Positive surgical margins in partial nephrectomy specimens: Urologist view

Ofer Nativ MD
Financial and Other Disclosures

- Off-label use of drugs, devices, or other agents: None or FILL IN HERE; including your local regulatory agency, such as FDA, EMA, etc.
- Data from IRB-approved human research is presented [or state: “is not”]

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<th>I have the following financial interests or relationships to disclose:</th>
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<td>Pfizer</td>
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In recent years, NSS for renal tumors has replaced RN as the standard procedure for treating localized RCC.

This change in surgical practice have resulted in increased rate of PSM.

The clinical relevance of PSM remains controversial.
Points for consideration

- Definition.
- Determination.
- Rate.
- Risk factors.
- Clinical implications.
- How to avoid PSM.
- Management.
Risk factors for positive surgical margins
Tumor related risk factors

- Size (both large and small tumors).
- Stage.
- Superior pole location (for MIPN).
- High grade.
- Complete pseudocapsule penetration.
- Papillary and chromophobe types.
- High complexity.
- Multiple/Bilateral lesions.
A Prospective, Multicenter Evaluation of Predictive Factors for Positive Surgical Margins After Nephron-Sparing Surgery for Renal Cell Carcinoma: The RECORd1 Italian Project

- 800 pts.
- 4.9% PSM.
- 2009-2012.
- 19 centers.

**Table 4** Multivariable Logistic Regression Models Accounting for the Significant Predictors of PSM

<table>
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<tr>
<th>Multivariate Analysis for PSM</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
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<tbody>
<tr>
<td>Continuous Variable, Age, Year</td>
<td>1.04</td>
<td>1.00-1.08</td>
<td>.01</td>
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<tr>
<td>Polar Superior Lesion Tumor Site versus Others</td>
<td>2.85</td>
<td>1.37-5.87</td>
<td>.005</td>
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<tr>
<td>Standard PN Technique versus SE</td>
<td>3.45</td>
<td>1.66-7.19</td>
<td>.004</td>
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<tr>
<td>Open Approach versus Minimally Invasive Approach</td>
<td>1.36</td>
<td>0.58-3.19</td>
<td>.48</td>
</tr>
<tr>
<td>Nuclear Grade 3/4 versus 1/2</td>
<td>4.81</td>
<td>1.63-14.16</td>
<td>.001</td>
</tr>
</tbody>
</table>

Schiavina R et al’*, Clinical Genitourinary Cancer, 2015
Parenchymal – tumor interface

Intact PC

Absent PC
Parenchymal – tumor interface

Complete PC invasion

Partial PC invasion
Surgery related risk factors

- Open vs Minimally invasive.
- Enucleation vs partial nephrectomy.
- Clamped vs off-clamped (↑bleeding).
- Teaching programs (un-experience surgeons).
- Academic vs community institutes.
- Solitary kidney.
- Imperative indication.
- African American.
The PSM rate ↑ over time in all pts and in those with APF.

Time, older age, larger tumor, community hospital, and robotic approach were associated with PSM in the setting of APF.

Maurice MJ et al’, BJUI, 2015
Utilization and quality outcomes of cT1a, cT1b and cT2a partial nephrectomy: analysis of the national cancer database

- Retrospective analysis.
- US NCDB.
- 43,749 PNs.
- 6.8% PSM.

Trends in PSM for cT1a, cT1b, cT2a

cT1a - 6.9%, cT1b - 6.5%, cT2a - 6.25%

Fero K et al”, BJUI, 2017
Trends in PSM: 2010 - 2013

PSM increased from 6.8% to 7.3%

Use of MIPN stratified by clinical stage

“...higher stage was not the main driver in terms of risk of PSMs, but rather it was the Increased adoption of minimally invasive approaches”
Objective: To assess the relationship of race and margin status in patients undergoing RPN for T1 renal tumors.

Methods: Using the National Cancer Database, 12,515 patients with cT1 lesions treated between 2010-2013 were identified.

Results: PSM was 7.9% for white pts, 8.8% for hispano/latino pts and 10.8% for AA pts. In multivariate analysis AA pts and treatment at non-academic center were associated with PSM.

Chen VS et al’, Urol Oncol, 2017
Clinical implications of positive surgical margins
Clinical implications of PSM

• Variables studied:
  – Local recurrence.
  – Distant metastases.
  – Cancer-specific survival.
  – Overall survival.

• The clinical and oncologic impact of PSMs after NSS is controversial.
Clinical implications of PSM

Kidney Cancer

Positive Surgical Margin Appears to Have Negligible Impact on Survival of Renal Cell Carcinomas Treated by Nephron-Sparing Surgery

*Bensalah K et al*, *Eur Urol*, 2010

Positive Surgical Margins Increase Risk of Recurrence after Partial Nephrectomy for High Risk Renal Tumors

*Shah PS et al*, *J Urol*, 2016
• Multicenter retrospective study.
• 111 patients with PSM were compared with 664 NSM patients.
• A second cohort of NSM patients was created by matching NSM to PSM for tumor size, grade and indication.
• End points:
  - LR.
  - Cancer-specific survival.
PSM following NSS may be associated with an increased risk of recurrence; however, it does not appear to influence cancer-specific survival.
A retrospective multi-institutional study of 1,240 patients undergoing PN between 2006 and 2013.

A positive margin was associated with an increased risk of relapse on multivariable analysis (HR 2.08)
A retrospective single institution study.

1863 RCC pts underwent PN (1990-2015).

1,8% PSM.

A 1:3 (34:100) matching was performed to a NSM cohort.

Median F-U: 62 months.

End points:
  – Predictors of PSM.
  – LR, Progression and survival.
Clinical outcome of pts with and without PSM after NSS

OS

LR

Free survival

Distant Mets

Free survival

Mets

Free survival
How to avoid positive surgical margins
How to avoid PSM

- A thorough understanding of surgical anatomy.
- Careful review of the pre-op. imaging.
- Use of simulators.
- Avoid intra-operative bleeding.
- Intraoperative US to delineate tu’ anatomy.
- Intraoperative FS from the tumor bed (?).
- Fulguration of the resection bed by cautery or by argon-beam coagulator.
Review of the pre-op. imaging
Review of the pre-op. imaging

Axial

Coronal
CT-based reconstruction of a 3-D model of left renal mass

Surgical planning and manual image fusion based on 3D model facilitate laparoscopic partial nephrectomy for intrarenal tumors
Virtual simulation on the model

3D image superimposed on the 2D laparoscopic image
Intra-operative image guided surgery
Utility of patient-specific silicone renal models for planning and rehearsal of complex tumour resections prior to robot-assisted laparoscopic partial nephrectomy.

A patient specific 3D model is reconstructed on the basis of the preop imaging.

A 3-D model of the kidney and tumor is then printed using mixtures of silicone rubber.

A standard lap trainer box and robotic instruments is used for the simulation.

von Rundstedt FC et al’, BJUI, 2016
Management of Positive surgical margins
Algorithm for management of PSM

PSM

Intra-op
  Resect tu’ bed

Post-op
  Observe
    LR
      Ablation
    Systemic Prog.
      TT/IO/Sx
    No rec.
      Observe
Summary

- PSM is relatively rare.
- PSM is associated with higher risk of local recurrence.
- PSM may impact progression and cancer survival, mainly in high risk cases.
- Efforts should be made to avoid PSM.
- Close F-U is recommended for cases with PSM that are detected postoperatively.
Thanks