Impact of Breast Cancer Surgery on Quality of Life Outcomes: What's new?

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Discussion of Abstracts GS6-05 and GS6-06

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SAN ANTONIO BREAST CANCER SYMPOSIUM®

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Dr. Ganz has no relevant financial relationships with commercial interests to disclose.

Historical Trends in Breast Cancer Surgical Management

- Changes in surgical approach to removal of breast cancer
  - Late 1970s - Abandonment of Halsted Radical Mastectomy
  - Mid- 1980s -Equivalency of breast conservation and modified radical mastectomy
- Changes in management of the axilla
  - Mid-1980s – axillary sampling through lower and mid-axillary nodes; used to determine risk of recurrence
  - Mid – 1990s-Introduction of sentinel node biopsy
  - Early 2000s –equivalency of SNLB and ALND
- Changes in breast reconstruction
  - Until late 1980s – surgical reconstruction delayed to second independent surgical procedure
  - 1990s-2000s – immediate reconstruction with a tissue expander becomes more common
  - 2000-present – immediate reconstruction with implant, autologous tissue flaps, skin sparing and nipple sparing procedures, oncoplastic surgery

Parallel changes in diagnosis and adjuvant treatments in past 40 years

- Mammographic screening detects smaller, node negative tumors
- Prognosis based on risk factors such as tumor size, age and hormone receptor status
- Development and validation of genomic risk classifiers
- Testing for germline mutations associated with hereditary breast cancer risk
- More extensive use of MRI breast imaging at time of diagnosis
- Promotion of bilateral mastectomy for gene carriers

What does the literature tell us about quality of life outcomes?

- Breast Conservation Surgery (BCS) vs. Mastectomy
- Mastectomy with and without reconstruction

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Cancer 1992, Medical Care 1993, JCO 1993, BCRT 1999

Breast Conservation *Versus* Mastectomy

Is There a Difference in Psychological Adjustment or Quality of Life in the Year After Surgery?

Patricia A. Ganz, MD,† C. Anne Coscarelli Schag, PhD,†‡ J. Jack Lee, PhD,§‖ Margaret L. Polinsky, PhD,† and Shu-Jane Tan, MS‖*

Predicting Psychosocial Risk in Patients With Breast Cancer

PATRICIA A. GANZ, MD,*† KARIM HIRJI, DSc,‡§ MYUNG-SHIN SIM, MS,§ C. ANNE COSCARELLI SCHAG, PhD,†¶ CAROL FRED, MSW,† AND MARGARET L. POLINSKY, PHD†

Characteristics of Women at Risk for Psychosocial Distress in the Year After Breast Cancer

By C. Anne Coscarelli Schag, Patricia A. Ganz, Margaret L. Polinsky, Carol Fred, Karim Hirji, and Laura Petersen

Report

Quality of life in the first year after breast cancer surgery: rehabilitation needs and patterns of recovery

Kojiro Shimozuma[1], Patricia A. Ganz[2,3], Laura Petersen[2], and Karim Hirji[4]

NCI P01 CA 43461

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What did we learn?

- 227 women prospectively enrolled between **1987 and 1990** in Los Angeles
- 40% had BCS, **more often in younger women;** associated with higher education and income, as well as university site of care
- Mood and QOL assessed 1 month post surgery and 12 months later
  - **Greater body image disruption with mastectomy**
  - Poorer QOL one year after surgery associated with greater mood disturbance and body image discomfort 1 month after surgery, as well as lymph node involvement
  - Having cancer and receiving chemotherapy was a more important driver of QOL than type of surgery

Life After Breast Cancer: Understanding Women's Health-Related Quality of Life and Sexual Functioning

By Patricia A. Ganz, Julia H. Rowland, Katherine Desmond, Beth E. Meyerowitz, and Gail E. Wyatt

Predictors of Sexual Health in Women After a Breast Cancer Diagnosis

By Patricia A. Ganz, Katherine A. Desmond, Thomas R. Belin, Beth E. Meyerowitz, and Julia H. Rowland

Role of Breast Reconstructive Surgery in Physical and Emotional Outcomes Among Breast Cancer Survivors

Julia H. Rowland, Katherine A. Desmond, Beth E. Meyerowitz, Thomas R. Belin, Gail E. Wyatt, Patricia A. Ganz

JCO 1998, 1999, JNCI 2000

NCI R01 CA63028

What did we learn?

- 1,957 breast cancer survivors, 1-5 years after diagnosis; cross-sectional survey focused on sexuality and intimacy; recruited from Los Angeles and Washington DC, between **1994-1997**
- Significant predictors of sexual interest: **body image** and emotional well-being
- Significant predictors of sexual dysfunction: vaginal dryness
- Significant predictors of sexual satisfaction: emotional well-being; age x partner problem

JCO, 1999

What about reconstruction?

- **57% had BCS**, 26% mastectomy alone, 17% had mastectomy with reconstruction; mean ages 55.9, 58.9, and 50.3 respectively
- No difference by surgery type in depressive symptoms, social support, QOL, or fear of recurrence
- **Significantly poorer body image for mastectomy patients, with or without reconstruction compared to BCS**
- Mastectomy patients experienced more physical symptoms and discomfort around the surgical site, including numbness, especially in those with reconstruction

JNCI, 2000

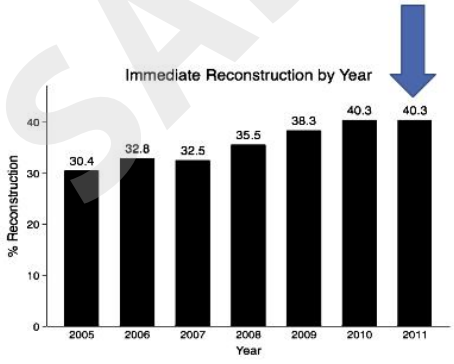
Impact of reconstruction on sex life

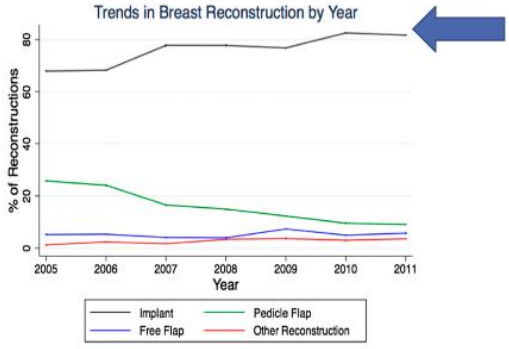
%

*All *P* values = .0001

Rowland, JNCI 1999

Increased Immediate Reconstruction in the Treatment of Breast Cancer





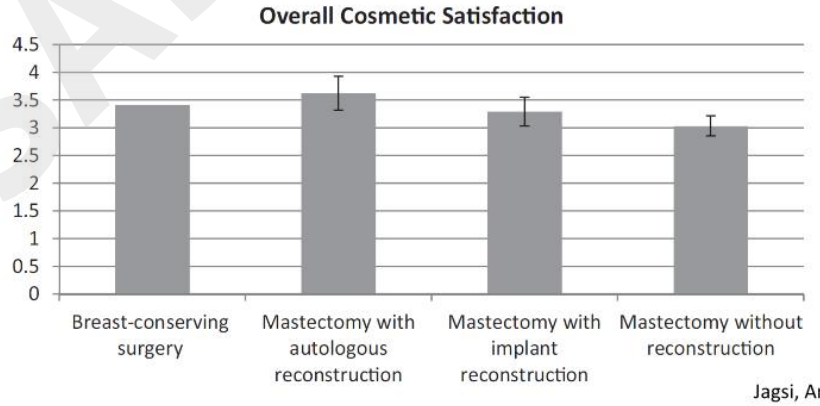
Sabino, American Surgeon, 2016

What does a more recent study show?

- Patients recruited from Los Angeles and Detroit SEER registries in **2005-2007**; 2290 surveyed 9 months after surgery and 1536 surveyed again 4 years later
- **1450** responded to both surveys; 963 BCS, 260 Mast without reconstruction, **222 mastectomy with reconstruction**
- Cosmetic satisfaction was similar between BCS and Mast with reconstruction
- Among those with Mast and reconstruction, satisfaction was associated with reconstruction type and radiation receipt (P<0.001)
- **Note: Mastectomy with reconstruction significantly associated with younger age; 30.7% had bilateral mastectomy**

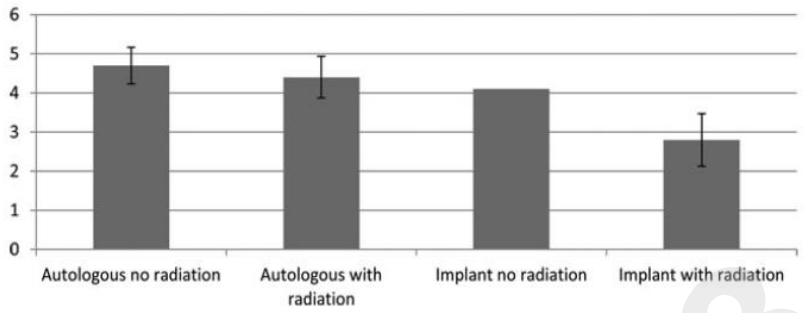
Jagsi et al., Ann of Surgery, 2015

Satisfaction with Cosmetic Outcomes



Jagsi, Ann Surg 2015

Cosmetic Satisfaction Related to Type of Reconstruction and Radiation



Jagsi, Ann Surg 2015

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The impact of breast cancer surgery on quality of life: Long term results from E5103

Shoshana M. Rosenberg, Anne O'Neill, Karen Sepucha,
Kathy D. Miller, Chau T. Dang, Donald W. Northfelt,
George W. Sledge, Bryan P. Schneider, Ann H. Partridge

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DANA-FARBER CANCER INSTITUTE
HARVARD MEDICAL SCHOOL

ECOG-ACRIN E5103

- Double-Blind Phase III Trial of Adjuvant Chemotherapy With and Without Bevacizumab in Patients With Lymph Node–Positive and High-Risk Lymph Node–Negative Breast Cancer

- 4,994 patients enrolled between November 2007-February 2011

Miller et al. JCO 2018

E5103: DM-QOL Objectives

- **Primary (pre-specified) objective:** To compare the QoL of patients randomized to receive AC+paclitaxel with either bevacizumab or placebo at 18 months post-enrollment
  - **Hypothesis:** Patient-reported physical and psychological symptoms will not differ between those treated with bevacizumab and those treated with placebo

- **Secondary (post-hoc) objective:** To evaluate the impact of breast cancer surgery on QoL at 18 months post-enrollment

- **Note: Study enrollment occurred in 2010**

Primary QoL Analysis: Placebo vs. Bev

	Mean score*			P**
	Arm A Chemo+Placebo	Arm B Chemo+Bev	Arm C Chemo+Bev (extended)	
FACT-B	113	110	111	0.23
EQ-5D-3L Index	0.83	0.82	0.81	0.81
EQ-VAS	80	80	79	0.79

- QoL at 18 months across treatment arms not different
- All treatment arms were combined for subsequent QoL analyses

Minimally important differences:
FACT-B: 7-8 points
EQ-5D-3L Index: 0.06 points
EQ-VAS: 7 points

*Higher scores=Better QoL
**Kruskal-Wallis test p-value

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QoL analysis: BCS vs. Mastectomy

	Mean score*		P**
	BCS	Mastectomy	
FACT-B	114	109	0.01
EQ-5D-3L Index	0.84	0.80	0.04
EQ-VAS	82	78	<0.01

Minimally important differences:
FACT-B: 7-8 points
EQ-5D-3L Index: 0.06 points
EQ-VAS: 7 points

*Higher scores=Better QoL
**Wilcoxon rank sum test p-value

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Summary

- **Primary QOL analysis:**

  The addition of bevacizumab, including among those who received extended duration therapy, did not negatively affect QoL at 18 months post-enrollment

  <u>Comment:</u> Nice to see this study completed, but no impact as this treatment is no longer in use

Summary

- **Post-hoc Surgical QOL analysis:**

  There was a trend towards more extensive surgery being associated with poorer QoL, including more problems with usual activities and physical functioning, and breast cancer-specific QoL

  <u>Comment</u>: Findings limited by multiple comparisons and little information on type of reconstruction and concurrent radiation

Local therapy and quality of life outcomes in young women with breast cancer

Laura Dominici, Jiani Hu, Tari King, Kathryn J. Ruddy, Rulla M. Tamimi, Jeffrey Peppercorn, Lidia Schapira, Virginia F. Borges, Steven E. Come, Ellen Warner, Ann Partridge, Shoshana Rosenberg

DANA-FARBER/BRIGHAM AND WOMEN'S CANCER CENTER

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The Young Women's Breast Cancer Study (YWS)

- Multicenter, prospective cohort study
- 12 participating hospitals (academic and community)
- Established to explore *biological*, *medical and psychosocial issues* in breast cancer patients (≤ 40 years old at diagnosis)
- Open to enrollment: October 2006 – June 2016
  - 2162 women identified, 1302 consented to participate
  - Patients are followed with serial surveys
- Median age at diagnosis: 37 (17-40) years

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Methods

- This analysis used a cross-sectional study design
- BREAST-Q was administered to all eligible YWS participants in active follow-up in 2016-2017, either as a stand-alone survey or as part of their 10-year follow-up
- **Median time from diagnosis to BREAST-Q completion: 5.8 years (range: 1.9-10.4 years)**
- Demographics and treatment information were obtained from serial surveys and chart review

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Local Therapy Characteristics/Sequelae

	N=560 (%)
Surgery	
Breast conserving surgery (BCS)	**160 (28%)**
Unilateral mastectomy	110 (20%)
Bilateral mastectomy	**290 (52%)**
Reconstruction (n=400)	
No reconstruction	**42 (11%)**
Implant based reconstruction	**276 (69%)**
Flap reconstruction	49 (12%)
Unknown/other	33 (8%)
Radiation	
BCS (n=160)	159 (99%)
Postmastectomy radiation (n=400)	**181 (45%)**
Lymphedema at 1 year*	163 (29%)

*Self report of any lymphedema at 1 year included as exposure due to potential impact on QOL

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BREAST-Q MEAN SCORES

p= 0.008 **p= 0.8**

Higher score = Better QOL

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BREAST-Q MEAN SCORES

p<0.001 **p<0.001**

Higher score = Better QOL

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Multivariable Results: Poorer Outcomes

- Satisfaction with breasts: **unilateral and bilateral mastectomy**, radiation treatment, and financial status associated with poorer outcomes
- Physical well-being: lymphedema, financial status, and more recent time since surgery associated with poorer outcomes
- Psychosocial well-being: **unilateral and bilateral mastectomy**, radiation, financial status, and BMI ≥25 associated with poorer outcomes
- Sexual well-being: **unilateral and bilateral mastectomy**, financial status, lymphedema, and BMI ≥25 associated with poorer outcomes

Study Conclusions: In Younger Women

- Mastectomy is more commonly being used, and is often bilateral; implant based reconstruction is most common.
- Mastectomy does not contribute to poorer physical function.
- Mastectomy is associated with poorer satisfaction with breasts, poorer psychosocial and sexual functioning.
- Being financially "uncomfortable" is an important variable associated with all aspects of well-being in younger women.

My Take Away Message…

- Mastectomy contributes to increased body image and sexual difficulties after a breast cancer diagnosis (in comparison to BCS); in some women there is greater psychosocial distress (younger women).
- Reconstruction may modify this outcome, but the benefits are complicated by type of reconstruction (implant vs. flap) and post-mastectomy radiation.
- Increased physical problems after mastectomy occur, but are more often associated with extent of axillary surgery, radiation, and chemotherapy, rather than type of surgery.

Final Thoughts

- How a woman feels about her body after breast cancer surgery—body image and adjustment to her new body—is an important driver of sexual and emotional well-being. This is often moderated by age.
- Clinicians need to prepare patients for the likely disruption in body image that occurs with any breast cancer surgery, and how this may potentially impact aspects of quality of life.