The impact of the SARS-COV-2 pandemic on the quality of breast cancer care in EUSOMA-certified breast centres

van Dam, Peter; Tomatis, Mariano; Ponti, Antonio; Marotti, Lorenza; Aristei, Cynthia; Biganzoli, Laura; Cardoso, Maria J; Cheung, Kwok L; Curigliano, Giuseppe; De Vries, Jakob; ...

Source / Izvornik: **European Journal of Cancer, 2022, 177, 72 - 79**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.1016/j.ejca.2022.09.027

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:184:716830

European Journal of Cancer 177 (2022) 72–79

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

The impact of the SARS-COV-2 pandemic on the quality of breast cancer care in EUSOMA-certified breast centres

Peter van Dam [a,*], Mariano Tomatis [b], Antonio Ponti [b,c], Lorenza Marotti [b], Cynthia Aristei [d], Laura Biganzoli [e], Maria J Cardoso [b,f], Kwok L Cheung [b,g], Giuseppe Curigliano [h,i], Jakob De Vries [j], Donatella Santini [k], Francesco Sardanelli [l,m], Isabel Teresa Rubio [n], Eusoma Working Group

[a] *Multidisciplinary Oncologic Center, Antwerp University Hospital, Edegem, Belgium*
[b] *European Society of Breast Cancer Specialists (EUSOMA), Florence, Italy*
[c] *CPO Piemonte, Turin, Italy*
[d] *Radiation Oncology Section, Department of Medicine and Surgery, University of Perugia and Perugia General Hospital Sant'Andrea delle Fratte Perugia, Italy*
[e] *"Sandro Pitigliani" Department of Medical Oncology, Hospital of Prato, Prato, Italy*
[f] *Breast Unit, Champalimaud Clinical Center/Champalimaud Foundation, Lisbon, Portugal*
[g] *Academic Unit for Translational Medical Sciences, School of Medicine University of Nottingham, Royal Derby Hospital Centre, UK*
[h] *Division of New Drugs and Early Drug Development for Innovative Therapies, European Institute of Oncology, IRCCS, Milan, Italy*
[i] *Department of Oncology and Hemato-Oncology, University of Milano, Italy*
[j] *University Medical Center Groeningen, the Netherlands*
[k] *Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy*
[l] *Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy*
[m] *Unit of Radiology, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy*
[n] *Breast Surgical Oncology, Clinica Universidad de Navarra, Madrid, Cancer Center Universidad de Navarra, Spain*

Received 9 August 2022; received in revised form 22 September 2022; accepted 23 September 2022
Available online 12 October 2022

KEYWORDS
Breast neoplasms;
COVID-19;
Data warehousing;
Quality indicators;
Healthcare;

Abstract ***Aims:*** We analysed the impact of the SARS-CoV-2 pandemic (COVID-19) on the quality of breast cancer care in certified EUSOMA (European Society of Breast Cancer Specialists) breast centres.
Materials and methods: The results of the EUSOMA quality indicators were compared, based on pseudonymised individual records, for the periods 1 March 2020 till 30 June 2020 (first COVID-19 peak in most countries in Europe) and 1 March 2019 till 30 June 2019. In addition,

* *Corresponding author*: Multidisciplinary Oncologic Units, Antwerp University Hospital, Drie Eycken straat 655, Edegem B2650, Belgium.
E-mail address: peter.vandam@uza.be (P. van Dam).

https://doi.org/10.1016/j.ejca.2022.09.027

SARS-CoV-2;
Surveys and
questionnaires

a questionnaire was sent to the participating Centres for investigating the impact of the COVID-19 pandemic on the organisation and the quality of breast cancer care.
Results: Forty-five centres provided data and 31 (67%) responded to the questionnaire. The total number of new cases dropped by 19% and there was a small significant higher tumour ($p = 0.003$) and lymph node ($p = 0.011$) stage at presentation. Comparing quality indicators (12,736 patients) by multivariable analysis showed mostly non-significant differences. Surgery could be performed in a COVID-free zone in 94% of the centres, COVID testing was performed before surgery in 96% of the centres, and surgical case load was reduced in 55% of the centres. Modifications of the indications for neoadjuvant endocrine therapy, chemotherapy, and targeted therapy were necessary in 23%, 23%, and 10% of the centres; changes in indications for adjuvant endocrine, chemo-, targeted, immune, and radiotherapy in 3%, 19%, 3%, 6%, and 10%, respectively.
Conclusion: Quality of breast cancer care was well maintained in EUSOMA breast centres during the first wave of the COVID-19 pandemic. A small but significantly higher tumour and lymph node stage at presentation was observed.

1. Introduction

The outbreak of the SARS-CoV-2 (COVID-19) pandemic has overwhelmed healthcare systems in many countries [1]. At the epicentre, the main focus of medical activities was on treating patients with severe COVID-19 disease, implicating that other forms of non-urgent medical care were often partially or completely halted [2]. Guidelines and recommendations were provided by multidisciplinary panels for prioritization, triage, and treatment of breast cancer patients in these difficult circumstances [3–6]. Several surveys showed that this pandemic had a significant impact on patients with cancer, often delaying their diagnosis and causing modifications in treatment [7–9]. In the present study, we performed a survey in EUSOMA-certified breast centres on adaptations of breast cancer care during the first and second wave of the COVID-19 pandemic and compared quality indicators (QIs) from March to June 2020 with those observed from March to June 2019. We hypothesise that the observed results depend on the certification process. It was previously shown that the EUSOMA certification process improves the quality of breast cancer care, and the present study suggests that EUSOMA certification creates robust structures capable to maintain high level standards of care in difficult circumstances [11].

2. Materials and methods

Forty-six EUSOMA centres (45 already certified and one in progress) were asked to participate in the project and to fill in a questionnaire about the measures taken in their hospital/country during the COVID-19 pandemic. All centres but one provided data via the eusomaDB and 31/46 (67%) additionally responded to the questionnaires focussing on the impact of the first wave of COVID-19 on the quality of breast cancer care in their centres.

2.1. The EUSOMA data warehouse (eusomaDB)

The eusomaDB is a central data warehouse of prospectively collected information that includes pseudonymised individual records on primary breast cancer patients diagnosed and treated at European Breast Centres that have provided their data according to EUSOMA requirements during the course of certification [11]. The database was started in 2006 and includes at December 2021 over 200,000 data sets on cancers from European breast centres. It collects 166 variables by patient record, including patient and tumour characteristics, information about preoperative work-up, multidisciplinary management, and follow-up data. No personal identifiers exist on the entire database. Data upload from each breast centre are performed yearly through an online application and represent a requirement to obtain and maintain certification. Participating centres agree to use the database for certification purposes, benchmarking, and for cooperative clinical research [10–13]. Breast centres participating in this project are located in Germany ($n = 2$), Switzerland ($n = 2$), Belgium ($n = 7$), Austria ($n = 1$), the Netherland ($n = 1$), Spain ($n = 1$), Portugal ($n = 3$), France ($n = 1$), Italy ($n = 25$), Sweden ($n = 1$) Croatia ($n = 1$), and Cyprus ($n = 1$).

2.2. Quality indicators and the certification process

Overall, 17 main QIs have been identified by EUSOMA by systematic search of the evidence and consensus by experts, respectively, seven on diagnosis; four on surgery and loco-regional treatment; two on systemic treatment; and four on staging, counselling, follow-up, and

rehabilitation, all with the specification, by consensus, of the desirable target and of the minimum standard [10,13]. Several of the EUSOMA QIs were listed in the National Quality Measures Clearinghouse of the US Agency for Health Care Research and Quality. EUSOMA has so far included 17 QIs in the certification process, 15 of which are included in this analysis (Table 1) [10,13]. Before starting the certification process, breast centres must validate their clinical database by uploading consecutive patients with primary breast cancer diagnosed in at least 6 months before, to the central eusomaDB in the required format.

2.3. Statistical analysis

All QIs are proportions. Univariable and multivariable analyses were performed for the before–after comparison, combining all breast centres. Given that the outcome of each indicator is binomial (fulfilled versus not fulfilled), a logistic regression analysis was performed with two covariates: time period (2019 versus 2020) and continuous age. The resulting odds ratios (ORs) for the two covariates were both included in the tables. The effect of age was separately studied by adjusting the OR for age by time period. Heterogeneity between results was assessed by using the χ^2 test. Statistical analyses were performed with program R (version 2.10.1).

3. Results

3.1. Questionnaire on adaptations on breast cancer care between February and June 2020 during the first wave of COVID-19

All 31 centres responding to the questionnaire reported that the COVID-19 pandemic had a severe impact on their functioning. Adaptations in the work flow were implemented during the first wave of COVID-19, respectively, taking place in February (one breast centre, 3%), March (29 breast centres, 94%), and April (one breast centre, 3%) 2020. Surgery could be performed in a COVID-19-free zone in 94% of the breast centres, COVID-19 testing was performed before surgery in 96% of centres, and surgical case load was reduced in 55% of the centres. Reconstructive surgery was stopped or reduced in 55% of centres. Modifications in the indications for neo-adjuvant endocrine therapy, chemotherapy, and targeted therapy were necessary in 23%, 23%, and 10% of the centres, while indications for adjuvant endocrine, chemo-, targeted, immune, and radiation therapy were changed in 3%, 19%, 3%, 6%, and 10% of the centres, respectively. Breast cancer screening was frequently suspended either on a national level (58%) or regional level (39%). Altogether, in 52% of the 31 centres patients requested more interaction by phone or video call with breast nurses, and in 26% of the 31 centres, more psychological support was necessary. One third of the centres (10 of 31) organised virtual informative events or produced informative material on the implications of COVID-19 on breast cancer. Palliative care was affected in 23% of the centres.

Table 1
EUSOMA quality indicators that were assessed in the present analysis.

1	Cancers with a pre-operative diagnosis (B5 or C5)
2	Invasive ca with histological type; grading; ER/Her2; pN; margins; vascular invasion & size recorded
3	Non-invasive ca with histological pattern; grading; size; margins & ER recorded
4	M0 invasive ca receiving postoperative RT after BCT
5	Invasive ca $\leq$ 3 cm (incl. DCIS component) treated with BCT
6	Non-invasive ca $\leq$ 2 cm treated with BCT
7	DCIS with no axillary clearance
8	Endocrine sensitive invasive ca receiving HT
9	ER- (T > 1 cm or N+) invasive ca receiving CT
10	Invasive ca receiving just 1 operation (excl. reconstruction)
11	DCIS receiving just 1 operation (excl. reconstruction)
12	SLNB in cN0 invasive ca (without neoadjuvant)
13	Immediate reconstruction after mastectomy
14	No more than 5 nodes excised in invasive ca with SLNB
15	Invasive Her2+ (T > 1 cm or N+) with adjuvant chemotherapy who received adjuvant biological drug

ER: oestrogen receptor; HER: human epidermal growth factor receptor; RT: radio therapy; BCT: breast conserving therapy; DCIS: ductal carcinoma in situ; HT: hormonal therapy; CT: chemotherapy; SLNB: sentinel node biopsy.

3.2. Comparison of March till June 2020 versus March till June 2019

The 45 centres providing data that were collected from a total of 12,736 patients; of which 9962 having an invasive carcinoma and 2774 a ductal carcinoma in situ. The total number of patients registered in the EUSOMA database dropped from 7035 to 5701 (minus 19%) when comparing the 4-month 2020 period versus the same 4-month period of the previous pre-pandemic year (2019). A slightly stronger drop was seen for DCIS (1546 versus 1228, minus 21%) as for invasive breast cancers (5489 versus 4473, minus 19%). We observed a small but significant higher tumour ($p = 0.003$) and lymph node ($p = 0.011$) stage at presentation in 2020 (Table 2).

Comparing of the QIs in the two time periods by multivariable analysis shows mostly no-significant differences. In fact, quality of pathology reporting (QI2: 94.6% versus 98.1%, $p < 0.0001$), endocrine sensitive invasive breast cancer receiving endocrine treatment (QI8: 93.7 versus 95.1%, $p = 0.013$) went up, while the percentage of patients with no more than five lymph nodes excised (QI14: 98.5% versus 97.6%, $p = 0.027$) went down during the first wave (Table 3).

Correction for age in the multivariable model showed that changes in the indications for mastectomy, adjuvant radiotherapy, chemotherapy, and endocrine treatment

Table 2
Characteristics of patients with invasive cancer included in the EUSOMA database comparing the registration 2020 to 2019.

Invasive		Total			2019			2020			
		N	%	Missing	N	%	Missing	N	%	Missing	
	Total	9962	100.0%		5489	100.0%		4473	100.0%		p-value*
	Median age (range)	62 (20–100)			62 (20–97)			62 (24–100)			
	Missing	18		0.2%	16		0.3%	2		0.0%	
pT	yT0-yTis-yTmic	455	4.9%		235	4.6%		220	5.3%		**0.003**
	yT1a-yT1b-yT1c	575	6.2%		320	6.3%		255	6.2%		
	yT2	221	2.4%		108	2.1%		113	2.7%		
	yT3-4	61	0.7%		38	0.7%		23	0.6%		
	T1mic	114	1.2%		63	1.2%		51	1.2%		
	T1a	506	5.5%		273	5.3%		233	5.6%		
	T1b	1662	18.0%		915	17.9%		747	18.1%		
	T1c	3340	36.2%		1935	37.9%		1405	34.1%		
	T2	2001	21.7%		1077	21.1%		924	22.4%		
	T3-4	300	3.2%		145	2.8%		155	3.8%		
	Unknown	727		7.3%	380		6.9%	347		7.8%	
PN	yN0	831	10.4%		434	9.8%		397	11.3%		**0.011**
	N0	4614	58.0%		2632	59.2%		1982	56.4%		
	yN1	234	2.9%		137	3.1%		97	2.8%		
	N1	1184	14.9%		675	15.2%		509	14.5%		
	yN2-3	174	2.2%		99	2.2%		75	2.1%		
	N2	306	3.8%		150	3.4%		156	4.4%		
	N3	214	2.7%		112	2.5%		102	2.9%		
	Nmi(sn)	404	5.1%		209	4.7%		195	5.6%		
	Unknown	2001		20.1%	1041		19.0%	960		21.5%	
ER	−	1121	13.4%		608	13.0%		513	13.9%		0.221
	+	7226	86.6%		4060	87.0%		3166	86.1%		
	Unknown	1615		16.2%	821		15.0%	794		17.8%	
PgR	−	2080	24.9%		1154	24.7%		926	25.2%		0.641
	+	6264	75.1%		3512	75.3%		2752	74.8%		
	Unknown	1618		16.2%	823		15.0%	795		17.8%	
Her2	0/1+	6065	73.6%		3423	74.1%		2642	72.9%		**0.002**
	2+ (Fish −)	11	0.1%		9	0.2%		2	0.1%		
	2+ (Fish +)	7	0.1%		5	0.1%		2	0.1%		
	2+ (Fish ?)	1439	17.5%		751	16.3%		688	19.0%		
	3+	720	8.7%		429	9.3%		291	8.0%		
	Unknown	1720		17.3%	872		15.9%	848		19.0%	
Ki67+	0–14	3154	42.0%		1764	41.7%		1390	42.3%		0.614
	15+	4360	58.0%		2464	58.3%		1896	57.7%		
	Unknown	2448		24.6%	1261		23.0%	1187		26.5%	
Grade	I	1498	16.9%		845	17.2%		653	16.4%		0.622
	II	5081	57.2%		2794	56.9%		2287	57.6%		
	III	2302	25.9%		1271	25.9%		1031	26.0%		
	Unknown	1081		10.9%	579		10.5%	502		11.2%	
Neoadjuvant CT	No	7229	82.3%		4055	83.1%		3174	81.3%		**0.026**
	Yes	1551	17.7%		822	16.9%		729	18.7%		
	Unknown	1182		11.9%	612		11.1%	570		12.7%	
Surgery	BCS	6322	67.1%		3525	67.8%		2797	62.5%		0.212
	Mastectomy	3099	32.9%		1675	32.2%		1424	31.8%		
	Unknown	541		5.4%	289		5.3%	252		5.6%	

*All p-values are from chi-squared test, except for Her2 where Fisher's exact test was used.

were observed in patients aged over 70 (Table 3). In addition, a univariable analysis of the performance of 15 EUSOMA QIs during these time periods was performed in patients younger than 70 years confirming that in this group there was only a small difference in the number of patients with mandatory histological reporting (96.5% versus 98.1%, p = 0.001), and no more than five axillary lymph nodes excised with invasive cancer (98.5 versus 97.4%, p = 0.029) were observed (Table 4). A similar univariable analysis in the patients above 70 years old (3628 patients) showed that the percentage of patients with endocrine sensitive invasive breast cancer receiving hormonal treatment (90.6% versus 93.5%, p = 0.018) and patients with ductal carcinoma in situ receiving just one operation (94.9% versus 85.2%, p = 0.033) differed significantly (Table 5).

Table 3
Multivariable analysis of 15 EUSOMA quality indicators between March and June 2020 compared to March and June 2019.

Indicator[c]	Eligible cases		Cases meeting the requirement		Effect of timing (being treated in 2020 vs. 2019) adj. by age			Effect of age adj. by timing		
	2019	2020	2019	2020	OR[a]	IC 95%	p-value	OR[b]	IC 95%	p-value
1	4190	3267	94.3%	95.1%	1.14	(0.92–1.40)	0.214	1.01	(0.99–1.01)	0.189
2	4014	3210	96.6%	98.1%	1.77	(1.30–2.40)	<0.001	1.00	(0.99–1.01)	0.478
3	504	375	90.5%	92.0%	1.22	(0.75–1.96)	0.419	0.99	(0.97–1.01)	0.349
4	2148	1446	92.5%	94.0%	1.32	(0.99–1.76)	0.056	0.89	(0.87–0.90)	<0.001
5	2311	1631	84.5%	85.7%	1.09	(0.91–1.30)	0.336	1.01	(0.99–1.01)	0.135
6	285	240	90.2%	89.6%	0.95	(0.53–1.68)	0.853	1.03	(1.00–1.06)	0.011
7	499	396	99.2%	99.2%	1.06	(0.23–4.80)	0.935	1.08	(1.00–1.16)	0.041
8	3480	2717	93.7%	95.1%	1.33	(1.06–1.65)	0.013	0.97	(0.96–0.98)	<0.001
9	315	281	86.3%	87.9%	1.29	(0.73–2.25)	0.376	0.88	(0.85–0.90)	<0.001
10	3787	3006	95.2%	94.6%	0.89	(0.71–1.10)	0.280	1.02	(1.01–1.02)	<0.001
11	514	401	91.8%	89.8%	0.77	(0.48–1.20)	0.253	1.01	(0.98–1.02)	0.563
12	2606	1905	95.3%	95.2%	0.93	(0.68–1.25)	0.632	0.87	(0.85–0.88)	<0.001
13	1344	1181	61.9%	63.8%	1.12	(0.91–1.36)	0.259	0.90	(0.89–0.90)	<0.001
14	2778	2180	98.5%	97.6%	0.63	(0.41–0.94)	0.027	1.00	(0.98–1.01)	0.878
15	205	133	96.1%	97.7%	1.72	(0.44–6.62)	0.430	1.01	(0.96–1.06)	0.543

[a] An OR > 1 means that it is more probable to meet the requirement in 2020, controlling per different age distributions in the two years. An OR < 1 means that it is less probable.
[b] An OR > 1 means that it is more probable for older patients to meet the requirement, controlling the effect of being treated in different years. An OR < 1 means that it is less probable.
[c] See Table 1 for indicators definition.

4. Discussion

This is the first multicentre international analysis on the effect of the COVID-19 pandemic on breast cancer care. The present analysis shows that although some adaptations had to be made, quality of breast cancer care was well maintained in EUSOMA centres during the first wave of the COVID-19 pandemic.

In our study, the number of patients newly diagnosed with invasive breast cancer was 19% lower in 2020 compared to a similar period in 2019. A reduction of new breast cancer diagnosis during the first wave of the SARS-CoV-2 pandemic, varying between 16% and 52%, has also been reported by several other authors at both sides of the Atlantic [9,14–16]. The above findings can be mainly explained by stopping breast cancer screening but also the reduced availability of non-COVID medical care and fear of patients to attend clinics and hospitals may have played a role [14]. The EUSOMA centres reported that screening was temporally halted on a national level in 59% or on a regional level in 38% in their neighbourhood. The psychological

Table 4
Univariable analysis of 15 EUSOMA quality indicators between March and June 2020 compared to March and June 2019 in patients up to 70 years old.

Indicator[a]	Eligible cases		Cases meeting the requirement		Effect of timing (being treated in 2020 vs. 2019)		
	2019	2020	2019	2020	OR	IC 95%	p-value
1	2869	2217	94.4%	95%	1.13	(0.88–1.45)	0.332
2	2667	2143	96.5%	98.1%	1.90	(1.31–2.76)	0.001
3	403	291	91.6%	92.1%	1.07	(0.62–1.86)	0.801
4	1423	927	97.3%	98.1%	1.39	(0.79–2.44)	0.260
5	1491	1016	85.2%	85.3%	1.01	(0.81–1.27)	0.913
6	226	182	90.7%	87.9%	0.75	(0.40–1.40)	0.362
7	403	306	99%	99%	1.01	(0.22–4.56)	0.987
8	2301	1798	95.2%	96%	1.20	(0.89–1.63)	0.232
9	225	196	97.3%	95.4%	0.57	(0.20–1.63)	0.294
10	2560	2032	94.5%	93.9%	0.90	(0.70–1.15)	0.391
11	412	313	91.3%	91.1%	0.97	(0.58–1.63)	0.922
12	1774	1287	98.8%	98.8%	1.02	(0.52–1.98)	0.963
13	957	858	78.7%	80.5%	1.12	(0.89–1.41)	0.329
14	1926	1526	98.5%	97.4%	0.58	(0.36–0.95)	0.029
15	158	93	96.8%	96.8%	0.98	(0.23–4.20)	0.979

An OR > 1 means that it is more probable for older patients to meet the requirement, OR < 1 that it is less probable.
[a] See Table 1 for indicators definition.

Table 5
Univariable analysis of 15 EUSOMA quality indicators between March and June 2020 compared to March and June 2019 in patients older than 70 years.

Indicator[a]	Eligible cases		Cases meeting the requirement		Effect of timing (being treated in 2020 vs. 2019)		
	2019	2020	2019	2020	OR	IC 95%	p-value
1	1308	1048	94.5%	95.2%	1.16	(0.8–1.68)	0.425
2	1331	1065	96.8%	97.9%	1.54	(0.92–2.6)	0.103
3	99	84	85.9%	91.7%	1.81	(0.69–4.72)	0.224
4	716	517	83%	86.7%	1.33	(0.97–1.84)	0.078
5	813	614	83.3%	86.2%	1.25	(0.93–1.68)	0.136
6	58	58	87.9%	94.8%	2.52	(0.62–10.2)	0.198
7	93	90	100%	100%	1.00		1000
8	1167	917	90.6%	93.5%	1.49	(1.07–2.06)	0.018
9	89	85	58.4%	70.6%	1.71	(0.91–3.2)	0.095
10	1215	972	96.7%	96.2%	0.86	(0.55–1.36)	0.517
11	98	88	94.9%	85.2%	0.31	(0.11–0.91)	0.033
12	823	616	87.6%	87.7%	1.01	(0.73–1.38)	0.975
13	382	323	20.2%	19.5%	0.96	(0.66–1.39)	0.829
14	844	652	98.5%	98%	0.77	(0.35–1.67)	0.507
15	47	40	93.6%	100%	–	–	0.995

An OR > 1 means that it is more probable for older patients to meet the requirement, OR < 1 that it is less probable.
[a] See Table 1 for indicators definition.

impact of the first wave of the COVID-19 pandemic on the cancer patients was high, and many centres tried to relieve this by setting up a system of teleconsultations (56%) and extra psychological support. Particularly, the use of telemedicine became an important tool to keep contact with the patients and to continue medical care during the COVID-19 pandemic [17,18].

Surgery could be performed safely after the introduction of SARS-CoV-2 polymerase chain reaction testing in nearly all EUSOMA units (96%). A monocentric study in Rome by Pelle *et al.* showed that a patient ascertainment for their COVID-19 status prior to hospital admission and hospital discharge, in association with protective measures allowed for a 'no-COVID-19 status' in their hospital with none of their healthcare providers developing any infection [17] although (controllable) cluster infections have been reported by others [19].

The National Cancer registry from the Netherlands showed that mastectomy or breast conserving surgery was less common, primary hormonal treatment more common and chemotherapy less common during the beginning of the first wave of the pandemic (weeks 9–11 and 13–15) but more frequent for patients diagnosed at the end (weeks 14–17) [9]. Specifically, ductal carcinoma in situ and stage I disease was less likely to be treated within 3 months (p 0.01) [9]. Surgical case load and particularly reconstructive surgery was reduced by an average of 55% in the EUSOMA centres. We observed a reduction in mastectomy rate in older patients above the age of 70 years. In order to postpone surgery as safely as possible, the indications for neoadjuvant endocrine therapy, chemotherapy, and targeted therapy were altered in 23%, 23%, and 10% of the EUSOMA-certified centres. Except for a change in the indication for adjuvant chemotherapy during the first wave, only very few changes were made on the decision making and delivery of adjuvant endocrine, targeted, immune, and radiotherapy in EUSOMA centres during the first wave of the pandemic.

Comparing of the performance of QIs in the 45 EUSOMA-certified centres between March and June 2019 versus March and June 2020 by multivariable analysis mostly shows small and non-significant differences. An analysis according to age in the multivariable model showed that adaptations of treatment were especially seen in the indications for mastectomy, adjuvant radiotherapy, chemotherapy, and endocrine treatment in the older patients above 70 years of age.

The question remains whether the changes made in breast cancer management during the COVID-19 pandemic have any impact on breast cancer specific survival. It is well known that treatment delay is associated with both lower overall and disease-specific breast cancer survival, particularly for the triple negative and human epithelial growth factor receptor (Her)-2-amplified breast cancer subtypes [20]. Papautsky and Hamlish showed that 44% of breast cancer patients, participating in a survey, reported cancer care treatment delays during the pandemic [21]. Excluding patients with a confirmed SARS-CoV-2 infection Satish *et al.*, in New York found that 42% out of 350 patients treated for breast cancer between 1 February 2020 and 20 April 2020 experienced a delay/or change and 51% a change of practice [22]. Toss *et al.* demonstrated that a 2-month stop in breast cancer screening in Emilia Romagna (Italy) produced a significant decrease in in situ (−10.4%) breast cancer diagnosis and an increase in node-positive (+11.2%) and stage III breast cancer diagnosis (+10.3%) [23]. Not surprisingly, the highest

impact was seen in the patients with breast cancer at high proliferation rates. A similar observation on a shift of nodal status was reported by Vanni *et al.* in a multicentric analysis of 432 patients having breast cancer surgery between 11 March 2020 and 30 May 2020, which showed on univariable analysis that lymph node involvement and tumour differentiation differed significantly [24]. These authors identified waiting time on list as a significant predictive factor for lymph node involvement by multivariable analysis. Despite a large sample size, we could only detect a small, but significant, increase in tumour stage and increased lymph node involvement in our population. Its clinical relevance is questionable and most probably very low, if any. Future follow-up analysis will clarify this issue.

Currently, there is no evidence that patients with early stage breast cancer are at higher risk to develop life-threatening COVID-19 infection. Zhang *et al.* could not identify differences in disease severity and outcomes between the COVID-19 patients with breast cancer and the other COVID-19 patients [25]. A prospective registry at the Institute Curie in Paris suggests that the COVID-19 mortality rate in breast cancer patients depends more on comorbidities than prior radiation therapy or current anti-cancer treatment [26]. Although modelling is very difficult in the present circumstances, Alagoz *et al.* concluded that it is likely that prolonged pandemic-related disruptions of breast cancer care will have a small long-term cumulative impact on breast cancer mortality [27]. Regardless, it remains particularly difficult to entangle all possible factors involved, and only long-term nation-wide breast cancer-specific mortality statistics will allow us to have an insight on the impact COVID-19 on breast cancer outcome.

In the present analysis, we do not have any direct evidence that breast cancer care was inferior during the first wave in EUSOMA-certified centres. Neoadjuvant treatment was used safely to delay surgery, and there was no reported underuse of various treatment modalities resulting in normal breast cancer quality of care standards in the entire breast cancer population treated in EUSOMA centres. Our study has limitations as follow-up data are lacking, and it is not clear whether the results of high-level EUSOMA-certified centres can be translated to breast cancer care in other situations. However, it is encouraging that this large data set proves that the quality of breast cancer care was well maintained in EUSOMA-certified centres during the first wave the COVID-19 pandemic. This confirms the underlying hypothesis that the certification process creates robust structures, audit, and quality control mechanisms capable of facing even unforeseen challenges.

5. Conclusion

This is the first multicentre international analysis on the effect of the COVID-19 pandemic on breast cancer care. Quality of breast cancer care was well maintained in EUSOMA-certified breast centres during the first wave of the COVID-19 pandemic. A small but significantly higher tumour and lymph node stage at presentation was observed.

Credit author statement

Conceptualisation and methodology: P. Van Dam, I. Rubio, A. Ponti. With regard to writing, review, and editing: all authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Dr. Musolino: I declare the following COI: **Advisory role**: Seagen, Daiichi-Sankyo, Novartis, EISAI, Gilead; **Research grants**: Roche, EISAI, Lilly. We will put this in the declaration of interest form. All remaining authors have declared no conflicts of interest.

References

[1] van Dam PA, Huizing M, Mestach G, Diercksens S, Tjalma W, Trinh XB, et al. SARS-CoV-2 and cancer: are they really partners in crime? Cancer Treat Rev 2020;89:102068. https://doi.org/10.1016/j.ctrv.102068.

[2] Castaldi M, Latifi R. Breast cancer care in a COVID-19 pandemic epicenter. Am Surg 2020;86(11):1513–4. https://doi.org/10.1177/0003134820952338.

[3] Society of Surgical Oncology. Resource for management options of breast cancer during COVID-19. March 30, 2020. https://www.surg.onc/wp-content/uploads/2020/03/Breats-Resource-during-COVID-19-3.30.30.20.

[4] Dietz JR, Mora MS, Isakoff SJ, Kurtzman SH, Willey SC, Burstein HJ, et al. Recommendation for prioritization, treatment and triage of breast cancer patients during the COVID-19 pandemic breast cancer consortium. Breast Cancer Res Treat 2020;181(3):487–97.

[5] Management of breast cancer during the COVID-19 pandemic: a stage and subtype specific approach. JCO Oncol Pract 2020;16:665–74. https://doi.org/10.1200/OP.20.00364.

[6] Facina G, Marques de Oliveira V. Breast cancer care during the coronavirus pandemic. Mastology 2020;30:e20200014.

[7] Schiaffino S, Pinker K, Magni V, Cozzi A, Athanasiou A, Baltzer PAT, et al. Axillary lymphadenopathy at the time of COVID-19 vaccination: ten recommendations from the European Society of Breast Imaging (EUSOBI). Insights Imaging 2021 Aug 20;12(1):119. https://doi.org/10.1186/s13244-021-01062-x. PMID: 34417642; PMCID: PMC8378785.

[8] Duffy SW, Seedat F, Kearins O, Press M, Walton J, Myles J, Vulkan D, Sharma N, Mackie A. The projected impact of the COVID-19 lockdown on breast cancer deaths in England due to

the cessation of population screening: a national estimation. Br J Cancer 2022 Feb 2:1–7. https://doi.org/10.1038/s41416-022-01714-9. Epub ahead of print. PMID: 35110696; PMCID: PMC8808468.

[9] Eijkelboom AH, de Munck L, Vrancken Peeters MJ, Broeders M, Strobbe LJ, Bos ME, et al. Impact of the COVID-19 pandemic on diagnosis, stage and initial treatment of breast cancer in The Netherlands: a population based study. J Hematol Oncol 2021;14:64. https://doi.org/10.1186/s13045-021-01073-7.

[10] Biganzoli L, Cardoso F, Beishon M, Cameron D, Cataliotti L, Coles CE, et al. The requirements of a specialist breast centre. Breast 2020;51:65–84. https://doi.org/10.1016/j.breast.2020.02.003.

[11] van Dam P, Tomatis M, Marotti L, Heil J, Wilson R, Rosselli De Turco M, the eusomaDB Working Group. The effect of EUSOMA certification on quality of breast cancer care. Eur J Surg Oncol 2015;41(10):1423–9. https://doi.org/10.1016/j.ejso.2015.06.006.

[12] van Dam P, Tomatis M, Marotti L, Heil J, Mansel RE, Roselli Del Turco M, et al. Time trends (2006-2015) of quality indicators in EUSOMA-certified breast centers. Eur J Cancer 2017;85:15–22. https://doi.org/10.1016/j.ejca.2017.04.040.

[13] Biganzoli L, Marotti L, D'Hart C, Catalotti L, Cutuli B, Kuhn T, et al. Quality indicators in breast cancer care: an update from the EUSOMA working group. Eur J Cancer 2017;86:59–81.

[14] Gathani T, Clayton G, MacInnes E, Horgan K. The COVID-19 pandemic and impact on breast cancer diagnosis: what happened in England in the first half of 2020. Br J Cancer 2021;124:710–2. https://doi.org/10.1038/s41416-020-01182z.

[15] Kaufman HW, Chen Z, Niles J, Fresko Y. Changes in the number of US patients with newly identified cancer before and during the Coronavirus Disease 2019 (COVID-19) pandemic. JAMA Open 2020;3(8):e2017267. https://doi.org/10.1001/jamanetworkopen.2020.17267.

[16] Filiper MD, van Deukeren D, Kip M, Doeksen A, Pronk A, Verheijen PM, Heikens JT, Witkamp AJ, Richir MC. Effect of the COVID-19 pandemic on surgical breast cancer care in The Netherlands: a multicenter retrospective cohort study. Clin Breast Cancer 2020;20(6):454–61.

[17] Pelle F, Cappelli S, Graziano F, Piarulli L, Cavicchi F, Magagnano D, De Luca A, et al. Breast cancer surgery during the COVID-19 pandemic: a monocentre experience from the Regina Elena National Cancer Institute of Rome. J Exp Clin Cancer Res 2020;39:171. https://doi.org/10.1186/s13046-020-01683-y.

[18] Rasschaert M, Vanclooster PJ, DePauw L, Mertens T, Roelant E, Coenen E, et al. Meeting the challenges in cancer care management during the SARS-CoV-2 pandemic: a retrospective analysis. Cancer Control 2021;28:1–9. https://doi.org/10.1177/10732748211045275.

[19] van Dam P, Huizing M, Roelant E, Hotterbeekx A, De Winter F, Kumar-Singh S, et al. Immunoglobulin G/total antibody testing for SARS-CoV-2: a prospective cohort study off ambulatory patients and health care workers in two Belgian Oncology Units comparing three commercial tests. Eur J Cancer 2021;148:328–39.

[20] Bleicher RJ, Ruth K, Sigurdson ER, Beck JR, Ross E, Wong YN, et al. The time to surgery and breast cancer survival in the United States. JAMA Oncol 2016;2(3):330–9. https://doi.org/10.1001/jamaoncol.2015.4508.

[21] Papautsky EL, Hamlish T. Patient reported treatment delays in breast cancer care during the COVID-19 pandemic. Breast Cancer Res Treat 2020;184:249–54. https://doi.org/10.1007/s10549-020-05828-7.

[22] Satish T, Raghunathan R, Prigoff JG, Wright JD, Hillyer GA, Trivedi MS, et al. Care delivery impact of the COVID-19 pandemic on breast cancer care. JCO Oncol Pract 2022;17(8):1215–20. https://doi.org/10.1200/OP.20.01062.

[23] Toss A, Isca C, Venturelli M, Nasso C, Ficarra G, Bellelli V, et al. Two-month stop in mammographic screening significantly impacts on breast cancer stage at diagnosis and upfront treatment in the COVID era. ESMO Open 2021;6(2):100055. https://doi.org/10.1016/j.esmoop.2021.100055.

[24] Vanni G, Tazzioli G, Pellicciaro M, Materazzo M, Paolo O, Cattadori F, et al. Delay in breast cancer treatment during first COVID-19 lockdown. A multicentric analysis of 432 patients. Anticancer Res 2020;40:7119–25.

[25] Zhang B, Xie R, Hubert SM, Yu Y, Zhang Y, Lei X, Deng W, Chen J, Li Y. Characteristics and outcomes of 35 breast cancer patients infected with COVID-19. Front Oncol 2020;10:570130. https://doi.org/10.3389/fonc.2020.570130.

[26] Vuagnat P, Frelaut M, Ramtohui T, Basse C, Diakite S, Noret A, et al. COVID-19 in breast cancer patients: a cohort at the Institute Curie Hospital in the Paris area. Breast Cancer Res 2020;22:55. https://doi.org/10.1186/s13058-020-01293-8.

[27] Alagoz O, Lowry KP, Kurian AW, Mandelblatt JS, Ergun MA, Huang H, et al. Impact of the COVID-19 pandemic on breast cancer mortality in the US: estimates from collaborative simulation modeling. JNCI 2021;113(11):djab097.