Protesi: rischio, sensibilità della mammografia e anticipazione diagnostica

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Gli effetti delle protesi sul cancro al seno

- Differenze d’incidenza?
- Differenze di mortalità?
- impatto sull’accuratezza della mammografia.
- ritardo diagnostico?
- Impatto sulla sopravvivenza?
- Impatto sulla partecipazione allo screening?

Aumenta il rischio?

Table 1. Results from Cohort and Case-Control Studies of Cosmetic Breast Implants and Risk of Breast Cancer

Reference	No. of Breast Cancers Observed	No. of Breast Cancers Expected	Risk Estimate (95% CI)
Cohort Studies			
Deapen et al., 1986[12]	9	15.7	0.57 (0.26–1.09)
Berkel et al., 1992[16]	41	86.2	0.48 (0.34–0.65)
Deapen and Brody, 1992[13]	21	31.7	0.66 (0.41–1.01)
McLaughlin et al., 1994[18]	1	4.2	0.24 (0.0–1.31)
Bryant and Brasher, 1995[17]	45	*	0.76 (0.55–1.02)
McLaughlin et al., 1995[22]	7	11.2	0.63 (0.3–1.3)
Deapen et al., 1997[14]	31	49.2	0.63 (0.43–0.90)
Friis et al., 1997[19]	8	7.8	1.0 (0.4–2.0)
Kern et al., 1997[25]	4	9.0	0.67 (0.20–2.17)
McLaughlin et al., 1998[23]	18	25.0	0.7 (0.4–1.1)
Park et al., 1998[26]†	0	<1	*
Mellemkjaer et al., 2000[20]	9	10.3‡	0.9 (0.4–1.7)
	8	7.2§	1.1 (0.5–2.2)
	16	17.3‖	0.9 (0.5–1.5)
Brinton et al., 2000[27]	136	152.2	0.89 (0.8–1.1)
Pukkala et al., 2002[28]	7	13.9	0.5 (0.2–1.0)
Friis et al., 2006[21]	18	22.8‡	0.8 (0.5–1.3)
	15	21.4§	0.7 (0.4–1.2)
	31	43.8‖	0.7 (0.5–1.0)
McLaughlin et al., 2006[24]	53	71.9	0.7 (0.6–1.0)
Brisson et al., 2006[29]	676	899.0	0.75 (0.70–0.81)
Deapen et al., 2007[15]	43	626.0	0.69 (0.50–0.93)
Case-control studies			
Malone et al., 1992[30]	6	9.0	0.8 (0.3–2.2)
Malone et al., 1992[30]	1	6.0	0.2 (0.1–1.3)
Brinton et al., 1996[31]	36	44.0	0.64 (0.4–1.0)

*Not provided by the authors.
†Authors characterize as cross-sectional prevalence study.
‡Hospital cohort.
§Clinic cohort.
‖Combined hospital and clinic cohort.

Le donne con protesi hanno minore rischio di cancro della mammella.
Minore BMI, minore tessuto

Deapen D, Plastic Recostr Surg, 2007

Mortalità

Table 4. Results from Studies of Breast Implants and Breast Cancer Mortality

Reference	Observed	Expected	Standardized Mortality Ratio	95% CI
Park et al., 1998[26]	6†	17†	0.33	0.11–0.92
McLaughlin et al., 1998[28]	‡	‡	0.5	0.1–2.0
Petit et al., 1998[53]	19†	30†	0.6	0.3–1.1
Brinton et al., 2000 and 2001[27,55]	23	¶	0.55	0.4–0.8
	23	8§	1.14	0.5–2.8
Koot et al., 2003[54]	4	6.7	0.6	0.2–1.6
Le et al., 2004[56]	101†	103†	0.54‖	0.42–0.67
Jacobsen et al., 2004[57]	7	7.4	1	0.4–2.0
Villeneauve et al., 2006[58]	37	82.6¶	0.45	0.32–0.62
	37	40§	0.76	0.48–1.19
Handel and Silverstein, 2006[51]	10.1%	10.5%	‡	$p = 0.65$

†Mastectomy.
‡Not provided by the authors.
§Comparison population.
‖Hazard ratio provided rather than standard mortality ratio.
¶Population mortality rates.

Quasi tutti gli studi mostrano una minore mortalità rispetto alla popolazione generale

Negli studi in cui si ha anche una popolazione di confronto con criteri di selezione simili il vantaggio scomare

Deapen D, Plastic Recostr Surg, 2007

Accuratezza della mammografia

Table 2. Sensitivity and Specificity of Mammography by Augmentation and Symptom Status

	Asymptomatic Women			Symptomatic Women		
	With Augmentation	Without Augmentation	*P* Value	With Augmentation	Without Augmentation	*P* Value
With cancer*						
Sample size, No. (%)	40 (29.2)	236 (34.7)		41 (29.9)	145 (21.2)	
Raw sensitivity (95% CI)	45.0 (29.3-61.5)	66.8 (60.4-72.8)	.008†	73.2 (57.1-85.8)	81.4 (74.1-87.4)	.25†
Adjusted sensitivity (95% CI)‡	46.5 (31.6-62.2)	67.2 (60.3-72.5)	.02§	74.0 (56.0-85.4)	77.4 (68.0-83.4)	.69§
Without cancer						
Sample size, No. (%)	9067 (83.6)	854 997 (84.1)		1006 (9.3)	62 625 (6.2)	
Raw specificity (95% CI)	97.7 (97.4-98.0)	96.7 (96.6-96.7)	<.001†	86.4 (84.1-88.4)	87.2 (87.0-87.5)	.43†
Adjusted specificity (95% CI)‖	98.2 (97.8-98.5)	97.3 (97.2-97.3)	<.001§	85.7 (82.5-88.5)	88.4 (88.1-88.7)	.06§

Abbreviation: CI, confidence interval.
*Among women with a mammogram within 1 year of cancer diagnosis.
†Based on χ^2 test.
‡Adjusted for age, breast density, first vs subsequent mammogram, and registry using logistic regression.
§Based on Wald test from logistic regression model.
‖Adjusted for age, breast density, first vs subsequent mammogram, race/ethnicity, menopausal status, current hormone therapy use, and registry using logistic regression.

Asintomatiche
Peggiore sensibilità
Migliore specificità
Differenze significative

Sintomatiche
Peggiore sensibilità
Peggiore specificità
Differenze non significative

Miglioretti et al, JAMA 2004

Ritardo alla diagnosi

Table 2. Results from Studies of Breast Implants and Detection of Breast Cancer

Reference	Women with Breast Cancer and Prior Implants		Women with Breast Cancer without Prior Implants
Deapen and Brody,1992,[13] and Deapen et al., 2000[46]	37 women 10.4% in situ 50.1% localized 39.5% regional or distant	=	Population data 8.7% in situ 52.6% localized 38.7% regional or distant
Birdsell et al., 1993[47]	41 women 65.9% ≤2-cm tumor size 31.7% positive lymph nodes 12.2% stage 0 83.0% stage I to IV 4.9% unknown 4.9% distant metastasis	<=	13,246 women 24.1% ≤2-cm tumor size 30.0% positive lymph nodes 6.2% stage 0 90.8% stage I to IV 3.0% unknown 5.0% distant metastasis
Clark et al., 1993[48]	33 women 18% in situ 82% invasive 19% positive lymph nodes* 82% ≤2-cm tumor size	<=	1735 women 15% in situ 85% invasive 41% positive lymph nodes 63% ≤2-cm tumor size
Cahan et al., 1995[49]	22 women(23 cancers) 1.2-cm tumor size (mean) 22% in situ 78% invasive 32% positive lymph nodes	=	611 women (636 cancers) 1.8-cm tumor size (mean) 19% in situ 81% invasive 23% positive lymph nodes
Brinton et al., 1996[31]	36 women 5.6% in situ 58.3% localized 36.1% distant		44 women †
Friis et al., 1997[19]	8 women 50% localized 50% regional	<=	Population data 50% localized 37% regional 13% distant or unknown
Brinton et al., 2000[27]	78 women 15.4% in situ 41.0% local 34.6% regional or distant 9.0% unknown	=>	36 women 27.8% in situ 52.8% local 16.7% regional or distant 2.8% unknown
Holmich et al., 2003[50]	23 women 4% distant 20.5-mm tumor size (mean) 2.7 positive lymph nodes (mean) 30% tumor in margins	=	253 women 4% distant 25.2-mm tumor size (mean) 2.2 positive lymph nodes (mean) 9% tumor in margins*
Handel and Silverstein, 2006[51]	129 women 27.3% stage 0 28.9% stage 1 37.5% stage 2 6.3% stage 3 or 4 23.2-mm tumor size (mean) 75.2% palpable	=>	3922 women 33.3% stage 0 31.7% stage 1 28.7% stage 2 6.2% stage 3 or 4 23.8-mm tumor size (mean) 54.4% palpable

*Not provided by the authors.
†Statistically significant.

Molti studi riportano migliore stadio alla diagnosi, minor diametro. Conferma che sono popolazioni molto differenti per attenzione ai controlli

Deapen D, Plastic Recostr Surg, 2007

Ritardo alla diagnosi

Le differenze sono soprattutto nelle sintomatiche

Table 3. Distribution of Tumor Characteristics by Augmentation and Symptom Status Among Women With a Mammogram Within 1 Year of Cancer Diagnosis

Characteristic	No. of Women (%)					
	Asymptomatic			Symptomatic		
	With Augmentation (n = 40)	Without Augmentation (n = 238)	*P* Value*	With Augmentation (n = 41)	Without Augmentation (n = 145)	*P* Value*
Type						
DCIS	10 (25.0)	52 (21.8)	.66	0	14 (9.7)	.04
Invasive	30 (75.0)	186 (78.2)		41 (100)	131 (90.3)	
AJCC stage						
0 or I	27 (71.0)	144 (69.6)	.85	17 (50.0)	73 (54.9)	.61
II, III, or IV	11 (29.0)	63 (30.4)		17 (50.0)	60 (45.1)	
Nodal involvement†						
No	22 (75.9)	133 (73.9)	.82	29 (70.7)	86 (68.2)	.77
Yes	7 (24.1)	47 (26.1)		12 (29.3)	40 (31.8)	
Grade†						
I or II	19 (76.0)	102 (68.5)	.45	29 (82.9)	53 (55.2)	.004
III or IV	6 (24.0)	47 (31.5)		6 (17.1)	43 (44.8)	
Estrogen-receptor status†						
Positive	18 (85.7)	95 (81.9)	.67	21 (95.5)	58 (76.3)	.05
Negative	3 (14.3)	21 (18.1)		1 (4.6)	18 (23.7)	
Tumor size, mm†						
No. of women	27	157		35	114	
Median (interquartile range)	15.0 (10.0-20.0)	12.0 (8.0-20.0)	.25‡	13.0 (10.0-20.0)	17.0 (12.0-27.0)	.02‡

Abbreviations: AJCC, American Joint Committee on Cancer; DCIS, ductal carcinoma in situ.
*Based on χ^2 test unless otherwise noted.
†Invasive only.
‡Based on Wilcoxon rank sum test.

and n = 102), estrogen-receptor status (n = 27 and n = 197), and tumor size (n = 8 and n = 43).

Miglioretti et al, JAMA 200

Rischio sopravvivenza e sopravvivenza libera da malattia

Table 3. Results from Studies of Breast Implants and Cancer Recurrence or Length of Survival

Reference	Length of Follow-Up (Range)	Women with Breast Cancer and Implants	Women with Breast Cancer without Implants	Risk of Recurrence or Death*
Georgiade et al., 1985[52]	3 (0.5–7.5)	101 women†	377 women	Relapse-free survival ($p = 0.30$)
Birdsell et al., 1993[47]	10.2 (1–18)	41 women 83% at 5 yr 73% at 10 yr	13,246 women 74% at 5 yr 62% at 10 yr	Data not provided
Petit et al., 1998[53]	13 (10–20)	146 women†	146 women	Local recurrence: RR = 0.5 (0.3–1.0)
		19 deaths	30 deaths	Distant metastasis: RR = 0.5 (0.3–1.0) Second breast primary: RR =1.0 (0.5–2.3)
Park et				80 1.0).83
				(0.21–3.13) Distant metastasis: OR = 0.73 (0.37–1.44)
Deapen et al., 2000[46]	18.7	37 women 88.5% at 5 yr	External rate 84.1% at 5 yr	Data not provided
Handel and Silverstein, 2006[51]	10.45 (0.5–37)	129 women 14.7% recurrence 10.5% death	3922 women 19.5% recurrence 10.1% death	

RR, relative risk; OR, odds ratio.
*Death caused by breast cancer.
†Reconstruction.

In questi 6 studi nessun effetto sulla sopravvivenza.
Anzi alcuni studi sono suggestivi di migliore sopravvivenza

Deapen D, Plastic Recostr Surg, 2007

Sopravvivenza e sopravvivenza libera da malattia

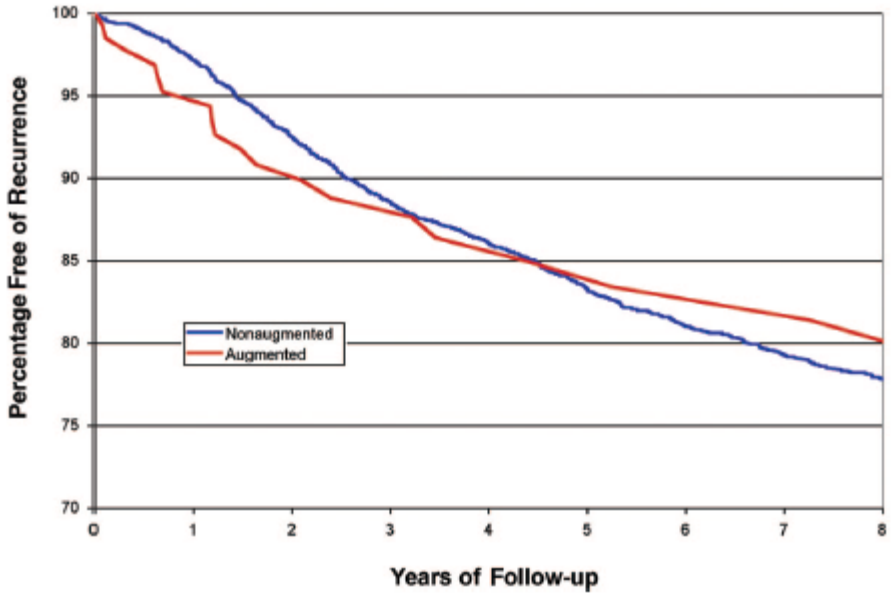

Fig. 8. Kaplan-Meier analysis of breast cancer recurrence in augmented and nonaugmented patients (no significant difference).

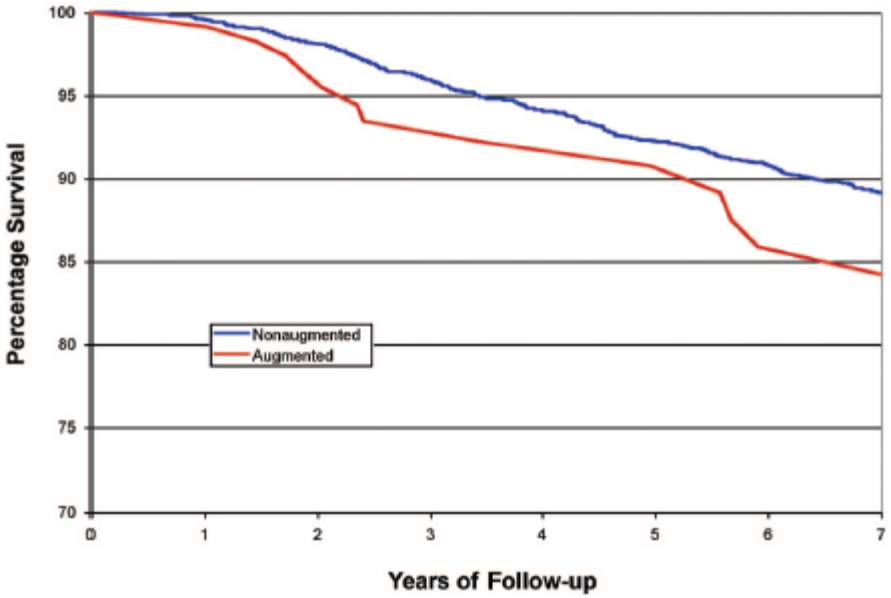

Fig. 9. Kaplan-Meier analysis of survival rates in augmented and nonaugmented breast cancer patients (no significant difference).

Nessuna differenza significativa, ma suggestivo di minore sopravvi

2235 no protesi
86 protesi
Stesso diametro alla diagnosi, 75% vs. 55% palpabili; stadio 2+ 44% vs 33%

Handel, Plastic Recostr Surg, 2007

Conclusioni sugli effetti

- Donne con impianti sono molto diverse dalla popolazione generale per rischio di base e per abitudini preventive:
  - Minore incidenza
  - Minore mortalità
  - Cancri meno aggressivi?
  - Molti controlli?
- Peggiora accuratezza della mammografia
- Negli studi che riescono a controllare per differenze, effetto sullo stadio alla diagnosi, soprattutto nelle sintomatiche
- Al netto delle differenze di rischio piccolo o nullo effetto sulla sopravvivenza
- Riduce la propensione alla mammografia (Jensen 2015)