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Reducing harms from treatment. Sixteen years of surgery of the axilla for screen-detected breast cancers in Italy

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ABSTRACT

Objectives: Available evidence on axillary surgery has accumulated dramatically in the last two decades in favor of less invasive care. The aim of this paper is to study 16-years trends in the surgical management of the axilla in a large population-based data set of screen-detected breast cancers in Italy and to document at what extent recommendations have been adopted in actual clinical care.

Material and methods: This is a retrospective cohort study documenting the surgical management of the axilla in primary breast cancer patients over time. We retrieved from the Italian database of screen-detected cancers 41213 cases diagnosed in women aged 50–69 between years 2000 and 2015 in twelve Italian Regions.

Results: In pN0 cases, an increasing trend ($p < 0.001$) in the number of patients who received sentinel lymph node biopsy (SLNB) as the only axillary staging procedure was observed. In pN + cases SLNB was the only staging procedure in an increasing number of patients ($p < 0.001$) especially since the publication of the ACOSOG-Z0011 paper. In ductal carcinoma in situ (DCIS) SLNB was more frequent in mastectomies and in high grade and large lesions. However, 45% of low grade, small DCIS over the whole time period had some form of axillary surgery.

Conclusion: This large series of screen-detected cases documents a strong time trend in the direction of reducing axillary surgery and hence potential harms from treatment. The continuing practice of SLNB in low risk DCIS is of concern in an era of increasing awareness towards overdiagnosis and overtreatment.

1. Introduction

Early diagnosis, associated with multimodality treatment by multidisciplinary team work, led to declining mortality and extended survival [1]. On the other hand, overdiagnosis and overtreatment are recognized as potential harms in the clinical care of screen-detected and non screen-detected breast cancer and efforts are made for their mitigation [1,2].

Limiting the impact of surgical morbidity is paramount for high-quality long-term survivorship: preservation of cosmesis and function and avoiding complications are regarded as increasingly important. Axillary lymph node dissection (ALND) has historically been a routine component of the staging and management of breast cancer, at the expense of worrisome complications (lymphoedema, nerve injury, shoulder reduced range of motion etc.). Concerns

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about overtreating the axilla in breast cancer patients have arisen at least since the publication of the NSABP-B04 randomized trial in 1977 [3]. This trial showed that variations in loco-regional treatment had no influence on survival, but, although ALND could be associated with significant morbidity, axillary lymph node status was one important predictor of long-term survival and, hence, an important guide to further treatment, together with the biological profile of the tumor.

Nowadays sentinel node biopsy (SLNB) is the standard approach for nodal staging in patients with early breast cancer and a clinically negative axilla. This minimally invasive technique allowed to abandon ALND without affecting outcome [4,5] and substantially reducing morbidity [6].

Physical examination, ultrasound, mammography and magnetic resonance are neither sensitive or reliable to ascertain the status of the axillary lymph nodes in invasive breast cancer, so surgical staging is generally still indicated, even in the setting of a clinically negative axilla, as the histology examination of removed lymph nodes is the most accurate method of assessing spread of the disease to these nodes [7,8].

The likelihood of axillary lymph node involvement increases as the size of the primary tumor increases, even in contemporary series [9,10]. Early breast cancer diagnosis is one of the most important means to avoid complete ALND and mammography screening may be the mainstay to reach this goal. On the other hand, overdiagnosis may put patients at risk of overexploring the axilla [11].

The aim of this paper is to describe the evolution of the management of the axilla for invasive and in situ breast cancer in a large Italian population-based database of screen-detected cancers for an extended period of time, in order to assess whether the trend in guidelines towards a more conservative approach has translated into practice.

2. Material and Methods

In Italy the organized, population-based (all women of the target age are actively invited) National Health Service mammography screening program is under the responsibility of the Regions with national co-ordination as for protocols, monitoring and training activities. The co-ordination bodies include the Italian Breast Cancer Screening Network (GISMa), a scientific association, and the National Center for Screening Monitoring (ONS). Since 1997 GISMa promotes the monitoring of the diagnostic and therapy management of screen-detected breast cancers. Individual data are collected retrospectively from medical records by local screening Units and recorded in a database and data warehouse called SQTM (Scheda computerizzata sulla Qualità del Trattamento del carcinoma Mammario) [12,13], freely available on the web with extensive bilingual documentation (www.qtweb.it). SQTM allows data providers to collect data in a structured way, calculate process indicators [14,15] and perform benchmarking. It also includes built-in data completeness and consistence tools. Data are recorded by the screening Units with the support of designated clinicians and are transferred yearly as de-identified files to the Regional co-ordination office, where they are collated, checked and transferred, still as anonymous individual data files, to the National co-ordination team, which performs further data quality control and data analysis. The results of the analyses are then published by ONS in yearly reports [13] and are presented at the GISMa and ONS

Table 1
Cases (n = 41213) by pT and lymph nodes status.

	pT										Lymphnode Status (invasive cancers)			
	X	IS	1mic	1a	1b	1c	2	3+	Unknown	Tot	N0	N+	Unknown	Tot
2000	5	161	23	72	274	426	154	35	35	1185	512	275	237	1024
	0.4%	13.6%	1.9%	6.1%	23.1%	35.9%	13.0%	3.0%	3.0%	100.0%	50.0%	26.9%	23.1%	100.0%
2001	3	208	49	77	334	475	141	19	90	1396	575	274	339	1188
	0.2%	14.9%	3.5%	5.5%	23.9%	34.0%	10.1%	1.4%	6.4%	100.0%	48.4%	23.1%	28.5%	100.0%
2002	6	281	53	74	353	585	225	22	66	1665	847	338	199	1384
	0.4%	16.9%	3.2%	4.4%	21.2%	35.1%	13.5%	1.3%	4.0%	100.0%	61.2%	24.4%	14.4%	100.0%
2003	11	334	52	93	449	754	253	29	69	2044	1076	408	226	1710
	0.5%	16.3%	2.5%	4.5%	22.0%	36.9%	12.4%	1.4%	3.4%	100.0%	62.9%	23.9%	13.2%	100.0%
2004	11	371	80	119	531	895	282	28	45	2362	1262	554	175	1991
	0.5%	15.7%	3.4%	5.0%	22.5%	37.9%	11.9%	1.2%	1.9%	100.0%	63.4%	27.8%	8.8%	100.0%
2005	15	443	68	155	637	1057	330	24	49	2778	1570	668	97	2335
	0.5%	15.9%	2.4%	5.6%	22.9%	38.0%	11.9%	0.9%	1.8%	100.0%	67.2%	28.6%	4.2%	100.0%
2006	9	443	94	154	672	1068	389	43	108	2980	1682	689	166	2537
	0.3%	14.9%	3.2%	5.2%	22.6%	35.8%	13.1%	1.4%	3.6%	100.0%	66.3%	27.2%	6.5%	100.0%
2007	15	471	64	167	684	1090	356	32	77	2956	1642	700	143	2485
	0.5%	15.9%	2.2%	5.6%	23.1%	36.9%	12.0%	1.1%	2.6%	100.0%	66.1%	28.2%	5.8%	100.0%
2008	7	449	76	148	706	1083	328	35	95	2927	1657	670	151	2478
	0.2%	15.3%	2.6%	5.1%	24.1%	37.0%	11.2%	1.2%	3.2%	100.0%	66.9%	27.0%	6.1%	100.0%
2009	12	431	60	145	607	1034	358	31	178	2856	1517	603	305	2425
	0.4%	15.1%	2.1%	5.1%	21.3%	36.2%	12.5%	1.1%	6.2%	100.0%	62.6%	24.9%	12.6%	100.0%
2010	16	399	52	125	594	1017	373	33	166	2775	1496	561	319	2376
	0.6%	14.4%	1.9%	4.5%	21.4%	36.6%	13.4%	1.2%	6.0%	100.0%	63.0%	23.6%	13.4%	100.0%
2011	19	395	45	122	551	964	352	29	194	2671	1471	496	309	2276
	0.7%	14.8%	1.7%	4.6%	20.6%	36.1%	13.2%	1.1%	7.3%	100.0%	64.6%	21.8%	13.6%	100.0%
2012	10	497	54	162	619	1056	403	51	221	3073	1624	613	339	2576
	0.3%	16.2%	1.8%	5.3%	20.1%	34.4%	13.1%	1.7%	7.2%	100.0%	63.0%	23.8%	13.2%	100.0%
2013	22	530	46	177	675	1059	416	36	278	3239	1721	541	447	2709
	0.7%	16.4%	1.4%	5.5%	20.8%	32.7%	12.8%	1.1%	8.6%	100.0%	63.5%	20.0%	16.5%	100.0%
2014	11	498	66	153	647	1073	427	49	230	3154	1525	561	570	2656
	0.3%	15.8%	2.1%	4.9%	20.5%	34.0%	13.5%	1.6%	7.3%	100.0%	57.4%	21.1%	21.5%	100.0%
2015	25	451	46	193	700	1065	437	37	198	3152	1772	566	363	2701
	0.8%	14.3%	1.5%	6.1%	22.2%	33.8%	13.9%	1.2%	6.3%	100.0%	65.6%	21.0%	13.4%	100.0%
Tot	**197**	**6362**	**928**	**2136**	**9033**	**14701**	**5224**	**533**	**2099**	**41213**	**21949**	**8517**	**4385**	**34851**
	0.5%	**15.4%**	**2.3%**	**5.2%**	**21.9%**	**35.7%**	**12.7%**	**1.3%**	**5.1%**	**100.0%**	**63.0%**	**24.4%**	**12.6%**	**100.0%**