The Natural History of Breast Cancer Related Lymphedema

Stav Brown MD, Joseph H. Dayan MD MBA, Michelle Coriddi MD, Lilian Boe PhD, Andrea Barrio MD, Babak J. Mehrara MD

Plastic & Reconstructive Surgery Division
Department of Surgery, Memorial Sloan Kettering Cancer Center

101st Meeting, May 1st, 2022, Chicago, IL
Speaker Financial Disclosure: Stav Brown

Payments of any denomination – public record on Open Payments Site

General Payments – None
Research Payments – None
Ownership and Investment Interest – None
Associated Research – None
The rate of lymphedema progression is highly variable

6 months
RVC=1.3%

12 months
RVC=3.2%

18 months
RVC=5.0%
The rate of lymphedema progression is highly variable

6 months  
RVC=44.9%

12 months  
RVC=52.5%

18 months  
RVC=79.6%
Current prediction models for lymphedema development

A model to estimate the risk of breast cancer-related lymphedema: combinations of treatment-related factors of the number of dissected axillary nodes, adjuvant chemotherapy, and radiation therapy

Current prediction models for lymphedema development

Development and Validation of an Intraoperative Nomogram to Predict Breast Cancer–Related Lymphedema Based on the Arm Lymphatic Distribution
Qiangqian Yuan 1, Jinxuan Hou 1, Rui Zhou 1, Yiqin Liao 2, Lewei Zheng 2, Chong Jiao 2, Wenbo Zhou 3, Gaoqiang Wu 4

Development and Validation of a Nomogram to Predict Lymphedema After Axillary Surgery and Radiation Therapy in Women With Breast Cancer From the NCIC CTG MA.20 Randomized Trial
Jeffrey P Gross 1, Timothy J Whelan 2, Wendy R Pecorelli 1, Bingshu E Chen 3, Alfred W Rademaker 4, Irene B Hiebert 2, Eric D Donnelly 4, Jonathan B Strauss 4

Risk of Lymphedema Following Contemporary Treatment for Breast Cancer: An Analysis of 7617 Consecutive Patients From a Multidisciplinary Perspective
Hwa Kyung Byun 1, Jee Suk Chang 1, Sang Hye Im 2, Youla M Kirou 3, 4, Alexandre Arsene-Henry 3, Seo Hye Choi 7, Young Up Cho 2, Huyong Soek Park 2, Jee Ye Kim 8, Chang-Ock Sun 9, 7, Ki Chang Keum 2, Joo Hyuk Sohn 7, Gun Min Kim 7, & Jae Lee 7, Jun Woong Kim 8, Yong Bae Kim 7

Risk factors for arm lymphedema following breast cancer surgery: a Japanese nationwide database study of 84,022 patients
Takaaki Kenishi 1, 2, Masahiko Tanabe 1, Nobusuke Michihara 4, 3, Hidoki Matsui 4, Kotaro Nishihara 2, Kiyohide Fushimi 4, Yasuyuki Sato 4, Hideo Yasunaga 5

Nomograms for predicting the risk of arm lymphedema after axillary dissection in breast cancer
José Luis B Bevilacqua 1, Michael W Kattan, Yu Changheng, Sergio Kollman, Ihsa E Mattos, Rosalina J Kollman, Anke Bergmann

Validation of a nomogram for predicting the risk of lymphedema following contemporary treatment for breast cancer: a large multi-institutional study (KROG 20-05)
Hwa Kyung Byun 1, Jee SukKim 2, Jee Suk Chang 1, Yeone Cho 3, Sung-Jae Ahn 4, Jung HanYoun 5, HyeYoung Kim 6, HaeKe Kim 6, EunChul Cho 7, HyoYoung Park 8, KyuBo Kim 9, Shin-HyoungPark 10, Chai-Hyon Kim 11, Hoon Ho 12, Kyun Yong Oh 13, & Jee Lee 1, Kyung Hoon Shin 14, Yong Bae Kim 7

Breast cancer–related lymphoedema: Risk factors and prediction model
Patricia Martinez-Jimenez 1, 2, Mariana Amorosa Verde 3, Carlos G Forens 4, Samantha Álvarez Salazar 4, Pilar Fuster Linares 4, Cristina Montforte-Royo 2, Jeane Masala 2, 9

Risk factors for lymphedema following breast cancer surgery: a Japanese nationwide database study of 84,022 patients
Takaaki Kenishi 1, 2, Masahiko Tanabe 1, Nobusuke Michihara 4, 3, Hidoki Matsui 4, Kotaro Nishihara 2, Kiyohide Fushimi 4, Yasuyuki Sato 4, Hideo Yasunaga 5

Breast cancer–related lymphoedema: Risk factors and prediction model
Patricia Martinez-Jimenez 1, 2, Miriam Amorosa Verde 3, Carlos G Forens 4, Samantha Álvarez Salazar 4, Pilar Fuster Linares 4, Cristina Montforte-Royo 2, Jeane Masala 2, 9

Affiliations 4 expand
Aims

1. Analyze the **natural history of BCRL** after ALND
2. Identify **predictive variables that regulate the trajectory** of the disease
3. Develop a **prediction model for volume changes** over time
Methods

Prospective longitudinal study

- **Inclusion criteria:** All patients undergoing ALND

- **Study Timeline:**

  - Baseline measurements
  - ALND
  - 6 month follow up
  - 12 month follow up
  - 18 month follow up
  - 24 month follow up
Methods

Analysis

• RVC = \( (A_2 U_1 / U_2 A_1) - 1 \)
• Four disease trajectories:

<table>
<thead>
<tr>
<th>Trajectory</th>
<th>I - No disease</th>
<th>II - Mild</th>
<th>III - Moderate</th>
<th>IV - Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVC</td>
<td>&lt;5%</td>
<td>5-10%</td>
<td>10-20%</td>
<td>&gt;20%</td>
</tr>
</tbody>
</table>

• Ordinal logistic regression model.
## Results

### Demographic and clinical information

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N = 255&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>27.1 (5.8)</td>
</tr>
<tr>
<td>Follow up</td>
<td>32.7 (6)</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>39.4%</td>
</tr>
<tr>
<td>Age</td>
<td>49 (11)</td>
</tr>
<tr>
<td>Affected arm is dominant</td>
<td>115 (45%)</td>
</tr>
<tr>
<td>Baseline Volume Differential</td>
<td>0.5 (5.1)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>168 (66%)</td>
</tr>
<tr>
<td>Asian</td>
<td>30 (12%)</td>
</tr>
<tr>
<td>Black/African American</td>
<td>57 (22%)</td>
</tr>
<tr>
<td>Total nodes removed</td>
<td>19 (8)</td>
</tr>
<tr>
<td>Lymphatic therapy</td>
<td>17 (6.7%)</td>
</tr>
<tr>
<td>Compression sleeve</td>
<td>14 (5.5%)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>176 (69%)</td>
</tr>
</tbody>
</table>

<sup>1</sup>Mean (SD); n (%)
# Model 1

RVC-based cumulative logit model

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR(^1)</th>
<th>95% CI(^1)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI(^2)</td>
<td>1.03</td>
<td>0.98, 1.08</td>
<td>0.2</td>
</tr>
<tr>
<td>Age</td>
<td>1.02</td>
<td>1.00, 1.05</td>
<td>0.041</td>
</tr>
<tr>
<td><strong>Affected Dominant</strong></td>
<td>0.58</td>
<td>0.34, 0.99</td>
<td>0.047</td>
</tr>
<tr>
<td><strong>BVD(^3)</strong></td>
<td>0.93</td>
<td>0.88, 0.98</td>
<td>0.012</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Asian</td>
<td>1.16</td>
<td>0.47, 2.71</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>African American</strong></td>
<td>2.34</td>
<td>1.24, 4.41</td>
<td>0.008</td>
</tr>
<tr>
<td>Total nodes removed</td>
<td>1.02</td>
<td>0.99, 1.06</td>
<td>0.2</td>
</tr>
<tr>
<td>Lymphatic Therapy</td>
<td>0.78</td>
<td>0.26, 2.10</td>
<td>0.6</td>
</tr>
<tr>
<td>Compression sleeve</td>
<td>0.90</td>
<td>0.26, 2.72</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Neoadjuvant chemotherapy</strong></td>
<td>1.82</td>
<td>1.03, 3.29</td>
<td>0.042</td>
</tr>
</tbody>
</table>

\(^1\)OR = Odds Ratio, CI = Confidence Interval  
\(^2\)Body mass index  
\(^3\)Baseline volume differential
Model 2
Prediction Equation - generalized estimating equation (GEE) approach

Patient 1
- 57 years old
- Caucasian
- BMI of 35
- BVD of 1%
- Affected is dominant
- No chemotherapy
- 12 nodes removed
- No physical therapy
- No sleeve
Model 2

Prediction Equation - generalized estimating equation (GEE) approach

**Patient 2**

- 57 years old
- **African American**
- BMI of 35
- BVD of 1%
- **Affected not dominant**
- **Chemotherapy**
- 12 nodes removed
- No physical therapy
- No sleeve
Model 2

Prediction Equation - generalized estimating equation (GEE) approach

\[ R^2_{\text{marg}} = 0.132 \]

RVC = 1.33%  
RVC = 8.19%
Conclusions

• Largest study to analyze the predictive factors associated with severe disease trajectory

• First study to provide a prediction equation of arm volume measurements

• The role of racial disparities in lymphedema

• Can be used to implement preventative strategies in high-risk patients.
Acknowledgments

Babak J. Mehrara, MD
Andrea Barrio, MD
Joseph H. Dayan, MD
Michelle Coriddi, MD
Lillian Boe PhD
Raghu P. Kataru, PhD