy: Postoperative Outcomes

Point estimates with 95% CI for difference between LOS between robotic partial nephrectomy and open or laparoscopic.

Robot vs. open
- Robot had fewer major complications

Robot vs. laparoscopic
- No difference in complications
Partial Nephrectomy: Functional Kidney Outcomes

Point estimates with 95% CI for difference between GFR and CKD upstaging between robotic partial nephrectomy and open or laparoscopic.

**Robot vs. open**
- Robot had slightly greater preservation of GFR
- Robot had lower incidence of CKD upstaging

**Robot vs. laparoscopic**
- Robot had greater preservation of GFR
- Robot had lower incidence of CKD upstaging
Partial Nephrectomy: Oncologic Outcomes

Point estimates with 95% CI for difference between cancer specific survival and recurrence between robotic partial nephrectomy and open or laparoscopic.

Robot vs. open
- No significant difference in cancer specific survival
- Robot had a lower recurrence rate

Robot vs. laparoscopic
- No significant difference in cancer specific survival or recurrence
## Partial Nephrectomy: Cost-Effectiveness

### Cost-effective analysis

<table>
<thead>
<tr>
<th>Source</th>
<th>Robot</th>
<th>Open</th>
<th>Lap</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mir, 2011</td>
<td></td>
<td></td>
<td>X</td>
<td>Lower LOS for lap &amp; high equipment costs for robot&lt;br&gt;Complication rates assumed to be similar across approaches</td>
</tr>
<tr>
<td>Buse, 2018</td>
<td>X</td>
<td></td>
<td></td>
<td>Lower in-hospital costs &amp; better clinical outcomes for robot&lt;br&gt;Excluded robot purchase and maintenance costs</td>
</tr>
</tbody>
</table>

### Cost studies

<table>
<thead>
<tr>
<th>Source</th>
<th>Robot</th>
<th>Open</th>
<th>Lap</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kates, 2015</td>
<td>X</td>
<td></td>
<td></td>
<td>Lower hospital charges for robot&lt;br&gt;Excluded capital costs of robot</td>
</tr>
<tr>
<td>Mano, 2015</td>
<td></td>
<td></td>
<td>X</td>
<td>Lower perioperative costs for open&lt;br&gt;Amortized capital costs of robot over 60 months</td>
</tr>
</tbody>
</table>

- ■ = approach was included in the study
- X = approach was more cost-effective/less expensive
Interim Summary: Partial Nephrectomy

<table>
<thead>
<tr>
<th></th>
<th>Robot vs open</th>
<th>Robot vs lap</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBL</td>
<td>↓</td>
<td>=</td>
</tr>
<tr>
<td>Intraop complications</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>WIT</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>OR time</td>
<td>=</td>
<td>↓</td>
</tr>
<tr>
<td>LOS</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Major complications</td>
<td>↓</td>
<td>=</td>
</tr>
<tr>
<td>GFR loss</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>CKD upstaging</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Recurrence</td>
<td>↓</td>
<td>=</td>
</tr>
<tr>
<td>CSS</td>
<td>=</td>
<td>=</td>
</tr>
</tbody>
</table>

***** Although seemingly positive results in favor the robotic approach for partial nephrectomy, the certainty of evidence is low based on data abstraction from studies with extensive limitations.
2A) What is the **clinical effectiveness** of robotic-assisted surgery compared to open or laparoscopic surgery for cystectomy?

- 5 RCTs (2 publications from the same study)
- 11 observational studies

2B) What is the **cost-effectiveness** of robotic-assisted surgery compared to open or laparoscopic surgery for cystectomy?

- 2 cost-effectiveness analyses
- 2 cost studies
Cystectomy: Intraoperative Outcomes

Point estimates with 95% CI for difference between EBL and between robotic cystectomy and open or laparoscopic.

**Robot vs. open**
- Robot had lower EBL
- Robot had longer OR time

**Robot vs. laparoscopic**
- Robot had similar EBL
- Robot had longer OR time
Cystectomy: Intraoperative Outcomes

Point estimates with 95% CI for difference between EBL and between robotic cystectomy and open or laparoscopic.

Robot vs. open
- No difference in LN harvest

Robot vs. laparoscopic
- No difference in LN harvest
Cystectomy: Intraoperative Outcomes

Point estimates with 95% CI for difference between EBL and between robotic cystectomy and open or laparoscopic.

Robot vs. open
• No difference in PSM

Robot vs. laparoscopic
• No difference in PSM
Cystectomy: Postoperative Outcomes

Point estimates with 95% CI for difference between EBL and between robotic cystectomy and open or laparoscopic.

**Robot vs. open**
- No difference in major complications
- No difference in length of stay

**Robot vs. laparoscopic**
- Limited data for length of stay or major complications but possibly favoring laparoscopy
Cystectomy: Oncologic Outcomes

Point estimates with 95% CI for difference between EBL and between robotic cystectomy and open or laparoscopic.

Robot vs. open
- No difference in RFS or Recurrence rate

Robot vs. laparoscopic
- No difference in overall recurrence
Robot vs. laparoscopic and open

- No statistically significant differences in major complications between patients treated with robot-assisted cystectomy compared to open cystectomy.

- RCT data are limited by sample size and follow-up to properly assess the long-term oncologic outcomes for robotic cystectomy versus the comparator procedures. Only 2 RCTs reported 5-year outcomes, and between them they included data on 40 robot-treated cases.
Robot vs. open or laparoscopic for four functional or cancer-specific outcomes: QoL for cancer patients receiving therapy, positive surgical margins, recurrence, and recurrence-free survival.

• With only a rare exception, no study reported statistically significant differences in any of these outcomes with robot and open or laparoscopic cystectomy.

• However, 95% CI are very wide, and clinically important differences cannot be excluded.
Summary: Cost-Effectiveness Studies

Cystectomy

- The first study used a propensity matched internal data set and did not incorporate randomized data, despite its existence.

- The second study included randomized data, but method of pooling was not well described and observational data was included. They found wide variation in estimates on sensitivity analysis. They did not include the latest RCT (RAZOR).

- While cost analysis of one study was granular and robust, the generalizability of operative time and LOS to contemporary practice is questionable.

- Further, time horizon for both studies was 90 days – too short to capture meaningful oncologic outcomes.
Summary: Partial Nephrectomy and Cystectomy

• Robotic surgery probably results in **less blood loss** than open (or laparoscopic) approaches, for both partial nephrectomy and cystectomy.

• Most other differences in outcomes probably are **small** or nonexistent (complications, lymph node sampling, warm ischemia time, etc.) however certainty of evidence is low or very low.

• **LOS may be shorter and major complications may be fewer** for robot-assisted cases of partial nephrectomy, but certainty of evidence is low.

• Procedure time for robotic cystectomy was longer (moderate certainty).

• On the important 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 evidence. Data only consider short-term outcomes and did not include long-term outcomes, including oncologic, that influence the cost/benefit ratio.
Applicability of Findings to VA Population

• No studies specific to VA populations.

• Applicability may depend on both similarity of the patients studied to VA and experience of surgical teams using the robot to VA surgical teams.

• Benefits for robotic approach may still be realized despite patient-level differences (VA patients greater burden of comorbidities), which will need to be confirmed in future studies.

• Urology as a surgical field has widely adopted robotic surgery, so the experience likely translates well to VA setting.
Research Gaps

- Need for randomized or propensity-matched data on robotic partial nephrectomy (short-term outcomes).

- Need for high quality evidence with long-term follow-up and statistical power to assess cancer outcomes for both partial nephrectomy and cystectomy.

- Despite what appears to better or equivalent technical outcomes for cystectomy and likely partial nephrectomy, acceptable functional outcomes need to be confirmed.
  - Kidney function for kidney cancer
  - Quality of life for bladder cancer

- Better quality cost-effectiveness studies are warranted – how to balance clinical benefits with increased cost of the procedure and perhaps savings (decreased blood loss, LOS).
## Acknowledgements

### Our Team
- Paul Shekelle
- Melinda Maggard-Gibbons
- Mark Girgis
- Christopher Childers
- Amber Tang
- Qiao Ruan
- Margherita Lamaina
- Selene Mak
- Meron Begashaw
- Marika Booth

### Operational Partners
- Mark Wilson
- William Gunnar

### Technical Expert Panel
- John Gore
- Jim Hu
- Mark Jordan
- John Leppert
- Joe Liao
- Matthew Rettig
- Kevin Win
If you have further questions, please feel free to contact:

Melinda Gibbons, MD, MSHS  
Melinda.Gibbons@va.gov

Mark Girgis, MD  
Mark.Girgis@va.gov

Full-length report and cyberseminar available on ESP website:

http://www.hsrд.research.va.gov/publications/esp/

This report is based on research conducted by the West Los Angeles Evidence Synthesis Program (ESP) Center, funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (e.g., employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.
Supplementary Materials
## Certainty of Evidence: Partial Nephrectomy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Certainty of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intraoperative outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraoperative complications</td>
<td>High</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Low</td>
</tr>
<tr>
<td>Robot = open/lap</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operating room time</td>
<td>High</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Very low</td>
</tr>
<tr>
<td>Robot = open/lap</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated blood loss</td>
<td>High</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Moderate</td>
</tr>
<tr>
<td>Robot &lt; open/lap</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warm ischemia time</td>
<td>High</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Very Low</td>
</tr>
<tr>
<td>Robot = open/lap</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Post-operative outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major complications</td>
<td>High</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Low</td>
</tr>
<tr>
<td>Robot &lt; open</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major complications</td>
<td>High</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Low</td>
</tr>
<tr>
<td>Robot = lap</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of stay</td>
<td>High</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Low</td>
</tr>
<tr>
<td>Robot &lt; open/lap</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Functional/Cancer Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All outcomes</td>
<td>High</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Very low</td>
</tr>
</tbody>
</table>
## Certainty of Evidence: Cystectomy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Certainty of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intra-operative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood Loss</td>
<td>RCT: Low</td>
<td>Consistent</td>
<td>Direct</td>
<td>Precise</td>
<td>High</td>
</tr>
<tr>
<td>Robot &lt; Open</td>
<td>Observational studies: High</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph Node Sampling</td>
<td>RCT: Low</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Low</td>
</tr>
<tr>
<td>Robot = Open</td>
<td>Observational studies: High</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operating Room Time</td>
<td>RCT: Low</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Moderate</td>
</tr>
<tr>
<td>Robot &gt; Open</td>
<td>Observational studies: High</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All comparisons to laparoscopic</td>
<td>RCT: Low</td>
<td>N/A</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Very Low</td>
</tr>
<tr>
<td>surgery</td>
<td>Observational studies: High</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Post-operative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major complications</td>
<td>RCT: Low</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Moderate</td>
</tr>
<tr>
<td>Robot = Open</td>
<td>Observational studies: High</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genitourinary complications</td>
<td>RCT: Low</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Moderate</td>
</tr>
<tr>
<td>Robot = Open</td>
<td>Observational studies: High</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of Stay</td>
<td>RCT: Low</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Moderate</td>
</tr>
<tr>
<td>Robot = Open</td>
<td>Observational studies: High</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All comparisons to laparoscopic</td>
<td>RCT: Low</td>
<td>N/A</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Very low</td>
</tr>
<tr>
<td>surgery</td>
<td>Observational studies: High</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Functional/Cancer Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All outcomes</td>
<td>RCTs: Low to High depending on</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Observational studies: High</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The cost effectiveness of robotic surgery for either partial nephrectomy or cystectomy is uncertain.

Different studies reaching different conclusions depending on how the fixed and variable costs of the robot were considered and how health outcomes (benefits or complications) were measured and valued.

Cost effectiveness data to date only consider short term outcomes and do not include longer term outcomes, including oncologic, that influence the cost/benefit ratio.