Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Onkoplastische und rekonstruktive Mammachirurgie
**Pubmed 2003 - 2017**

Cochrane data base (z.B. Cochrane Breast Cancer Specialised Register)

Suchbegriffe: breast reconstruction; ... AND random allocation, ... AND cohort study

**Einteilung in EBM-Grade nach**


**Verwendete Guidelines zu Diagnostik und Therapie des Mammakarzinoms**

National Institute of Health (NIH) – National Cancer Institute:
http://www.cancer.gov/cancertopics/pdq/treatment/breast/HealthProfessional/

American Association of Clinical Oncology (ASCO) and Technology Assessments:
http://www.asco.org/portal/site/ASCO/menuitem. (Practice Guidelines),
Japanese Medical Association (CMA): http://www.cmaj.ca/cgi/content/full/158/3/DC1
NCCN 2016
Regeln zur Überarbeitung der AGO Empfehlungsdiagramm Stand 01/ 2019


3. Optimizing breast cancer adjuvant radiation and integration of breast and reconstructive surgery. Kuerer H, et al. ASCO Educational Book 2017; Memorial Sloan Kettering Cancer Center, Fig. 2 und 3

1. AWMF Leitlinien: S3-LL. Brustrekonstruktion mit Eigengewebe. Registernummer 015 – 075, Stand: 01.04.2015 , gültig bis 31.03.2020


7. Prosthetic breast reconstruction in previously irradiated breasts: A meta-analysis. Lee KT, Mun GH. J


19. Patient-reported cosmetic satisfaction and the long-term association with quality of life in irradiated breast cancer patients.


**Possible Associations between Implants and rare Diseases**

- US FDA Breast Implant Postapproval Studies (LPAS)
  *Long-term Outcomes in 99,993 Patients*
  *(Primary Augmentation: N= 71,937 / Primary Reconstruction: N= 9942)*
  - 56% of implants were silicone implants

- Possible Associations:
  - Sjogren syndrome: (SIR 8.14)
  - Scleroderma: (SIR 7.00)
  - Rheumatoid arthritis: (SIR 5.96)
  - Stillbirth: (SIR 4.50)
  - Melanoma: (SIR 3.71)

- At 7 years, reoperation rate is 11.7% for primary augmentation, and 25% for primary/revision reconstruction.

- One case of Bf-ALCL

Associations need to be further analyzed with patient-level data to provide conclusive evidence.

---

**New Background slide**

**Statistical Analysis:**

LPAS data is expressed relative to normative population rates using standardized incidence ratios (SIRs).

Systemic harm rates in the study population are calculated per 10,000 person-years.

Normative population rates for systemic harms, self-harm, and reproductive outcomes are obtained from the literature; rates reflect LPAS demographics for female sex, age, and race in the United States.

### Possible Associations between Implants and rare Diseases

#### Rare Systemic Harms Compared With the General Population:

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Study Events</th>
<th>Study Event Rate (Per 10,000 Person Yr)</th>
<th>General Population Event Rate (Per 10,000 Person Yr)</th>
<th>SIR</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fibromyalgia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergan</td>
<td>9</td>
<td>1.8</td>
<td>112.8</td>
<td>0.02</td>
<td>0.01-0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mentor</td>
<td>36</td>
<td>28.4</td>
<td>112.8</td>
<td>0.25</td>
<td>0.22-0.28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergan</td>
<td>4</td>
<td>0.8</td>
<td>5.4</td>
<td>0.15</td>
<td>0.04-0.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mentor</td>
<td>34</td>
<td>32.2</td>
<td>5.4</td>
<td>5.96</td>
<td>5.35-6.62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>46</td>
<td>4.2</td>
<td>0.6</td>
<td>7.00</td>
<td>5.12-9.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sjogren syndrome</td>
<td>62</td>
<td>5.7</td>
<td>0.7</td>
<td>5.14</td>
<td>6.24-10.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>3</td>
<td>0.6</td>
<td>5.4</td>
<td>0.11</td>
<td>0.02-0.33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mentor</td>
<td>66</td>
<td>6.0</td>
<td>5.4</td>
<td>1.11</td>
<td>0.86-1.41</td>
<td>0.398</td>
</tr>
<tr>
<td>Cancer</td>
<td>80</td>
<td>16.0</td>
<td>43.3</td>
<td>0.39</td>
<td>0.31-0.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allergan</td>
<td>532</td>
<td>63.8</td>
<td>43.3</td>
<td>1.54</td>
<td>1.42-1.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>116</td>
<td>13.9</td>
<td>12.1</td>
<td>1.11</td>
<td>0.92-1.33</td>
<td>0.26</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>5</td>
<td>0.6</td>
<td>5.2</td>
<td>0.12</td>
<td>0.04-0.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Brain cancer</td>
<td>3</td>
<td>0.4</td>
<td>0.8</td>
<td>0.67</td>
<td>0.14-1.90</td>
<td>0.639</td>
</tr>
<tr>
<td>Melanoma</td>
<td>65</td>
<td>7.8</td>
<td>2.1</td>
<td>3.71</td>
<td>2.87-4.73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neurological disorder</td>
<td>18</td>
<td>3.6</td>
<td>22.3</td>
<td>0.16</td>
<td>0.09-0.25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allergan</td>
<td>394</td>
<td>35.8</td>
<td>22.5</td>
<td>1.59</td>
<td>1.44-1.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>47</td>
<td>4.3</td>
<td>2.5</td>
<td>1.72</td>
<td>1.06-2.29</td>
<td>0.041</td>
</tr>
<tr>
<td>Myasthenia</td>
<td>17</td>
<td>1.5</td>
<td>0.8</td>
<td>1.88</td>
<td>1.05-3.80</td>
<td>0.038</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Study Events</th>
<th>Study Event Rate (Per 10,000 Person Yr)</th>
<th>General Population Event Rate (Per 10,000 Person Yr)</th>
<th>SIR</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergan</td>
<td>9</td>
<td>1.8</td>
<td>112.8</td>
<td>0.02</td>
<td>0.01-0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mentor</td>
<td>36</td>
<td>28.4</td>
<td>112.8</td>
<td>0.25</td>
<td>0.22-0.28</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### New Background slide

Brust-Implantat-assoziiertes großzellig-anaplastisches Lymphom (BIA-ALCL)

- Selten, 3% aller Non-Hodgkin-Lymphome, 0,04–0,5% aller malignen Brusterkrankungen
- geschätzte jährliche Inzidenz 0,6–1,2 je 100,000 Frauen mit Implantaten (medianes Patientenalter 54 J.)
- Auftreten überwiegend bei texturierten Implantaten
- 5-Jahres-OAS 89%
- Intervall zur Lymphomdiagnose: 8 Jahre (Median)
- Klinische Präsentation
  - Schwellung und Serom (60%)
  - Tumoröse Raumforderung (17%)
  - Serom und Raumforderung (20%)
- Histologisch: CD30+/ALK-T-Zell-Lymphom
- Meldepflicht als SAE nach §3 MPSV an das BfArM

Reviews


BIA-ALCL – Therapie


BIA-ALCL
– Schemata zum Management (n. Noah 2017) –

Periprothetisches Serom oder Tumormasse > 3 Jahr nach Implantatansatz

Ausschluss Trauma oder Infektion

Ultraschalluntersuchung

Serom: Punktion Untersuchung (ggf. mit CD30-ImC)

Tumormasse

Unklar

+ALCL

Operative Exploration mit Kapselbiopsie

Besprechung Tumorboard

Bestätigte ALCL Fälle

Tumorboardbesprechung

Operative komplette und totale Kaspelektomie, Tumorexzision nach onkologischen Standards, Lymphknotenentfernung bei Verdacht, keine neuen Implantate ggf. kontralateral ebenfalls

Komplette Resektion R0

RS oder positive Lymphknoten

Klinische Verlaufskontrolle Ultraschall und CT alle 6 Monate für 2 Jahre, danach jährlich für 5 Jahre

Chemotherapie; CHOP ggf. Immunotherapie

Ggf. Bestrahlung
### Stadiumspezifische Therapie des BIA-ALCLs

<table>
<thead>
<tr>
<th>TNM</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor extent</td>
</tr>
<tr>
<td>T2</td>
<td>Early capsule infiltration</td>
</tr>
<tr>
<td>T3</td>
<td>Cell aggregates or sheets infiltrating the capsule</td>
</tr>
<tr>
<td>T4</td>
<td>Lymphoma infiltrates beyond the capsule</td>
</tr>
<tr>
<td>N0</td>
<td>No lymph node involvement</td>
</tr>
<tr>
<td>N1</td>
<td>One regional lymph nodes positive</td>
</tr>
<tr>
<td>N2</td>
<td>Multiple regional lymph nodes positive</td>
</tr>
<tr>
<td>M0</td>
<td>No metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Spread to other organs/distant sides</td>
</tr>
</tbody>
</table>

**IA-IIC/IIIA:**
- chirurgische vollständige Resektion der Implantatkapsel, des Implantates, auffälliger knotiger Veränderungen und ggfs. auffälliger LK
- Keine Indikation für Mastektomie, SNB oder Axilladissektion

**IIA/IIB-IV:** 2-18%
- Chirurgische Entfernung s.o.
- CHO(EJ) (Cyclophosphamid, Vincristin, Doxorubicin, Prednisol) +/- Etoposid
- **Brentuximab Vedotin** (Adcertis™)
  - Antikörper-Wirkstoff-Konjugat (ADC), in dem Konjugat ist ein monoklonaler Antikörper, der sich gegen humanes CD30-Antigen richtet, kovalent an drei bis fünf Moleküle des Zytototikums Monomethylauristatin E gebunden
- **CHT & Stammzelltransplantation** und Strahlentherapie sind Fällen mit unvollständiger Resektion und fortgeschrittenem Erkrankungsstadium vorbehalten

BIA-ALCL – EUSOMA-Recommendation

- Despite an increase of BIA-ALCL in association with texture implants the use of textured implants is still permitted!

„For the moment, textured implants can safely continue to be used with patient’s fully informed consent, and that women that have these type of implants already in place don’t need to remove or substitute them, which would undoubtedly cause harm to many tens of thousands of women, to prevent an exceptionally rare, largely curable and currently poorly understood disease.”

Cardoso MJ, Wyld L, Rubio IT, et al EUSOMA position regarding breast implant associated anaplastic large cell lymphoma (BIA-ALCL) and the use of textured implants.


7. Clinical outcome and patient satisfaction with the use of bovine-derived acellular dermal matrix.


1. AWMF-Leitlinie „Autologe Fetttransplantation“, Klasse: S2k Registernummer: 009/017, 11/2015
8. Oncological outcomes of lipofilling breast reconstruction: 195 consecutive cases and literature


6. Tamoxifen may increase the risk of microvascular flap complications. Surgeons should consider...


17. A Multicenter Analysis Examining Patients Undergoing Conversion of Implant-based Breast Reconstruction to
**Gestielter vs. freier Gewebetransfer**

- Muskelsparende Techniken und sorgfältiger Verschluss der Bauchdecke führen zu niedrigen Komplikationsraten unabhängig von der verwendeten Methode
- Autologer Gewebetransfer von der Bauchdecke hat die höchste Zufriedenheitsrate (PROM) in allen Patientengruppen
- Morbidität der Spenderregion (z.B. reduzierte Muskelfunktion) kann bei allen Lappentechniken auftreten

---

1. AWMF Leitlinien: S3-LL. Brustrekonstruktion mit Eigengewebe. Registernummer 015 – 075, Stand: 01.04.2015 , gültig bis 31.03.2020
7. Autologous options for postmastectomy breast reconstruction: a comparison of outcomes based on


6. Nipple-sparing mastectomy using a hemi-periareolar incision with or without minimal medial-lateral extensions; clinical outcome and patient satisfaction: A single centre prospective observational study.


