Management of the Recurrent Laryngeal Nerve at the Ligament of Berry: Implications for the patient, endocrinologist and surgeon

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I have nothing to disclose
Recurrent Laryngeal Nerve: Embryology

- **Thyroid**: fusion of the medial thyroid anlage (derived from the primitive pharynx) and the lateral thyroid anlage (derived from the neural crest)

- **The tubercle of Zuckerkandl**: represents this fusion site, a posterior lateral projection from the thyroid \(^1,2\)

- **Superior parathyroid gland** originates from the fourth branchial pouch of the primitive pharynx \(^3\)

- **RLN**: arises from the vagus nerve and carries motor, sensory, and parasympathetic fibers
Recurrent Laryngeal Nerve: Anatomy

a: superior parathyroid gland
b: tubercle Zuckerlandl
c: superior pole of thyroid gland
d: RLN
n: inferior thyroid artery
p: superior thyroid muscles
s: approximate level of entry RLN beneath cricopharyngeus
t: superficial vascular fascial layer containing branches inferior thyroid artery overlying the RLN

Serpell JW, Annals of surgical oncology. 2010
Recurrent Laryngeal Nerve: Anatomy

- **a**: superior parathyroid gland
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Recurrent Laryngeal Nerve: Anatomy
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Randolph, 2016
Recurrent Laryngeal Nerve: Anatomy

Randolph GW, 2016
Non Recurrent Recurrent Laryngeal Nerve: Anatomy

Illustration Netter
Photo courtesy of Nathan Hales
Recurrent Laryngeal Nerve: Branching

Left RLN

Courtesy of Nathan Hales
Recurrent Laryngeal Nerve: Approaches

Randolph et al, 2013
Ligament of Berry: Anatomy

Randolph, 2016
Recurrent Laryngeal Nerve: Risk of Injury

- Subjective post-thyroidectomy voice complaints occur in 30-87%.
- Traditionally quoted rates of RLN injury (3-5%) significantly underestimate the true incidence, which is likely closer to 10%.\textsuperscript{9-10}
- EBSLN injury remains unknown, it may be as high as 58%.\textsuperscript{11-12}
Recurrent Laryngeal Nerve: Inconsistencies?

- Lack of standardization of postoperative laryngeal examination practices
- Reporting biases from large thyroid centers where complication rates are low
- High incidence of concurrent LPR (acid reflux)
- Subtlety and variability of nerve paralysis symptoms. 13-16
Recurrent Laryngeal Nerve Injury: Symptoms

Unilateral
- dyspnea from air escape
- dysphonia (hoarseness, vocal fatigue, breathy voice)
- dysphagia with potential aspiration.

Bilateral
- Stridor
- respiratory distress
- airway compromise due to obstruction

EBSLN injury
- voice fatigue
- changes in vocal range
- pitch changes
ATA Guidelines 2015: RECOMMENDATION 40

All patients undergoing thyroid surgery should have preoperative voice assessment as part of their preoperative physical examination. This should include the patient’s description of vocal changes, as well as the physician’s assessment of voice.
ATA Guidelines 2015: RECOMMENDATION 41

Preoperative laryngeal exam should be performed in all patients with:
(A) Preoperative voice abnormalities
(B) History of cervical or upper chest surgery, which places the RLN or vagus nerve at risk
(C) Known thyroid cancer with posterior extrathyroidal extension or extensive central nodal metastases
“I have noticed in operations of this kind, which I have seen performed by others upon the living, and in a number of excisions, which I have myself performed on the dead body, that most of the difficulty in the separation of the tumor has occurred in the region of these ligaments….This difficulty, I believe, to be a very frequent source of that accident which so commonly occurs in removal of goiter, I mean division of the recurrent laryngeal nerve.” Berry (1887)
Types of nerve injury

1. Traction (neuropraxia) at points of relative nerve fixation
2. Compression from a ligature, clip, surgical instrument or crossing taut blood vessel
3. Direct sharp or thermal trauma

Generally, only the latter remains as potentially a permanent RLN injury
## RLN monitoring

<table>
<thead>
<tr>
<th>Study</th>
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<th>Transient Injury</th>
<th>Permanent Injury</th>
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<tr>
<td>Higgins et al 2011 (^{17})</td>
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<td>Lombardi et al 2016 (^{21})</td>
<td>14 articles</td>
<td></td>
<td>no</td>
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Revision cases, pre operative unilateral cord paralysis, large substernal goiters, patient or endocrinologist request
Risk of Injury: Does Surgeon Volume Matter?

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<th>Surgeon Volume</th>
<th>Increase in odds of complication</th>
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<td>1 case/year</td>
<td>87%</td>
</tr>
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<td>(51% of total)</td>
<td></td>
</tr>
<tr>
<td>2-5 cases/year</td>
<td>68%</td>
</tr>
<tr>
<td>6-10 cases/year</td>
<td>42%</td>
</tr>
<tr>
<td>11-15 cases/year</td>
<td>22%</td>
</tr>
<tr>
<td>16-20 cases/year</td>
<td>10%</td>
</tr>
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<td>21-25 cases/year</td>
<td>3%</td>
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Median 7 cases /year

16,954 patients TT

Adam et al, 2016

23
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<td>2-5 cases/year</td>
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<td>6-10 cases/year</td>
<td>&gt;26 thyroidectomies / year (P &lt; 0.01)</td>
</tr>
<tr>
<td>11-15 cases/year</td>
<td>22%</td>
</tr>
<tr>
<td>16-20 cases/year</td>
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Median 7 cases /year

Adam et al, 2016
Risk of Injury: Does Surgeon Volume Matter?

Highest volume thyroid surgeons = >100 thyroidectomies / year
perform 5% of all thyroidectomies in the US (90% are white)

Sosa et al, 2007

16,878 patients
Why does all this matter to the Endocrinologist?

Patient Satisfaction and Outcomes Matter

Preventing Complications
- RLN injury
- Hypoparathyroidism

Improved Outcomes
- Residual Disease
Case 1: Mary Ann

52 year old female with a 2 cm papillary thyroid cancer undergoes a total thyroidectomy at an outside hospital. She reports dysphonia and coughing in the recovery room. She is noted to have severe dysphagia and aspiration. Her PTH post op is <10. She develops symptomatic hypoparathyroidism 24-48 hours post op which worsens over the next 5 days. She spends 10 days in the hospital and 3 weeks in a rehab center due to her complications. She presents to the office seeking options for voice and swallow restoration. She remains on daily calcium supplements.
Case 1: Mary Ann
Case 1: Mary Ann, Complications

- Left Recurrent nerve injury
  - dysphonia
  - dysphagia
  - aspiration
- Hypoparathyroidism permanent
- Prolonged hospital stay
- Residual disease
RECOMMENDATION 42:

(A) Visual identification of the RLN during dissection is required in all cases.
Why does all this matter to the Endocrinologist?

- Preventing Complications
  - RLN injury
  - Hypoparathyroidism
  - Residual disease
Identifiable areas of uptake as seen on single photon emission computerized tomography-computed tomography (SPECT-CT) post total thyroidectomy.

Zeuren et al, 2015
Identifiable areas of uptake as seen on single photon emission computerized tomography-computed tomography (SPECT-CT) post total thyroidectomy.

Zeuren et al, 2015

- 79%
- 46%
- 87%
BRAF and RAI

BRAF + \(\downarrow\) sodium-iodine symporter expression \(\downarrow\) RAI uptake

Chakravarty D et al, 2011
**BRAF and RAI**

<table>
<thead>
<tr>
<th>134 patients</th>
<th># of patients</th>
<th>Macroscopic recurrence</th>
<th>Stim Tg &gt;1</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAI (30mCi)</td>
<td>97</td>
<td>2.6%</td>
<td>13% **</td>
</tr>
<tr>
<td>BRAF +</td>
<td>39</td>
<td>2.6%</td>
<td></td>
</tr>
<tr>
<td>BRAF -</td>
<td>58</td>
<td>1.7%</td>
<td>1.7%</td>
</tr>
<tr>
<td>No RAI</td>
<td>37</td>
<td>0 (24% BRAF +)</td>
<td></td>
</tr>
</tbody>
</table>

Small study, lack of randomization
Role of molecular testing in guiding post operative RAI is yet to be firmly established

Elisei et al 2012
BRAF and RAI

BRAF + \(\downarrow\) sodium iodine symporter expression \(\downarrow\) RAI uptake
BRAF and RAI

It has NEVER been so important to choose wisely the right surgeon and obtain a complete and safe surgery….post op RAI may not salvage inadequate surgery in BRAF + patients.
<table>
<thead>
<tr>
<th>Study</th>
<th>Primary Surgery</th>
<th>Revision Surgery</th>
<th>Risk of RLN injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yarbrough et al 2004</td>
<td>2%</td>
<td>12%</td>
<td>Risk of RLN injury</td>
</tr>
<tr>
<td>Martensson et al 1985</td>
<td></td>
<td>14%</td>
<td>Risk of RLN injury</td>
</tr>
<tr>
<td>Beahrs et al 1963</td>
<td></td>
<td>8% / 22%</td>
<td>Benign ds</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12% / 36%</td>
<td>Malignant ds</td>
</tr>
<tr>
<td>Matthias et al 2009</td>
<td>6.2%</td>
<td>11.6%</td>
<td>Risk of RLN injury</td>
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Parathyroid risk? ↑↑↑
1. Management of the RLN at the Ligament of Berry is complex and key to safe and successful thyroid surgery. It matters to the patient…it matters to the endocrinologist…..it matters to the surgeon

2. Complications rates are increased in revision cases.

3. Surgeon experience and volume matters. Am I referring my patients to the most qualified surgeon?

4. With emerging evidence suggesting post op RAI resistance in BRAF positive disease complete and thorough surgery, the first time, has never been more important.


8. Medial approach to the recurrent laryngeal nerve. Courtesy of Dave Aten, Illustrator and Mark Zafereo


31. Matthias Echternach, MD; Christoph Maurer, MD; Thomas Mencke, MD, Martin Schilling, MD; Thomas Verse, MD; Bernhard Richter, MD. Laryngeal Complications After Thyroidectomy Is It Always the Surgeon? Arch Surg. 2009;144(2):149-153.
Racial Disparities in Clinical and Economic Outcomes in Thyroid Surgery

<table>
<thead>
<tr>
<th>Race</th>
<th>16,878 patients</th>
<th>LOS</th>
<th>In hospital mortality</th>
<th>Overall Complication rates</th>
<th>Total costs (per patient)</th>
<th>Surgery Low Volume Surgeons (1-9 cases/yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>71%</td>
<td>1.8 days</td>
<td>0.1%</td>
<td>3.8%</td>
<td>$5447</td>
<td>44%</td>
</tr>
<tr>
<td>Black</td>
<td>14%</td>
<td>2.5 days</td>
<td>P&lt;.001</td>
<td>0.4%</td>
<td>$6587</td>
<td>52%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>9%</td>
<td>2.2 days</td>
<td>0.1%</td>
<td>3.6%</td>
<td>$6294</td>
<td>55%</td>
</tr>
<tr>
<td>Other</td>
<td>6%</td>
<td></td>
<td></td>
<td></td>
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Highest Volume surgeons (>100 cases per year) = 5% of thyroidectomies = 90% where white (p<0.001)

Sosa et al, 2007