Patterns of care and prognosis of older women with breast cancer

Kiderlen, M.

Chapter 4

Variations in compliance to quality indicators by age for 41,871 breast cancer patients across Europe: a European Society of Breast Cancer Specialists database analysis

Kiderlen M, Ponti A, Tomatis M, Boelens PG, Bastiaannet E, Wilson R, van de Velde CJ, Audisio RA; eusomaDB Working Group.

Published: Eur J Cancer. 2015 Jul;51(10):1221-30

ABSTRACT

Objective. The aim of this study is to assess age-specific compliance to quality indicators (QIs) regarding the treatment of breast cancer as defined by the European Society of Breast Cancer Specialists (EUSOMA) for patients across Europe.

Methods. All patients entered into this study were affected by in situ or invasive breast cancer, diagnosed and treated between 2003 and 2012 at 27 Breast Units across Europe, who were entered into the EUSOMA database. Patients were categorized according to age; compliance to thirteen QIs was assessed for each age group and per time period (2003-2007 and 2008-2012). Compliance to QIs was tested by multivariable logistic regression models adjusted for breast unit, incidence year, and tumour characteristics.

Results. Overall, 41,871 patients with a mean age of 59.6 years were available for analysis. The highest compliance was reached for patients aged 55-64 years and in the time period 2008-2012, while the lowest compliance was observed for women aged over 74 or under 40 years and in the earlier time period. In multivariable logistic regression models, a significant difference between age categories was shown for 12 out of 13 QIs ($P<0.001$). Compliance to the QIs for patients aged ≥75 years was significantly lower when compared to patients aged 55-64 years for ten QIs, while for patients in the youngest age group this was true for seven QIs.

Conclusion. In conclusion, we found that among the 27 included breast units across Europe, compliance to QIs for breast cancer treatment is often lower in the youngest and oldest breast cancer patients, with a tendency to *over*treatment in the youngest patients, and to *under*-treatment in the elderly.

INTRODUCTION

Numerous national and international guidelines and recommendations are available to physicians treating breast cancer patients. However, a significant variation in patterns for breast cancer care has been reported throughout Europe.[1,2] This variation in treatment is accompanied by variation in breast cancer survival rates.[3]

The European Society of Breast Cancer Specialists (EUSOMA) aims to improve and standardize the level of patients care throughout Europe. To accomplish this, the measurement of quality indicators in breast cancer care is essential, in order to monitor the effectiveness and to guide improving the healthcare.[4] To identify the appropriate indicators for quality assurance in breast cancer care, EUSOMA organized a workshop in 2008 where 24 experts from different disciplines defined a set of quality indicators (QIs) on the whole process of breast cancer management based on the international literature, which was published in 2010. For each QI, the experts defined minimum and target standards.[4] Breast centres certified in compliance with the standards of the EUSOMA guidelines are required to hold a Breast Unit (BU) database for the purpose of auditing as well as for research purposes.[5]

The QIs are defined without any age-specific comments, and also, the minimum standards are not age-specific. However, probably it is desired to take into account age-specific issues in treatment recommendations for breast cancer treatment.

For instance, it is questionable if deviation from standard treatment has the same impact on patient outcomes across all age groups. Population-based data from Europe and North America have shown that among older women, large differences in *locoregional* treatment between countries have not led to survival differences .[1,6-9] This leads to the question if 'non-inferior' locoregional treatment strategies result in worsened outcomes among elderly. On the other hand, with regards to systemic therapy, a few randomized trials have shown that chemotherapy regimens which are considered inferior (but more patient-friendly, such as oral capecitabine), result in an inferior prognosis for both younger and older patients[10,11], implying no age-specific impact on outcome.

However, when interpreting trial results, it has to be taken into account that in contrast to the growing population of elderly with cancer, older patients are underrepresented in current clinical oncological studies.[12] Moreover, it has been shown that the older subjects who are included in a clinical trial, are not always representative for the general older population.[13] Therefore, the external validity of clinical trial results should be questioned when it concerns older patients.

With regards to younger breast cancer patients, it is opted that these patients probably deserve a different approach and management than older women, taking

into account their longer general life expectancy, but also, their other, more aggressive tumour biology.[14]
In summary, it is understandable to observe differences in treatment approach across age groups, accompanied by varying compliance to QIs by age. To test this hypothesis, the aim of this study is to assess age-specific compliance to the EUSOMA QIs regarding treatment for patients across Europe.

METHODS

The EUSOMA database (db) is a central data warehouse of prospectively collected information which includes individual records on primary breast cancer cases diagnosed and treated at European breast units (BUs) providing patients data in a standardized format. The database was started in 2006 and collects 108 variables for each patient record, including patient and tumour characteristics, information about preoperative work-up, multidisciplinary management, and follow-up data. Different BUs started entering patients in the db on different points in time, but it has been formally checked that the patients that were included in the database are consecutive patients. Records are anonymous but BUs can identify their own patients by the use of an ID code. The data transfer from each Unit database to the EUSOMA db occurs yearly through an online application and represents a requirement to obtain and to continue holding certification. BUs can access the EUSOMA db to check data quality, calculate QIs, perform data analysis and benchmarking and agree to use it for certification purposes and for co-operative clinical research.[15] For research purposes, the data are fully anonymized, as well on case record level, as on BU level. To assure the data quality, there have been several consistency checks built into the database, as is a report on missing values. In order to maintain EUSOMA certification, BUs are required to minimize inconsistencies an incompleteness and may send several data transfers in order to achieve this.

Patients

All patients with a diagnosis of in situ or invasive breast cancer diagnosed between 2003 and 2012 from 27 certified BUs from Austria, Belgium, Germany, Italy, and Switzerland who provided their data to the EUSOMA db before August 2013 were included into this analysis. Patients with missing data on age or with non-epithelial tumours or other neoplasms were excluded. Age was categorized as <40 years, 40-54 years, 55-64 years, 65-74 years, and ≥75 years.

Outcome measures

Primary outcome measure was the compliance to EUSOMA QIs by age.[4] We selected the thirteen QIs considering treatment (rather than diagnosis, staging, follow-up or counselling). QIs were divided into five groups: appropriate surgical approach, post-operative radiotherapy (RT), avoidance of overtreatment, appropriate hormonal therapy, appropriate chemotherapy, and other medical therapy. Data on trastuzumab were incomplete; therefore, QIs regarding this treatment modality were disregarded from the present investigation.

Statistical analyses

All analyses were performed using IBM SPSS Statistics 20 or R (v.3.0.0). All tests of significance were two-sided and *P*-values smaller than 0.05 were considered statistically significant.

For each QI, the appropriate selection of patients was used (based on tumour stage or type of treatment). Patients with missing data on the treatment of interest for a specific QI, were excluded from the analyses (per QI). The EUSOMA db datacentre considers outcomes of QIs with more than 25% missing values as highly unstable and therefore, QI compliance is not calculated when the proportion of missing values exceeds 25%.

Proportions of compliance to each QI were stratified by age group and time period (2003-2007 and 2008-2012).

Primary outcome measure was the proportion of compliance to each QI. Multivariable logistic regression analyses were performed to calculate adjusted odd's ratios (ORs) and 95% confidence intervals (CIs) by age group, with the middle age group (55-64 years) as reference category. The results were adjusted for BU, incident year, and, when appropriate, tumour characteristics (stage, grade, morphology, and hormone receptor expression). In case of missing data in one of the adjustment variables, these patients were not excluded from the multivariable models, but the missing data were taken into account as a separate value of the variable.

With the purpose of presenting the results into a more intuitive way, adjusted ORs were converted to risks using the formula: adjusted OR/ 1 - adjusted OR.[16]

RESULTS

In total, 41,871 patients from the EUSOMA db were included into this study. The mean age was 59.6 years (Standard Deviation (SD) 13.0). The majority of patients were categorized into the middle three age groups, 5% were <40 years, and 13% were ≥75 years. There was an increasing trend in the number of patients per year, from

2.6% in the year of initiation of the database (2003), to 18.8% in 2011. Most patients had stage I or II breast cancer (39.5% and 31.4%, respectively). Most cancers were hormone receptor positive (81.5%) and invasive ductal carcinoma (72.2%) (Table 1).

Table 1. Patient and tumour characteristics.

	Age categories											
	< 40		**40-54**		**55-64**		**65-74**		**75+**		**All ages**	
	N=2,260		N=13,701		N=10,706		N=10,323		N=5,475		N=41,871	
	N	%	N	%	N	%	N	%	N	%	N	%
Incidence year												
2003	69	3.1	380	2.9	335	3.1	205	2.0	97	1.8	1,086	2.6
2004	127	5.6	565	4.3	519	4.8	370	3.6	190	3.5	1,771	4.2
2005	157	6.9	779	5.9	713	6.7	531	5.1	281	5.1	2,461	5.9
2006	179	7.9	904	6.9	820	7.7	727	7.0	329	6.0	2,959	7.1
2007	210	9.3	1113	8.5	902	8.4	916	8.9	372	6.8	3,513	8.4
2008	238	10.5	1,471	11.2	1,227	11.5	1,266	12.3	570	10.4	4,772	11.4
2009	334	14.8	2,027	15.5	1,674	15.6	1,801	17.4	831	15.2	6,667	15.9
2010	360	15.9	2,221	16.9	1,827	17.1	1,870	18.1	1,023	18.7	7,301	17.4
2011	386	17.1	2,552	19.5	1,868	17.4	1,849	17.9	1,212	22.1	7,867	18.8
2012	200	8.8	1,095	8.4	821	7.7	788	7.6	570	10.4	3,474	8.3
Stage												
in situ	205	9.1	1,767	13.5	1,366	12.8	1,083	10.5	358	6.5	4,779	11.4
I	802	35.5	5,064	38.6	4,584	42.8	4,428	42.9	1,677	30.6	16,555	39.5
II	780	34.5	4,077	31.1	3,110	29.0	3,127	30.3	2,055	37.5	13,149	31.4
III	289	12.8	1,371	10.5	1,033	9.6	1,057	10.2	758	13.8	4,508	10.8
IV	40	1.8	216	1.6	184	1.7	202	2.0	132	2.4	774	1.8
missing	144	6.4	612	4.7	429	4.0	426	4.1	495	9.0	2,106	5.0
Grade												
1	139	6.2	2,058	15.7	1,727	16.1	1,646	15.9	757	13.8	6,327	15.1
2	901	39.9	6,433	49.1	5,619	52.5	5,766	55.9	3,138	57.3	21,857	52.2
3	1054	46.6	3,902	29.8	2,897	27.1	2,538	24.6	1,447	26.4	11,838	28.3
missing	166	7.3	714	5.4	463	4.3	373	3.6	133	2.4	1,849	4.4
Hormone receptor (ER and/or PR)												
negative	680	30.1	2,108	16.1	1,617	15.1	1,372	13.3	721	13.2	6,498	15.5
positive	1,483	65.6	1,0523	80.3	8,774	82.0	8,708	84.4	4,633	84.6	34,121	81.5
missing	97	4.3	476	3.6	315	2.9	243	2.4	121	2.2	1,252	3.0
Morphology												
Ductal	1,851	81.9	9,422	71.9	7,611	71.1	7,294	70.7	4,043	73.8	30,221	72.2
Lobular	99	4.4	1,495	11.4	1,350	12.6	1,545	15.0	742	13.6	5,231	12.5
Combined/other	91	4.0	492	3.8	403	3.8	410	4.0	329	6.0	1,725	4.1
missing	219	9.7	1,698	13.0	1,342	12.5	1,074	10.4	361	6.6	4,694	11.2

Percentages indicate the proportion of patients within an age-group. ER=estrogen receptor. PR=progesterone receptor.

The thirteen scrutinized QIs with definitions are listed in Table 2, which also displays the minimum standards as defined by EUSOMA[4] and the absolute numbers of QI compliance by time period, including the number and proportion of missing values. The proportions of QI compliance by age and time-period are shown in Webtable 1. The highest compliance to QIs was reached in patients aged 55-64 years, where the minimum standard was reached for ten QIs during 2008-2012 and for six during 2003-2007. In patients aged ≥75 years, the minimum standard was reached in the two time periods for three and seven QIs respectively, while in women <40 for four and six QIs.

In multivariable logistic regression models (Webtable 2), a significant difference between age categories was shown for 12 of 13 QIs (P<0.001). No difference between age groups was shown for QI 13e (p=0.07). The adjusted proportions of guideline adherence per age group are shown in Figure 1. Compliance to QIs for patients aged ≥75 years differed significantly from patients in the middle age group (55-64 years) for almost all QIs, except QI 11b. For two indicators, 9a and 9b, the compliance was higher among the oldest patients. However, for the remaining ten QIs, compliance of patients aged ≥75 years was significantly lower, when compared to patients aged 55-64 years.

Table 2. Definition of QIs and compliance by time period.

Definition		Minimum standard	Time period	Compliance		Missing	
				N	%	*N*	%
Surgery and locoregional treatment							
Appropriate surgical approach	9a. % of patients with invasive cancer who received a single operation (excluding reconstruction)	80%	2003-2007	10254	75.0%	19	0.2%
			2008-2012	25432	**82.0%**	45	0.2%
			Total	35686	**80.0%**	64	0.2%
	9b. % of patients with DCIS who received only one operation	70%	2003-2007	1218	53.9%	3	0.2%
			2008-2012	3300	64.8%	1	0.0%
			Total	4518	61.8%	4	0.1%
	9c. % of patients with cN0 who had a SNB.	90%	2003-2007	9590	44.9%	173	1.8%
			2008-2012	23376	81.1%	171	0.7%
			Total	32966	70.5%	344	1.0%
	9d. % if patients with ALND performed, with at least 10 LNs examined	95%	2003-2007	5896	84.7%	261	4.2%
			2008-2012	8476	90.3%	333	3.8%
			Total	14372	88.0%	594	4.0%
Post-operative RT	10a. % of patients with RT after BCS for M0 invasive cancer.	90%	2003-2007	4982	**95.8%**	1418	22.2%
			2008-2012	15714	**94.2%**	1227	7.2%
			Total	20696	**94.6%**	2645	11.3%
	10b. % of patients with pN2a or more who received postmastectomy RT	90%	2003-2007	589	**91.9%**	190	24.4%
			2008-2012	1225	85.2%	128	9.5%
			Total	1814	87.4%	318	14.9%

Table 2. Definition of QIs and compliance by time period. (*continued*)

Definition		Minimum standard	Time period	Compliance		Missing	
				N	%	*N*	%
Avoidance of overtreatment	11a. % of patients with invasive cancer not greater than 3 cm who underwent BCT	70%	2003-2007	7398	**75.0%**	158	2.1%
			2008-2012	16967	**82.3%**	658	3.7%
			Total	24365	**80.1%**	816	3.2%
	11b. % of patients with non-invasive cancer not greater than 2 cm who underwent BCS	70%	2003-2007	801	**77.8%**	36	4.3%
			2008-2012	1882	**87.0%**	149	7.3%
			Total	2683	**84.3%**	185	6.5%
	11c. % of patients with DCIS who do not undergo ALND	95%	2003-2007	1130	86.4%	18	1.6%
			2008-2012	3236	**96.0%**	8	0.2%
			Total	4366	93.5%	26	0.6%
	11d. % of invasive breast cancer patients with pN0 who do not undergo ALND	80%	2003-2007	5818	48.7%	2	0.0%
			2008-2012	15824	**86.4%**	4	0.0%
			Total	21642	76.3%	6	0.0%
Systemic treatment							
Appropriate hormonotherapy	12a. % of patients with HR+ invasive cancer who received hormonotherapy	80%	2003-2007	5403	**96.5%**	3116	36.6%
			2008-2012	18994	**93.8%**	3385	15.1%
			Total	24397	**94.4%**	6501	21.0%
Appropriate chemotherapy and other medical therapy	13a. % of patients with HR- (T>1 or N+) invasive cancer who received adjuvant chemotherapy	80%	2003-2007	1266	**91.7%**	324	20.4%
			2008-2012	2806	**90.6%**	178	6.0%
			Total	4072	**90.9%**	502	11.0%
	13e. % of patients with inflammatory cancer or locally advanced irresectable cancer who had neoadjuvant chemotherapy	90%	2003-2007	27	11.1%	15	35.7%
			2008-2012	111	78.4%	21	15.9%
			Total	138	65.2%	36	20.7%

Numbers shown in bold type indicate that the minimum standard is reached. Patients with missing values were excluded for calculating the proportion of compliance per QI. The proportion of missing values indicate the missing values of the treatment of interest in the selection that was made for the specific QI.

DCIS=ductal carcinoma in situ. cN0=clinically node negative. SNB=sentinel node biopsy. ALND=axillary lymph node dissection. LN=lymph node. RT=radiotherapy. BCS=breast conserving surgery. M0=non-metastatic. HR=hormone receptor

Furthermore, for eight QIs, compliance for the patients in the youngest age group differed significantly compared to those aged 55-64 years (Webtable 2). The compliance was lower, with the exception of QI 13a.

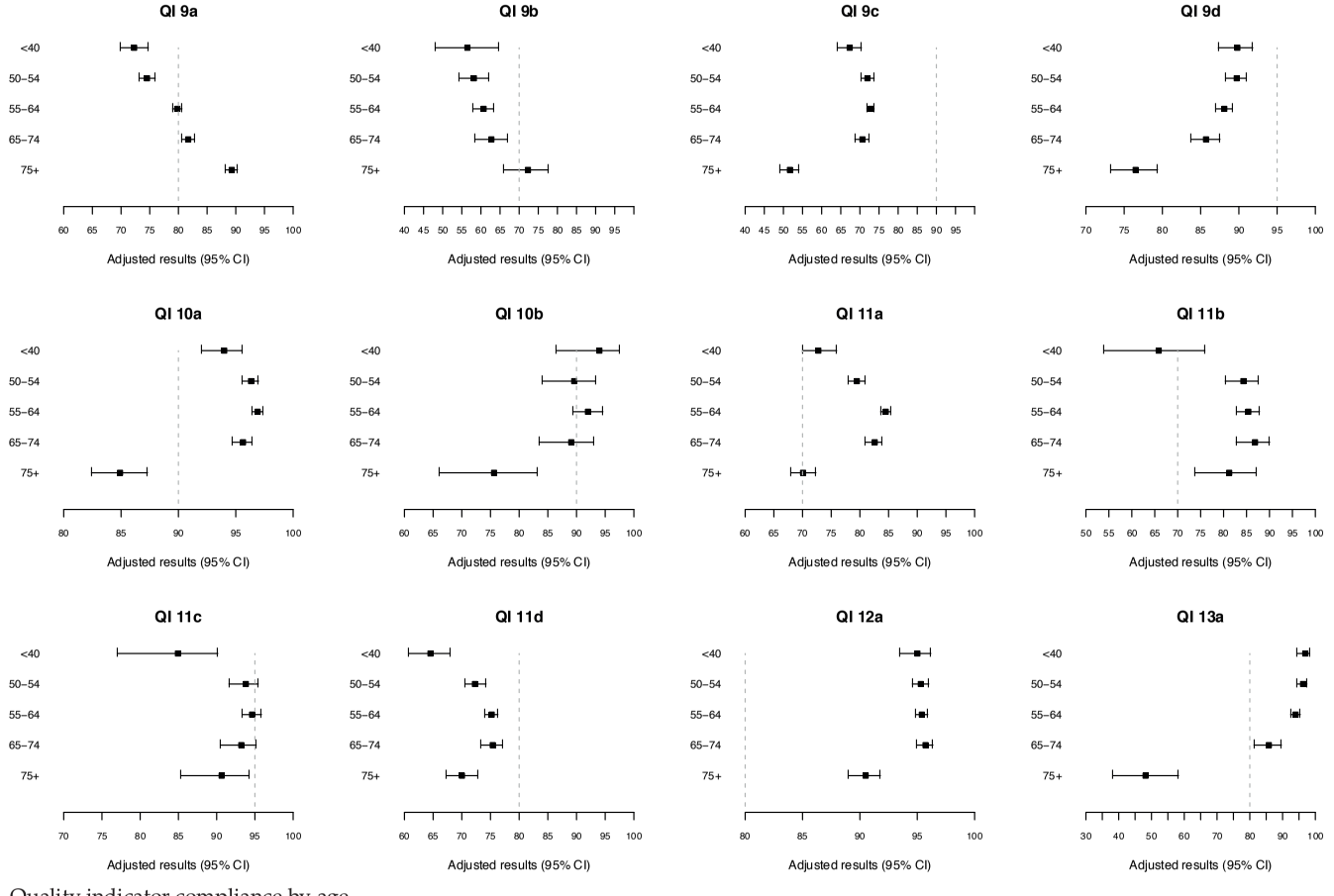

Figure 1. Quality indicator compliance by age

DISCUSSION

This observational study conducted on the largest European breast cancer database demonstrates a low compliance to quality indicators among the youngest (<40 years) and the oldest (≥75 years) patients. Below we will discuss compliance to the specific QIs per treatment category.

The category "Appropriate surgical approach" includes four QIs. Firstly, we observed that the proportion of patients receiving only one operation for invasive cancer (9a) increases with age. A possible explanation is that there is a more reluctant approach to older patients with positive margins, whereas in younger breast cancer patients, positive margins are considered unacceptable, with regards to a higher risk on local recurrence.[17] The same applies for QI 9b: the proportion of patients with ductal carcinoma in situ (DCIS) receiving only one operation; only patients aged ≥75 years met the minimum standard. For QI 9c; the proportion of clinically node negative patients receiving sentinel node biopsy was lower in the youngest and the oldest age group. Again, this is probably reflecting a more aggressive treatment approach in the youngest patients (axillary lymph node dissection), and a more reluctant approach to elderly. The time-period analyses showed almost twice as much compliance in the period 2008-2012 as compared to 2003-2007, reflecting the increasing use of sentinel node procedures.[18] For QI 9d; the proportion of patients with axillary clearance with at least ten lymph nodes examined, the compliance declined with increasing age. This is in keeping with previous studies.[19,20]

QIs for "Post-operative radiotherapy" are separated for radiotherapy after breast conserving surgery (BCS) for non-metastatic invasive cancer (10a), and after mastectomy for pN2a or more (10b). The minimum standard for QI 10a was reached, except in the oldest group (≥75 years). Our observation is a confirmation of many population-based studies showing a decrease in the receipt of RT after BCS in older breast cancer patients, but still a proportion of 82% in the EUSOMA db is higher than previous observations.[1,21,22] The compliance to QI10b was lower in patients aged ≥75 years, which again reflects a more reluctant treatment approach towards older patients.[23] Interestingly, the compliance to QI 10b was higher in the time period 2003-2007. The decrease over time might be explained by the increasing use of aromatase inhibitors, which are considered more tolerable than other (chemotherapeutic) systemic therapies, and moreover probably more effective than tamoxifen for advanced hormone receptor positive breast cancer.[24]

The category "Avoidance of overtreatment" comprises four QIs. QI 11a and 11b consider the proportion of patients with small invasive and non-invasive breast cancers receiving BCS, respectively. We have found that compliance decreases with

increasing age, in line with previous studies which showed an increase in mastectomies with increasing age.[21,25] In contrast, for non-invasive cancer the compliance was lowest for the youngest age group, indicating more extensive surgery. For QIs 11c and 11d, considering the avoidance of axillary lymph node dissection (ALND) for patients with non-invasive lesions or for pathologically confirmed N0 disease (pN0), the minimum standards were not reached in any of the age categories before 2008, which can be explained by the limited use of sentinel node procedures at that time.[26] From 2008 onwards, this QI compliance increased dramatically, and the minimum standard for both QIs was reached in all age groups, except for patients aged <40 years. This indicates a possible overtreatment of the young patients, because there is no hard evidence and no guidelines that justify the use of ALND in non-invasive cancers.[4]

The relatively greater overtreatment in the youngest patients group is probably due to the attempt to assure the lowest risk of recurrence, although this practice should be challenged by considering the balance between benefits and harms.

The category "Appropriate hormonal therapy" comprises one QI (12a), which describes the proportion of patients with hormone receptor (HR) positive invasive breast cancer who received endocrine therapy. This is the only QI for which the minimum standard was achieved in all age categories, indicating good consensus on the provision of hormonal therapy for hormone receptor positive breast cancer.

The last category is "Appropriate chemotherapy and other medical therapy". The standard for QI 13e (chemotherapy for HR-, T>1 or N+) was reached for all patients, except for the oldest patients, where the compliance dropped to 53%. Reluctance to administer chemotherapy in the elderly has been described in previous studies. Reluctance is probably related to the expectation of as well physicians and patients that older patients have a lower treatment tolerability, but also to patient preferences.[4,21,27]

For QI 13e (the proportion of patients with inflammatory cancer or locally advanced irresectable cancer who had neoadjuvant chemotherapy) we showed the same trend in reluctance with chemotherapy with increasing age; although the minimum standard was not reached in any age category, the compliance was by far the lowest in patients aged ≥75 years (44%).

Summarizing our results, we found that treatment of breast cancer patients <40 years and ≥75 years was most often not compliant to the quality indicators as defined by EUSOMA. In the youngest age group, this non-compliance can most probably be explained by *over*-treatment rather than *under*-treatment. In 2012, EUSOMA published recommendations for the treatment of young women (<40 years) with breast cancer.[14] In 2007, the first recommendations for treatment of older patients with breast cancer were published by SIOG (International Society of

Geriatric Oncology), which were updated in 2012 in collaboration with EUSOMA (a summary of treatment recommendations is provided in Webtable 3).[28,29]

The largest difference between these recommendations regards the use of systemic therapy: EUSOMA advises to offer chemotherapy to all young patients with stage I-III breast cancers while EUSOMA/SIOG advises to restrict the provision of chemotherapy to older patients for node-positive, ER negative disease.

With regards to the older patients, our findings raise the question whether a minimalistic attitude results into poorer outcomes. In the last decade, several studies have documented the omission of certain treatments. A small number of clinical trials omitting radiotherapy for selected groups of older, HR positive patients, have been performed[30] none of them showing a deterred survival. However, the risk of locoregional recurrence was higher, as was also shown in the EBCTCG overview.[31] In addition, Martelli et al. published a two-armed trial in which axillary dissection versus no axillary dissection in elderly patients without clinically suspicious nodes.[32] After a median follow-up of 15 years, no significant difference in breast cancer mortality was shown. More on, only a restricted number of randomized studies takes into account the omission of local surgery for older breast cancer patients. A meta-analysis of these trials showed that primary endocrine therapy with tamoxifen associates with inferior local disease control but non-inferior cancer specific survival after surgery.[33] On the other hand, a few trials that studied the effectiveness of more tolerable chemotherapy regimens have shown that these regimens are, less effective in older patients, similar to the younger breast cancer population.[10,11] However, the question is if the older patients that were included in these trials are comparable to the general older cancer patients in terms of, for example, tumour characteristics and comorbidity. Therefore, the generalizability of these trial results should be further explored.[13] From these studies, among others, it is clear that the treatment of breast cancer for older women should not be always the same as the treatment for their younger counterparts, at least not for all treatment modalities. Therefore, in quality of care research regarding breast cancer treatment, it is probably worth considering to define age-specific QIs in the future, or at least to re-define the minimum standards by age category.

One limitation of our study rests on the voluntary certification of contributing breast centres, implying that enrolled patients are likely to be subjected to a selection of top performing breast units.[5] A further limitation of the data is that hospitals did not start recruiting patients' information at the same point in time. Furthermore, the QIs have been prepared in 2008 and published in 2010, whilst the patients in the database are included from 2003 onwards.[4] The expected increasing trend in QI compliance due to the increasing awareness of these quality measurements has indeed been observed in our stratified analyses. Another limitation of our study

is one that often arises in observational studies, namely the existence of missing data. For the majority of treatment modalities, patients with missing values were limited to a proportion of lower than 10%, with the exception of data on systemic treatments, where the proportion was somewhat higher, but still not exceeding the preliminary defined limit of 25%. For our analyses regarding QI compliance, we excluded patients with missing data per QI. It is unknown if the missing data are 'missing at random', therefore, it was not justified to use imputation techniques to fill in the missing data. Theoretically, in the case of 'non-missing at random' data, it is possible that our results slightly over- or underestimate the real compliance. However, we have no reason to believe that the missing data are related to the level of QI compliance, and therefore, we believe that the low proportion of missing data will not impact our results.

Further insight in patterns of care is mandatory to improve the quality of care and outcomes of cancer patients across Europe. The inclusion of follow up information in the EUSOMA db is on-going but not yet available, therefore we were not able to analyse the impact of QI compliance on patient outcome in our current study.

The European Registration of Cancer Care, or in short European Cancer Audit (EURECCA) aims at improving outcome of cancer care through registration and auditing.[34] The aim of EURECCA is to create a population-based audit structure that covers all breast cancer patients across Europe: anonymous patient and tumour data, including treatment and outcome information will be registered in an uniform way across countries. The aim is to develop an extensive data source with the ultimate goal to define high-quality care and monitor the quality of care of all European cancer patients. EURECCA aims to investigate best practices and learn from them, as well as perform analysis on patient groups that deviate from guidelines such as the young and elderly.

In conclusion, we found that among twenty-seven BUs across Europe, compliance to quality indicators for breast cancer treatment is often lower for the youngest and oldest breast cancer patients, with a tendency to *over*treatment in the youngest patients, and to *under*-treatment in the elderly. In the near future EURECCA, in close collaboration with EUSOMA, will map patterns of care and the clinical outcome of European breast cancer patients and will develop an international audit structure to improve quality of care.

ACKNOWLEDGEMENTS

The authors would like to thank Lorenza Marotti, EUSOMA Executive Director, Laura Biganzoli, member of the EUSOMA database advisory board, and Marco Rosselli del Turco for their advice, and Teresa Natali of the EUSOMA Secretariat for her kind assistance. The authors did not receive specific funding for this study.

REFERENCES

1. Kiderlen M, Bastiaannet E, Walsh PM, et al: Surgical treatment of early stage breast cancer in elderly: an international comparison. Breast Cancer Res Treat 132:675-682, 2012
2. Allemani C, Storm H, Voogd AC, et al: Variation in 'standard care' for breast cancer across Europe: a EUROCARE-3 high resolution study. Eur. J. Cancer 46:1528-1536, 2010
3. De AR, Sant M, Coleman MP, et al: Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE-5-a population-based study. Lancet Oncol 15:23-34, 2014
4. del Turco MR, Ponti A, Bick U, et al: Quality indicators in breast cancer care. Eur. J. Cancer 46:2344-2356, 2010
5. Wilson AR, Marotti L, Bianchi S, et al: The requirements of a specialist Breast Centre. Eur. J. Cancer 49:3579-3587, 2013
6. Ess S, Joerger M, Frick H, et al: Predictors of state-of-the-art management of early breast cancer in Switzerland. Ann. Oncol 22:618-624, 2011
7. van de Water W, Bastiaannet E, Dekkers OM, et al: Adherence to treatment guidelines and survival in patients with early-stage breast cancer by age at diagnosis. Br. J. Surg 99:813-820, 2012
8. Showalter SL, Grover S, Sharma S, et al: Factors influencing surgical and adjuvant therapy in stage I breast cancer: a SEER 18 database analysis. Ann. Surg. Oncol 20:1287-1294, 2013
9. Giordano SH, Duan Z, Kuo YF, et al: Use and outcomes of adjuvant chemotherapy in older women with breast cancer. J. Clin. Oncol 24:2750-2756, 2006
10. Muss HB, Berry DA, Cirrincione CT, et al: Adjuvant chemotherapy in older women with early-stage breast cancer. N. Engl. J. Med 360:2055-2065, 2009
11. Jones S, Holmes FA, O'Shaughnessy J, et al: Docetaxel With Cyclophosphamide Is Associated With an Overall Survival Benefit Compared With Doxorubicin and Cyclophosphamide: 7-Year Follow-Up of US Oncology Research Trial 9735. J. Clin. Oncol 27:1177-1183, 2009
12. Hurria A, Dale W, Mooney M, et al: Designing therapeutic clinical trials for older and frail adults with cancer: U13 conference recommendations. J. Clin. Oncol 32:2587-2594, 2014
13. van de Water W, Kiderlen M, Bastiaannet E, et al: External validity of a trial comprised of elderly patients with hormone receptor-positive breast cancer. J. Natl. Cancer Inst 106:dju051, 2014
14. Cardoso F, Loibl S, Pagani O, et al: The European Society of Breast Cancer Specialists recommendations for the management of young women with breast cancer. Eur. J. Cancer 48:3355-3377, 2012
15. Garcia-Etienne CA, Tomatis M, Heil J, et al: Mastectomy trends for early-stage breast cancer: a report from the EUSOMA multi-institutional European database. Eur. J. Cancer 48:1947-1956, 2012
16. Grant RL: Converting an odds ratio to a range of plausible relative risks for better communication of research findings. BMJ 348:f7450, 2014
17. Elkhuizen PH, van Slooten HJ, Clahsen PC, et al: High local recurrence risk after breast-conserving therapy in node-negative premenopausal breast cancer patients is greatly reduced by one course of perioperative chemotherapy: A European Organization for Research and Treatment of Cancer Breast Cancer Cooperative Group Study. J. Clin. Oncol 18:1075-1083, 2000

18. Rescigno J, Zampell JC, Axelrod D: Patterns of axillary surgical care for breast cancer in the era of sentinel lymph node biopsy. Ann. Surg. Oncol 16:687-696, 2009
19. Olaya W, Wong J, Wong J, et al: When is a lymph node dissection a lymph node dissection? The number of lymph nodes resected in sentinel and axillary lymph node dissections. Ann. Surg. Oncol 20:627-632, 2013
20. Schaapveld M, de Vries EG, van der Graaf WT, et al: The prognostic effect of the number of histologically examined axillary lymph nodes in breast cancer: stage migration or age association? Ann. Surg. Oncol 13:465-474, 2006
21. Bastiaannet E, Liefers GJ, de Craen AJ, et al: Breast cancer in elderly compared to younger patients in the Netherlands: stage at diagnosis, treatment and survival in 127,805 unselected patients. Breast Cancer Res. Treat 124:801-807, 2010
22. Lavelle K, Downing A, Thomas J, et al: Are lower rates of surgery amongst older women with breast cancer in the UK explained by co-morbidity? Br. J. Cancer, 2012
23. Jagsi R, Abrahamse P, Morrow M, et al: Patterns and correlates of adjuvant radiotherapy receipt after lumpectomy and after mastectomy for breast cancer. J. Clin. Oncol 28:2396-2403, 2010
24. Milla-Santos A, Milla L, Portella J, et al: Anastrozole versus tamoxifen as first-line therapy in postmenopausal patients with hormone-dependent advanced breast cancer: a prospective, randomized, phase III study. Am. J. Clin. Oncol 26:317-322, 2003
25. Louwman WJ, Vulto JC, Verhoeven RH, et al: Clinical epidemiology of breast cancer in the elderly. Eur. J. Cancer 43:2242-2252, 2007
26. van Steenbergen LN, Voogd AC, Roukema JA, et al: Time trends and inter-hospital variation in treatment and axillary staging of patients with ductal carcinoma in situ of the breast in the era of screening in Southern Netherlands. Breast 23:63-68, 2014
27. Schonberg MA, Marcantonio ER, Li D, et al: Breast cancer among the oldest old: tumor characteristics, treatment choices, and survival. J. Clin. Oncol 28:2038-2045, 2010
28. Biganzoli L, Wildiers H, Oakman C, et al: Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA). Lancet Oncol 13:e148-e160, 2012
29. Wildiers H, Kunkler I, Biganzoli L, et al: Management of breast cancer in elderly individuals: recommendations of the International Society of Geriatric Oncology. Lancet Oncol 8:1101-1115, 2007
30. van de Water W, Bastiaannet E, Scholten AN, et al: Breast-Conserving Surgery With or Without Radiotherapy in Older Breast Patients With Early Stage Breast Cancer: A Systematic Review and Meta-analysis. Ann. Surg. Oncol, 2013
31. Darby S, McGale P, Correa C, et al: Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet 378:1707-1716, 2011
32. Martelli G, Miceli R, Daidone MG, et al: Axillary dissection versus no axillary dissection in elderly patients with breast cancer and no palpable axillary nodes: results after 15 years of follow-up. Ann. Surg. Oncol 18:125-133, 2011
33. Hind D, Wyld L, Reed MW: Surgery, with or without tamoxifen, vs tamoxifen alone for older women with operable breast cancer: cochrane review. Br. J. Cancer 96:1025-1029, 2007
34. EURECCA - European Registration of Cancer Care, 2014. http://www.essoweb.org/projects/eurecca-cancer-care/

APPENDIX A

EusomaDB Working Group participants:

Dr. Mahmoud Danaei, (Clinical Director), Brustcentrum Aachen-Kreis Heinsberg Marien Hospital Aachen, Germany. Univ. Prof. Dr. med Nikolai Maass (Clinical Director), Breast Cancer Centre Aachen City, University Hospital Aachen, Germany. Dimitri Sarlos, MD, Director of Breast Unit, Kantonsspital Aarau, Switzerland. Dr. Annemie Prové and Dr. Luc Verkinderen, Campus Sint Augustinus, GZA Ziekenhuisen, Antwerp, Belgium. Dr. Olivia Pagani, Medical Oncologist and Dr. Marzia Conti Beltraminelli Medical Oncologist/Clinical Director, the Breast Unit of Southern Switzerland, Switzerland. Margherita Serra MD, U.O. and Alice Pellegrini, MD U.O. Chirurgia Generale Policlinico Sant' Orsola Malpighi, Bologna, Italy. Dr. Romano Polato, Chirurgia Generale and Dr.ssa Elisabetta Cretella, Oncologia Medica, Bolzano, Italy. Dipl. Med Andreas Denk (Clinical Director), Brustzentrum, Krankenhaus St. Joseph Stift, Bremen, Germany. Dr. Giuseppe Catalano, head of RT Dept and Dr. Luis Guillermo Bassani, Breast surgeon, Breast Unit at Multimedica Castellanza, Italy. Prof. Dr. Rainer Kimmig and Dr. Peter Kern, Dpt. of Obstetrics and Gynecology, West German Cancer Center, University Hospital Essen, Germany. Sherko Kuemmel, MD, PhD and Frank Stoeblen, MD, Breast Center Essen, Kliniken Essen Mitte, Essen, Germany. Prof. Dr. Volker Moebus (Unit Clinical Director), Breast Unit Frankfurt a.M./Hoechst, Klinikum Frankfurt Hoechst, Academic Hospital, Germany. Prof. Günter Emons and Dr. Adelgund Emons, Breast Cancer Centre, University Medicine Göttingen, Göttingen, Germany. PD, Dr. Kay Friedrichs, (Clinical Director), Mammazentrum Hamburg Krankenhaus Jerusalem, Hamburg, Germany. Prof. Christof Sohn and Prof. Andreas Schneeweiss, University of Heidelberg, Germany. Dott. Corrado Tinterri, Direttore Unità di Senologia, Humanitas Cancer Center, Rozzano, Italy. Daniel Egle MD and Michael Hubalek MD, Dept. Gynaecology and obstetrics, Breast Cancer Centre Tirol, Medical University of Innsbruck, Austria. Prof. Dr. Walter Jonat, Frauenklinik, Universitaetsklinikum Schleswig Holstein, Kiel, Germany. Dr. Gracienne Staelens, Breast Centre Coordinator and Dr. Marleen Borms, Dept. of Medical Oncology, AZ Groeninge, Kortrijk, Belgium. Prof. Dr. med. U. Köhler, Head of Breast Center, Klinikum St. Georg gGmbH, Leipzig, Germany. Prof. Dr. Marion Kiechle, Director, and Dr. Johannes Ettl, Senior physician, Dept. for Gynecology and Obstetrics, Technical University Munich, Germany. Prof. Nadia Harbeck, Department for Gynecology and Obstetrics, Breast Centre München, Germany. Prof. Jutta Engel, MD, Munich Cancer Registry (MCR) of the Munich Cancer Center (MCC), Dept. of medical Informatics, Biometry and Epidemiology (IBE), Ludwig-Maximilians-University, München, Germany. Lorenzo Pavesi, Md Head of Oncological Dept.

and Lea Regolo Md Senior Assistant Surgical Dept, Maugeri Foundation, IRCCS Pavia, Italy. Dr.ssa Adele Sgarella and Dr.ssa Giuseppina Riboni, Struttura Semplice dipartimentale di Senologia, afferente al Dip. Oncoematologico, Fondazione IRCCS Policlinico San Matteo, Italy. Christian F Singer, MD, MPH - Professor of Clinical-Translational Gynecological Oncology, Breast Centre, Dept of Obstetrics and Gynecology - Medical University of Wien, Austria. Dr. Fatemeh Lorenz-Salehi, Brustzentrum - Dr. Horst Schmidt Kliniken Wiesbaden, Germany. Christoph Tausch, MD, and Christoph Rageth, MD, Brust-Zentrum 8008 Zürich, Switzerland.

Webtable 1 QI compliance by age and time period

Webtable 2 QI compliance by age, multivariable logistic regression analyses

Webtable 3 EUSOMA and SIOG recommendation for the treatment of young and older breast cancer patients